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Testicular Mesothelioma

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1. Introduction

The testicular mesothelioma is one of the rare tumor from other types of mesotheliomas (less than 1%)[9, 43, 81, 104]. In light of this are clear of the difficulties encountered by some clinicians, radiologists, pathologists and cytologists in differential diagnosis. In addition, they are so rare that there is no more the researcher, which would focus in his hands a sufficient number of his own observations to make serious conclusions. That is why, apparently, the question of the tumor so far in the literature are not systematically developed. The lack of sufficient information on the morphology of mesothelioma are often a cause of incorrect diagnosis. It should also be recognized that a lack of sufficient morphological data about testicular mesothelioma considerably narrows the diagnostic possibilities for dissector and thereby restricts the advice assistant to clinic in establishing the correct diagnosis. In this regard, it seems appropriate to offer for the attention of specialists is one of the literary reviews, focusing on the pathological anatomy of this enigmatic tumor, thereby making an attempt to systematize to some extent, knowledge of mesothelial tumors. We hope that the proposed work will be useful and necessary in the daily work of professionals and will be of interest for researchers studying and developing one of the important problems in oncology - the problem of testicular mesothelioma.

2. Synonyms and definition

Testicular mesothelioma is one of the testis-specific and aggressive form of cancer that develops from the mesothelium covering the tunica albuginea as well as parietal and visceral sheets of the tunica vaginalis of the testis, epididymis, and spermatic cord, and surrounding it, thereby providing protection and support of this body [68, 79]. Among the primary tumors of serous integument mesothelioma (synonyms: adenofibroma, adenofibromyoma, adenoma, adenoma of Müllerian moves, adenomatoid genital tract tumor, adenomatoid leiomyoma, adenomatoid tumor, adenomatous tumor, angiomatoid tumor, angiomatoid tumor of endothelium, cancerous endothelioma, carcinosarcoma, celomic cancer, celothelioma, cystadenoma, endothelial cancer, endothelioma, fibroadenoma, lymfangioendothelioma, lymphangioma, malignant epithelioma, malignant epithelioma of serosa, malignant tumor of the serous covering of cells, primary carcinoma, sarcomatous endothelioma) of the testis is a relatively rare [49, 96, 99].

3. Epidemiology: Frequency and age

Considered a type of cancer in this chapter is most common with a high socio-economic status, mainly in the elderly, but is in young and even in the children, and the incidence has two peaks: the first in 20-30 years, the second after 50 years [110]. Testicular tumors are about 1% of the total number of tumors in men [25]. They occur with a frequency of 20-25 per 1 million men, most aged 20-35 years (3, 40). Testicular tumors in 60% of the observations affect the boys up to 3 years of age, with 80% of them are malignant [5, 60, 67] . The high incidence of testicular tumors for 1998-2002 is registered in most countries of Western Europe: Denmark (9.2 per 100 000 population), Germany (8.1), Scotland (7.6), Italy (7.3), Switzerland (6.9), Czech Republic (6. 5), Netherlands (6.0), Russia, St. Petersburg (1.7); among the white U.S. population (6.0-6.8) [110]. Throughout the second half of the last century there has been an increase of morbidity by testicular cancer. In 2002 in Russia revealed 1189 testicular cancer, representing 1.8 per 100 000 population[64]. Most often, these tumors were observed in age from 0 to 4 years, 30 to 34 years and older than 75 years. The countries with high mortality (> 0.5) from testicular cancer are almost all represented by the WHO the countries of Eastern and Central Europe (Croatia, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Romania, Slovakia, Slovenia, etc.) [44, 71]. In Western Europe and the U.S., that is, in regions with a high morbidity of testicular cancer, the mortality rate is low, which can be attributed to advances in the treatment of tumors of the body. Mortality, respectively, is low and in countries with low morbidity, namely in East Asia. In Russia, the mortality statistics from testicular cancer is not provided and there is still no national registry of mesothelioma.

However, Kashansky [51] in Russia for the period from 1881 to 2006 has conducted a time-consuming retrospective analysis of published by Russian-speaking authors of 872 papers containing descriptions of 3576 observations of mesotheliomas in different locations, including 29 (0.8%) - of testis, but without a clear representation of literary references proving the obtained data that undoubtedly reduces the quality of his work. The decrease of the reliability of this work also can be attributed to a lack of the Russian national mesothelioma registry. Currently, the epidemiology of the disease being studied in the Altai Territory and the Sverdlovsk region of Russia, and the mesothelioma monitoring was organized in St. Petersburg.

According to Butnor, et al [15] revealed 80 observations of paratesticular adenomatoid tumor, and Murai [78] reports only 6 (0.3%) cases of malignant mesothelioma from 1785 of mesotheliomas of various localizations during 1958-1996, arising from the tunica vaginalis of testes.

Testicular mesothelioma occurs at various ages, from newborns to 80 years. Over the past 50 years, have been documented about 100 cases of testicular mesothelioma [113]. About 80 cases of malignant testicular mesothelioma are reported in the literature, and the frequency of mesothelioma is 1: 1 000 000 [43]. Al-Qahtani, et al. [4] indicate that 73 surveillances of malignant mesothelioma arising from the testicular serous membranes, are published in the literature for the period 1966-1997. Mesothelioma varies in a wide range from 0.6 cases per 1 million inhabitants per year in Tunisia, and 35 in Australia [63]. The background morbidity is 1-2 cases per 1 million of population per year (39). According to forecasts Peto, et al. [84] the mortality from mesothelioma in Western European countries will grow from 5,000 cases

in 1998 to 9,000 in 2018 and over the next 35 years from mesothelioma dies about 250 000 people.

According to the International Agency for Research on Cancer, in Europe there is a significant variation between the levels of mesothelioma morbidity in different countries [10, 110]. Thus, in 1993-1997 the largest number of cases of mesothelioma among men are registered in Scotland and the Netherlands - 34 cases per million, whereas in Estonia and Belarus - only 3 cases per million. The situation with the frequency of detection of mesothelioma in the USA and Canada is different from Australia, France and Great Britain, where the number of cases is much higher and continues to grow [85]. For example, in Australia in 1993-1997 were recorded an average of 23 cases with mesothelioma per million among men. In 2000, there were already 60 cases per million in men [45].

Among the economically developed countries of Western Europe, only in Sweden is a similar situation to the United States. In 1993-1997 the morbidity among Swedish men was at the level of the13 cases per million population, but in recent years, the downward trend of these indicators. Projected to peak IARC mesothelioma in Western Europe will be in the 2015-2030 years. According to the International Agency for Research on Cancer the peak of mesothelioma morbidity in Western Europe will be in the 2015-2030 [11, 110].

Thus, epidemiological data about this type of cancer are inconsistent and is explained by the fact that some authors consider the testicular tumors with the positions of germ cell tumors, not considering the mesothelioma of the paratesticular zone, other researchers lead only statistics of the mesotheliomas of other more frequent localizations, not focusing its attention on the testicular mesothelioma because of its great rarity, and numerous publications on the paratesticular mesothelioma are, unfortunately, mostly descriptive in nature. That is why out of the contradictory situation is advisable to establish national centers of pathology with the formation of these cytology, biopsy and autopsy banks, followed by an examination of questions of etiology, epidemiology, patho-and morphogenesis of tumor diseases and, in particular, testicular mesothelioma, as well as analysis of the intravital diagnosis of pathological processes in order to the timely treatment and prevention [116].

4. Etiology and pathogenesis

The exact cause of the testicular mesothelioma is not installed, but the known risk factors that may contribute to its development [20, 64]. Factors of the testicular tumors are as follows: 1. Age. The majority of cases of the testicular cancer are detected from 15 to 40 years. However, the tumor may occur at any age, including infants and the elderly. 2. Cryptorchidism, in which the possibility of the tumor defeat is growing at 40-60 times. 3. Professional career: the miners, firefighters, utility workers, leather, printing, oil and gas industry have an increased risk of testicular cancer. Rather, it involves the use of certain solvents and dyes. Therefore, the risk group usually consists of firefighters, miners, plumbers, builders and gasman. 4. AIDS. Men living with human immunodeficiency virus, there is an increased role in the development of the testicular cancer. 5. Race. The probability of occurrence of the testicular cancer among white Americans is 5-10 times higher than among African-American men. The risk of the testicular cancer in men of Asia and Africa is low. 6. Nutrition. The excessive consumption of animal fat is a risk factor for the testicular

cancer. 7. A small increase in risk of the testicular cancer is associated with the trauma of the scrotum. 8. The risk of the testicular cancer raised among young people whose mothers used to maintain the pregnancy is estrogenic drugs, in particular, diethylstilbestrol, and who were, respectively, in vitro exposed to estrogens.

In recent years actively accumulates information indicating about polyetiology of the disease [83]. There is increasing works on mesothelial activity of chemical (salts of nickel, beryllium, silica, tobacco, iron oxide, manganese, carbon black, polyurethane, polysilicon, ethylene oxide, wollastonite, erionite, etc.), physical (microwave and ionizing radiation) and biological (fungi , mycobacterium tuberculosis, viruses of the avian leukemia (MS 29) and simian virus 40) agents [30, 37, 42, 77, 82, 111]. Presently, a considerable role in the development of mesothelioma is assigned to viral etiology, with the Simian virus 40 being isolated in 47-83% of human mesotheliomas, yet the currently available epidemiological evidence seems insufficient to duly evaluate the impact of this virus on the increased incidence of mesothelioma in the second half of the last century [17, 20]. Among the carcinogenic factors contributing to the emergence of mesothelioma, the asbestos is in the first place, especially the impact of asbestos and its derivatives (actinolite, zeolite, amosite, anthophyllite, chrysotile, crocidolite and tremolite), which are classified by the International Agency for Research on Cancer in Group 1 of the carcinogen risk to human where asbestos can be both a stimulant and an initiator of carcinogenesis, it has its own cancer-causing properties and, moreover, can enhance the carcinogenic effect of other factors [12, 33, 62, 90]. Like all other types of mesothelioma, testicular mesothelioma is believed to be caused by exposure to asbestos [7, 87]. In 40% of patients had contact with asbestos, and notes the synergy effects of smoking and asbestos at risk of developing mesothelioma [43]. Despite the fact that in some developed countries reduces production and use of asbestos, the morbidity and mortality from mesothelioma continues to rise. This can be explained to the delayed effect of asbestos. It is known that for development of malignant tumor the latency period is required, the duration of which depends from the carcinogenic factor could be 20 years or more. However, it is possible that increases in the morbidity of mesothelioma is related to other unknown factors [29, 32]. Since the beginning of 1970 in the XX century in Western countries, the development of mesothelioma were due solely to the inhalation of asbestos-containing dust, and, above all, amphibole asbestos, especially crocidolite, and tremolite asbestos, which currently have a crucial role in the etiology of the disease [22, 36]. Human exposure occurs through inhalation of asbestos fibers from the polluted air in the working environment, as well as from the ambient air near of the sources of such pollution, or in rooms that contain the fragile asbestos materials. Such exposure may occur during the installation and use of asbestos-containing materials, and of the vehicle maintenance. In 1977 in Germany, then in France, Japan, Finland, USA and other countries, and since 1996 in Russia the mesotheliomas through law were classified as occupational diseases associated with exposure to asbestos [51]. In a number of countries have established national cancer registers of mesothelioma and operate numerous government agencies and public associations, to examine various aspects of this pathology. The incidence of diseases caused by asbestos is related to fiber type, size of fibers, the dose and the industrial processing of asbestos [89].

The mechanisms of carcinogenicity of asbestos may be associated with the formation in target organs of the active forms of oxygen, which are known to be capable of damaging cell

membranes, including the genetic structure of cells [91]. Under the influence of iron contained in large quantities in the amphibole asbestos minerals, oxygen is restored to superoxide with subsequent formation of hydrogen peroxide and later hydroxyl radical. In addition, the active forms of oxygen appear as a result of damage to the phagocytes by asbestos fibers longer than 10 μm (0. 01 mm — the so-called "long fibers") and the emergence of "oxidative stress" is directly into the phagocytes.). In the literature there are data that the short asbestos fibers (up to 10 μm - and thickness of elementary fiber in 26 nanometers) can directly damage the chromosomes and cell division apparatus (fragmentation of the chromosomes, micronuclei, mitotic spindle damage). The initial event in a row, leading to a malignant tumor is the emergence of cells with damaged hereditary structures, which is either removed from the body or remains and gives rise to a tumor. Recent results revealed that asbestos carcinogenesis in humans and in rodents is linked to the activation of the AP-1 pathway, which induces cell division, and to the secretion of TNF-alpha (and the expression of its receptor) by mesothelial cells and by nearby macrophages exposed to asbestos [18]. In mesothelial cells, TNF-alpha signaling through NF-kappaB activation prevents apoptosis and cell death, allowing mesothelial cells to survive the genetic damage induced by asbestos and divide. In addition, mutagenic oxygen radicals released mainly by lung macrophages may contribute to asbestos carcinogenesis. Very recent results indicate that mineral fiber carcinogenesis can be influenced by genetics and microbial infections [19]. Genetic susceptibility to the mineral fiber erionite has been demonstrated in some Turkish families and causes a malignant mesothelioma epidemic in Cappadocia, Turkey. In these mesothelioma families, exposure to minimal amounts of erionite or asbestos appears sufficient to cause mesothelioma. Recent results demonstrate that SV40 and crocidolite asbestos are cocarcinogens and that, in the presence of SV40, significantly lower amounts of asbestos suffice to induce malignant mesothelioma [55]. These findings indicate that the risk varies among asbestos- and erionite-exposed individuals because of their genetic background or because of exposure to other carcinogens. Moreover, these data provide a rationale for the observation that only a fraction of heavily exposed asbestos workers developed mesothelioma, and novel targets for prevention and therapy.

How the fibers reach the testicular area has yet to be determined, but it is understood that asbestos fibers can cause tumors to form in that region of the body. While there is currently no theory to explain why asbestos exposure might cause a primary tumor to develop in the testicles, it is understood that once the asbestos fibers are in the body, they can become lodged in organs and cause inflammation or infection that can result in the development of mesothelioma. The fibers cause cancerous cells to divide abnormally, causing build up of fluid and the development of tumors. Once cells have become cancerous, they are no longer able to regulate their own cycles of growth and division. A primary tumor that develops in the testicle is formed from cancerous cells that divide without restraint, which causes the thickening of the tunica vaginalis and can eventually lead to the formation of tumors.

Thus, the etiology and pathogenesis of testicular mesothelioma to date until the end are unknown, although there are various factors that may influence for the occurrence of the disease, and may play a significant role to asbestos and its derivatives, and these issues require careful further study on the modern level.

5. Pathological anatomy: The macroscopic and cyto-histopathological features

Serous membranes in general, and the testicular membranes, in particular, are difficult to built connective tissue membranes, which have a rich network of blood and lymph vessels, and their surface is covered by one layer of mesothelial cells - mesotheliocytes located on the basement membrane.

Like any cancer testicular mesothelioma can be categorized generally into two types according to the type of cancerous cells. These are benign mesothelioma and malignant mesothelioma. The former one is a non cancerous condition while the latter is the more dangerous one as it spreads to other body parts. The first is the so-called adenomatoid tumor of genitals (mesotheliomas of sex organs), as well as fibrous mesothelioma. All other types of mesotheliomas, including localized in the large serous cavities are malignant.

In International histological classification of tumors of the testis number 16, in section VII «"Tumors of the straight tubules, network testis, epididymis, spermatic cord, the capsule, supporting structures and vestigial structures" under the letters "A" and "B" are introduced such titles as "Adenomatoid tumor" and "Mesothelioma", respectively [48, 49]. According to the international histological classification of tumors of soft tissue № 3 distinguish predominantly epithelioid, predominantly fibrous (spindle) and a two-phase form of benign and malignant mesothelioma [46, 47]. In the modern classification of tumors of the urinary system and male reproductive organs and tumors of the lung, pleura, thymus and heart differentiate the: diffuse malignant mesothelioma and its types - epithelial, sarcomatoid, desmoplastic, biphasic (a combination of epithelial and sarcomatoid features) and localized (nodal) [106, 107]. It should be noted that macro-and microscopic pattern of testicular mesothelioma is usually no different from similar tumors of other localizations.

Adenomatoid tumor is often benign, usually unilateral tumor of the epididymis , sometimes of the testicular tunica albuginea, which is about 69% of all cancers of the epididymis, but they can meet as malignant analogues of neoplasms [56]. Macroscopically, it is represented by an encapsulated, rarely plaque-like node in diameter from a few millimeters to 5 cm, consisting of soft or compact tissue, ivory. The tumor is usually detected in the lower pole of the epididymis, most of the right testicle. The histological pattern is the same everywhere. It does not depend on the location, but depends on the phase of the tumor development. Golovin [35] distinguishes the epithelial, endothelial-like, and fibromatous stage. At the epithelial stage the tumor is represented a conglomerate of small tubules lined by mostly a cuboidal epithelium. The next stage is characterized by a unique, peculiar only to the tumor, changes in the epithelial cells that vacuolating, flatten and become similar to endothelial (or mesothelial) elements. The last stage is "strangling" of the parenchymatous elements by growing fibrous tissue with an admixture of smooth muscle fibers, the tumor becomes a so-called fibroma, in which only here and there is saved the remnants of the adenomatoid structures. The fibrous stroma may be by hyalinized, there is lymphoid infiltration. Often seen the smooth muscle elements, which should not be seen as a sign of invasion [34]. However, the confusion that reigns in the literature about its supposed histogenesis and, consequently, the classification provisions still exists. As potential sources of tissue called the endothelium, mesothelium and derivatives of mezonefron and müllerian remnants of moves (adenomatoid tumors in the fallopian tubes) [59]. Most of the authors believe the

most likely the mesothelial origin. Hence the another name - a benign mesothelioma of genital tract. Thus adenomatoid tumor and testicular mesothelioma, as would put on an equal footing, that is totally unjustified and could only lead to confusion. These two tumors anything among themselves do not have any clinical behaviour, histological pattern or histogenesis. If true mesothelioma develops in the mesothelium covering the testicular membranes, then adenomatoid tumor because of its epithelial nature, it is obvious in the early stages of development - most likely from embryonic remnants or Wolf and Müllerian duct. Therefore, these tumors are confused and unite under one name can not be. Testicular mesotheliomas grow diffusely in the form papillae, causing dropsy, the cytoplasm of tumor cells is not vacuolated, tumors never exposed to total fibrosis. Adenomatoid tumors originating from the testicular membranes, do not grow diffusely, but as a node, the papillary structures do not form, the dropsy do not give, their cells have characteristic large vacuole; tumors over time are converted into fibroma, leiomyoma rarely [35].

Squamous cell carcinoma and adenocarcinoma in the area of testis epididymis and spermatic cord are extremely rare and do not have here any special clinical and morphological features that distinguish them from similar tumors at other sites [59].

In addition to the adenomatoid tumor which are viewed as a derivative of the mesothelium, is the tumor proliferation of mesothelium benign or malignant nature, but sometimes the differences between the two tumors is very difficult to establish [23]. The tumor must also distinguish between hyperplasia, often papillary, and desquamation of the mesothelium in inflammatory lesions [49]. From the testicular membranes may develop benign mesothelial tumors. In rare instances in the testes mesothelium can be a source of papillary tumors. The structure of these tumors resembles that of similar tumors originating from ovarian membrane[34].

The type of benign mesothelioma is the non cancerous form of the mesothelioma and is rare [108]. Recently it was referred to as the "solitary fibrous tumor." It is not a cancer itself but can develop into cancerous forms. The benign mesothelioma usually starts in the sub mesothelium layer that lies beneath the mesothelium of the testicular membranes.

The structure of benign mesotheliomas is rather monotonous [105]. On the connective tissue basis with small lymphoid cell clusters are highlighted a cellular bands of the solid structure or in the form of tubes, closely contacting each other, anastomosing and branching. In the interstitial tissue are sometimes found smooth muscle fibers. Careful examination of the tumor proves that solid cell bands and tubular structures are a continuation of the same cell formations. Tumor bands are surrounded by argyrophilic frame and formed large cells with acidophilic cytoplasm and large round nucleus with a centrally located nucleolus. Sometimes the tumor bands are soft and formed a single row of cells, sometimes bands are wider and consist of several rows. In this case there may be gaps that have irregular shape and are always formed between the tumor cells in tumor bands, rather than between them and argyrophilic frame. These gaps include the slightly mucikarminofil liquid. The gaps may expand and connect with each other, and the cells on the edge of the gap are first cube, and then acquire the endothelial form. The cellular bands turn into tubes. Some cells are separated and placed in the cavity gaps. Depending on the case and the location, as well as in different parts of the same tumor may dominate the solid cellular bands or tubular formation. In the latter case, the tumor resembles and is often mistakenly regarded as a

lymphangioma. This similarity is enhanced by the presence in the interstitial tissue of the lymphoid clusters. Proof of their origin is the mesothelial brush fringe lining the cavity. A detailed study revealed that the apical surface of endothelial-like cells is not smooth, like endothelial cells, and is provided with a cuticular border and even ciliate formations. No similar formations in vascular endothelium and they are unique to the mesothelium. Can thus be considered reliable, such that tumor formation is not lymphangioma, and certainly not with cancer, and a benign mesothelioma. It still remains to clarify why only mesothelium of genital tract leads to such tumors [26, 27, 68, 69].

Fibrous mesothelioma is a slowly growing, well-delimited node (no more than 3 cm in diameter) has a conical shape, the apex is directed upwards along the spermatic cord, grow together at the base of the epididymis, a very dense, layered on the section, whitish or light brownish. Only in tissue culture can prove the mesothelial origin of the tumor cells. On histological pattern, it has the structure of fibroma, rich in cellular elements, so it is called fibrous mesothelioma [26, 27, 68, 69, 96]. The structure of malignant mesothelioma in its main features is everywhere the same and different only in its details of macroscopic pattern and clinical course associated with the anatomical features of each serous cavity [13, 75]. Macroscopically, the tumor is in the form of a dense infiltrate, causing a dramatic thickening (2-3 cm, and sometimes more) of the serous membranes in a limited area or extends to the entire parietal and visceral sheets of the tunica vaginalis surrounding the body in the form of the shell, sometimes has the form of the mild delimited node from 0.5 to 6 cm oval, or merging several nodes with the villous surface resembling moss, destroys the epididymis and causes the testicular atrophy. It is white, yellow or brownish color, granular, often crumbles easily, in its upper part can move in the spermatic cord, and lower - in the epididymis [26, 27, 79]. In the thicker of infiltrates and nodes is a lot of cracks and cystic cavities with serous, bloody or cloudy mucus content. In the serous cavity, if it is not obliterated, accumulated serous or hemorrhagic exudate, often in large quantities [96]. Mesothelioma is prone to rapid dissemination through the lymph vessels of the serous membrane, resulting in the latter occurs tumor 'lymphangitis' and formed the small nodular lesions. Typical regional and distant metastases in lymph nodes, namely, inguinal, iliac and para-aortic. Hematogenous metastases is usually not excessive, but it may metastasize to the lungs, liver, kidneys, heart, bone, brain, thyroid, adrenal gland, skin, soft tissue. The tumor may grow into other body, mainly on the connective tissue interlayers with the formation in it of small nodules and tumor brands, but the invasive growth is not typical for mesothelioma, it has the exophytic growth in the thickened serous membrane. In the presence of a large tumor node in the body is always an assumption to metastatic lesion of serous membrane.

Microscopic pattern is expressed in the appearance of papillary, solid, alveolar, glandular (tubular), cystic, myxomatous, fibrous, perithelial, sarcomatoid and angioma-like structures, which in some cases may dominate [74, 80, 101, 115]. All this creates considerable polymorphism of the microstructure of the tumor [96]. The types of malignant tumor or cancer cells involved in the development of mesothelioma are of three main types namely epithelioid, sarcomatoid and mixed or biphasic cells [46, 106]. Among the most frequent histological variants of mesothelioma is epithelioid (50-70%) as a set of buds with delicate gripping growths covered with prismatic, cubic or polygonal cells with pale vacuolated cytoplasm and with evidence of cellular polymorphism, hyperchromatosis of the nuclei, the

presence of pathological mitoses and giant cells, as if spun from each other, that is, in our opinion, the pathognomonic morphological sign of mesothelioma, and for which can not be wrong [115]. The other type is sarcomatoid which is much more serious than the epithelioid, and it affects the secondary tissues including the bone, muscles, cartilage or fat [94]. This type of cancer cell is a much more rare type that occurs in 7-20% of the cases. Mixed (biphasic) refers to both types of cancers that occurs simultaneously, and making up the rest of the 20-35% of the mesothelioma cases that are reported. A feature of the tumor is large variety of morphological structure, as well as the ability to form structures characteristic of both epithelial and connective tissue for growth. Connective tissue differentiation is less common than epithelial. It is expressed in the transformation of mesothelial cells into elongated elements, such as fibroblasts, which are formed into bundles, severed in various directions. Between the tumor cells are elongated in one way or another including argyrophilic and collagenous fibers. Tumor cells were clearly involved in their formation. These special morphogenetic potency are disclosed already in conditions of inflammation and tissue culture [26, 27]. Histological structure of the epithelial type of mesothelioma is typical enough: they are not similar to any other epithelial tumors and are recognized easily [76]. Connective tissue options is more difficult to distinguish from fibrosarcoma. And they both consist of elongated cells that produce collagen fibers. But fibrosarcomas are small-spindle-cells tumors and relatively rich in mitoses, whereas fibroblasts of mesothelial origin differ by polymorphism and this polymorphism in a strange way contrasts with the paucity of mitoses. In general, cells of all types of mesotheliomas is rarely share by mitosis and is a valuable diagnostic feature.

In the study of tumors of this region has to overcome some difficulties to determine their exact location. Of course, when the tumor is small and not adherent to surrounding tissues, then we can easily establish that it is within the epididymis, spermatic cord, or testicular membranes. But often fall into the hands of a pathologist large tumors that were released outside the body in which they are evolved, and spliced to the surrounding tissues. In such cases, the localization can be expected speak only. This circumstance creates a condition where in each case it would be better to speak in favour of mesothelioma of paratesticular zone, but without precise localization. However, I would like to focus on those cases where the tumor location is beyond doubt.

According to Klimanova [54], the cellular composition of the exudate with mesothelioma in each case differs significantly by originality, but on aggregate the most of common cytomorphological features all cytograms can be summarized in three main groups. When cytograms having a picture of glandular cancer, tumor cell elements are arranged as a circular complexes, rosettes, and glandular-like and papilla-like structures, clusters and isolated. According to the degree of polymorphism and anaplasia of tumor cells in each case the cytograms are somewhat different. However, as a rule, the cell structure consists mainly of rounded cells, there are cubic and prismatic cells. Sometimes there is a sharply pronounced nuclear and cellular polymorphism, in the cytoplasm along with the large cells are small and giant cells, the latter are often multinucleated. Cell nuclei predominantly round and oval, of different sizes, coarse-grained chromatin pattern or small-grained, sometimes thin with non-uniform illumination. Sharply hypertrophied nucleoli are seen in the nuclei. With a low differentiation of cellular elements the cytogram looks more monomorphic, since the basic number of elements are rounded cells of medium size with a narrow zone of basophilic cytoplasm.

Among cytograms of mesothelioma, like cytograms for regenerative proliferative processes, can be identified two types. When one of these cellular elements are very similar to the lining of a serous cover under physiological conditions, and only the abundance of them in the exudate indicates a pathology. The cells are arranged as a vast, one-layer clusters, bands, and layers, are enlarged to the round, polygonal and elongated shape. Signs of atypia of the cellular elements are expressed mild. However, there are discomplexation of nuclei, their polymorphism, the uneven pattern of chromatin (granular or small-grained with broad achromatic zones). The hypertrophied nucleoli are visible in the nuclei. In part of the nuclei with large size have revealed signs of severe dystrophy. In the second form of mesothelioma cells cytograms by location is very similar to the elements of a well differentiated glandular cancer or of proliferating mesothelium. They are mostly round-shaped, medium sized, form a round, or similar to the papillae complexes, glandular-like structure, rows and clusters of other shapes. Enlarged cell nuclei are located centrally and eccentrically, the cytoplasm is colored differently intensively, smile-grained or fine-vacuolated.

In cytograms of mixed type are present both epithelial and connective tissue cells. Epithelial cells are arranged in the form of the layers, papilla-like, glandular-like structures, and clusters and isolated. They are the same type, mostly rounded, sometimes cubic, vary considerably in size. Cell nuclei are rounded or oval shape of various sizes, located centrally or eccentrically. The structure of chromatin in some nuclei are uniformly grained, in other small-grained. Many nuclei are hyperchromatic, some of them contain the hypertrophied nucleoli. The cytoplasm surrounds the nucleus in a narrow or wide rim, is stained unevenly. In some cells more intensely it is stained in the center around of the nucleus, the other reveals a bright ring in the middle of the cytoplasm. There are cells with the morphological characteristics of secretion (the signet ring cell is a cell type with a narrow intensively stained rim of the cytoplasm, which surrounds the vacuole filled with grainy masses of secretion). The cells form of connective tissue similar to the fibroblasts or fibrocytes, are arranged in bundles, bands, clusters and isolated. They are small in size, of the spindle or elongated shape, often with spines of different lengths. The cell nuclei are of round and oval shape, average sizes, sometimes large. Many nuclei are hyperchromatic stained, with irregular contours and uneven chromatin pattern. The cytoplasm of most cells are stained weakly basophilic, granular or has bands. Both types of cellular elements (epithelial and connective tissue) as is mixed in cytogram and often formed intimately the interrelated clusters. Cytologic differential diagnosis of mesothelioma in exudate is very difficult Most often, the cytogram has a pattern of the glandular cancer. Suspected mesothelioma, in this case can only be a careful examination of the entire cellular composition, when I find an abundance of cells and different cell groups, characteristic of epithelial tumors, some types of connective tissue cells and structural formation of them. It should be noted that the mesothelioma even with sharply expressed atypia cells has elements similar to proliferating or dystrophic mesothelium. Especially valuable if all three types of cellular elements (specific to cancer, similar to the mesothelium and the connective tissue nature) are in close contact, and often in direct connection. In the absence of pronounced signs of mesothelioma cells atypia have many similarities with their mesothelium in able of regenerative proliferation, diagnosis can be made only when taken into account the clinical data for this disease.

Cytological diagnosis of mesothelioma is set in the mixed cellular composition of cytograms if, in addition to the cells and structures of the epithelial type observed a large number of fibroblastic cells type and structures with the nature of the connective tissue growth.

Thus, in accordance with the macroscopic, histological and cytological study of tumor substrate of paratesticular zone are released the benign and malignant mesotheliomas, cyto-histological pattern which it is extremely polymorphic and not always pathologists, experiencing the considerable difficulties, can reliably determine their precise localization, namely, the testicular membranes, spermatic cord or its epididymis.

6. Clinical data: Signs and symptoms

Clinical picture is made up of symptoms caused by the presence of the primary paratesticular tumor and its metastases, or a combination thereof [92]. Mesothelioma originating from the serous membranes of the testis, epididymis or its spermatic cord, accompanied by increased and in most cases combined with a hydrocele [28, 83, 100]. Initially the testicular tumor is asymptomatic. The speed of its development is uncertain. However, most often asymptomatic tumor growth lasts no more than 1-2 months. The most frequent symptoms of primary paratesticular tumor are pain, increasing in size or swelling of the body with the appearance of palpable tumor in their formation. With the growth of tumor the testis increases, it becomes dense, lumpy due to the appearance of testicular lumps, which are pathognomonic diagnostic symptom of testicular mesothelioma, and later joins the adhesion process associated with the skin of scrotum [57, 95]. The increase of the testis as the main and only symptom noted in 54% of patients. The pain is the result of a significant increase of intratesticular pressure, germination of the tunica vaginalis of testis or elements of the spermatic cord and is often a sign of far-gone of the disease. Acute pain in the testicle and his the increasing simulate the clinical picture of acute epididimoorhit, the accession of hydrocele in 10% of the cases is typical for tumor lesion. The pain may radiate to the groin, thigh and lower back before the emergence of metastases. In 5% of cases the only symptom may be pain in the back. Often the symptoms associated with the presence of metastases predominate over local symptoms of the testicular lesion. Thus, severe pain in the back may indicate to an increase in the retroperitoneal lymph nodes, which squeeze the nerve rootlets, or to the involvement in the process of the psoas muscle. Often there are gastrointestinal symptoms (nausea or vomiting, diarrhea, abdominal pain), loss of weight, fatigue, muscle weakness, and sometimes in the abdominal cavity on palpation is revealed a tumor. The spread of the tumor above the diaphragm can lead to the discovery in the left supraclavicular area of the visible tumor masses and to the complaints of shortness of breath, chest pain, cough, hoarseness, and heart palpitations.

7. Diagnosis and differential diagnosis

The rarity of the testicular mesothelioma makes it extremely difficult to diagnose [61].The primary malignant neoplasm of the testis serous membranes, its epididymis and the spermatic cord is very difficult for intravital diagnosis, not only in earlier, but in the later stages of the disease. In addition, the diagnosis of mesothelioma is imperfect, usually heavily delayed and it is no accident that this tumor remains an enigma for the oncologist [53]. The cancer typically progresses to the later developmental stages before the patients learned of their diagnosis in the documented cases of the testicular mesothelioma.

Its an accurate diagnosis is obtained at best from pathologic study of resected tumor and at worst from postmortem examination [114]. A combination of clinical, X-ray, laboratory, and instrumental techniques is used to make the diagnosis. The diagnosis should be based primarily on the exclusion of the primary tumor in various internal organs, and first of all, lung, stomach, pancreas, gall bladder and others. The diagnosis is based on precise localization of the tumor and the availability in it of ciliated epithelial cells (primitive cells of the coelom), while using the testicle self-examination can be established an early diagnosis of the testicular cancer. Be that as it may be, any tumor in the testis should be considered as a possible his cancer, and every patient with suspected to a malignant tumor of the testicular region should be examined promptly by a surgeon-urologist, or oncologist. Diagnosis is made up of data history, physical examination, palpation, laboratory tests, radionuclide diagnostics, ultrasound, positron emission tomography, remote infrared thermography, magnetic resonance imaging for detection of metastases and a biopsy [39]. The palpation study is the first diagnosis stage of testicular mesothelioma. With continued examination the doctor should carefully to investigate the status of inguinal, abdominal, supraclavicular, and other lymph nodes accessible to research, to draw an attention to the breasts to detect a possible gynecomastia. Transillumination, which allows to distinguish a tumor that does not transmit light from a cyst filled with fluid, refers to an affordable and highly informative survey techniques [3]. In all patients with suspected to the testicular malignant tumor is necessary to conduct an ultrasound of the scrotum [70]. An ultrasound is a noninvasive and relatively inexpensive method, and accuracy of study in testicular tumors is very high and reaches 90% [14, 25]. Testicle ultrasound is used for differential diagnosis of testicular tumors and other diseases, such as epididymitis. However, basing a diagnosis solely on ultrasound imaging can not, because based on the results of the study can not clearly differentiate tumor from inflammation. Magnetic resonance imaging is more accurate method, but because of the high cost is not always used in routine practice. Nevertheless, in some observations the magnetic resonance imaging should be used to resolve disagreements arising between the ultrasound and physical examination [6]. Cytological examination of the tumor punctate has supporters and opponents. The puncture of the tumor is a danger of its dissemination. In addition, the puncture biopsy does not give the full picture of the morphological features of the tumor, but negative cytology does not exclude the existence of neoplasms. However, in recent years strengthened the view that the puncture in suspected testicular tumor is very valuable, simple and harmless study [1, 52]. Hydropic fluid from the testicular membranes should be subjected to compulsory cytology. Radiacal orchiectomy with subsequent histological examination of obtained material allows to diagnose a testicular tumor.

After identifying of the primary tumor is necessary to determine the stage of disease in the light of the lesion of lymph nodes and presence of distant metastases [73]. Computed tomography is the most accurate method of determining the lesion of the lymph nodes, mainly retroperitoneal. However, be aware that 25-30% of patients with testicular tumor and the absence of data computed tomography showing the lesion of the lymph nodes, and morphological study revealed the microscopic metastases in the last. Other frequently used methods of diagnosis of retroperitoneal lymph node metastases are cavography and lymphangiography. With a significant increase of retroperitoneal lymph nodes in the excretory urogram is possible to detect a displacement or compression of the ureter. The lungs are the most frequent localization of distant metastases of testicular tumor. To identify

them it is need perform not only lung X-rays in two projections, but also computed tomography of the chest, allowing to detect metastases in diameter up to 3 mm [26]. Metastatic liver lesions can be detected by ultrasound and scintigraphy of the liver, and the presence of metastases in the brain of an informative role in the diagnosis is given of magnetic resonance imaging. Experts are reserved to the primary tumor biopsy, and with great enthusiasm to the removal of metastases for histological examination. So much activity can be explained by three reasons. First, the biopsy helps to determine the extent of distribution of the tumor process. Secondly, if you delete metastasis, in addition to histological examination, it is possible that he was single and, of course, the procedure would be of great benefit to the patient. Third, the histological study of metastasis, despite the fact that there is a conclusion of the primary tumor, can make a change in the morphological verification of diagnosis, and consequently in the nature of the treatment. The task of staging process is to determine the prevalence and nature of both the primary tumor and its metastases. The level of serum markers of human chorionic β-gonadotropin, α-fetoprotein and lactate dehydrogenase to be determined in pre-and postoperative period, and in the future - with weekly intervals. The situation in which after the operation the level of α-fetoprotein and human chorionic β-gonadotropin is not normal, indicates the prevalence of the disease, which makes justified those serological tests. In this case, shortly after radical orhiectomy should be performed computed tomography (an advantage of magnetic resonance imaging has not yet proved) of the chest, abdomen and pelvis. When using classification by the TNM system is required histological confirmation of the diagnosis [8]. Histological verification of both mature and immature mesotheliomas is very difficult. Histogenesis and morphology of testicular tumors can be reliably determined only by histotopographical, and sometimes even serial sections. Therefore, the best way to determine the diagnosis is to obtain a tissue sample from the area. The sample may then be biopsied and examined for the presence of cancerous cells. Once a diagnosis is confirmed, the patient will be referred to an oncologist to determine a course of treatment.

Differential diagnosis between mesothelioma and their simulating metastatic tumors is based on the combined of anatomical, histological and clinical data. On the basis of a microscopic examination of mesothelioma from adenocarcinoma is difficult to differentiate [2]. In the analysis of the microstructure is of great importance to the presence of polymorphism of the tumor areas resembling to the angioendothelioma, spindle-polymorphocellular sarcoma, etc., which is not characteristic of cancerous tumors. The structure of mesothelioma is also unlike to any the testicular disgerminoma. The latter has a pronounced solid-alveolar structure, and is too small glandular differentiation, to assume that it occurs in the epididymis or testicular tubules [26].

Recently, using different immunohistochemical markers for mesotheliomas, in particular, they are positive for cytokeratin, cytokeratin 7, γ-glutamylcysteine synthetase, vimentin, mesothelin, epithelial membrane antigen, thrombomodulin, calretinin, and mesothelial antibody, whereas mesotheliomas are negative for cytokeratin 20 and carcinoembryonic antigen [24, 50, 65, 112]. However, it is not always and not all the conventional tumor markers allow you to make a diagnosis [16, 97]. For example, the carcinoembryonic antigen, usually is determined at low concentrations, whereas, the tissue polypeptide specific antigen and the cytokeratin fragment 21-1 are identified only occasionally in high concentrations. Differential diagnosis of testicular tumor have to spend with specific and

nonspecific inflammatory diseases of the testis, as well as with a hydrocele, hematocele, hematoma, hernia, and testicular torsion [66]. Tuberculous orchitis is confirmed by the tuberculous lesion of kidney, prostate, seminal vesicles. The gender history and Wasserman'reaction have an important role in cases of suspected syphilis in the testis. If you suspect a diagnosis of brucellosis orchitis is specified by the agglutination test, at Wright-Haddlson, complement fixation reaction with allergic intracutaneous test. In doubtful cases, for the differential diagnosis of chronic orchitis and testicular tumor is shown holding of an emergency open biopsy on the operating table. Accurate diagnosis can be made using the immunohistochemical typing with the use of monoclonal antibodies, as well as the method of tissue culture.

Thus, the difficulty of the diagnostic process in the diagnosis of testicular mesothelioma is obvious. Therefore, a breakthrough in improving its diagnosis should be sought in the widespread institutional arrangements, consisting in close collaboration of the various medical specialties in specialized medical centers a qualitatively of new level.

8. Treatment

Over the past two decades in the treatment of testicular cancer has been quite remarkable, resulting in 5-year survival rate in the U.S. and Europe has reached 90-95% [3, 31]. However, in many countries rates of 5-year survival rate is much lower. In Russia (St. Petersburg), 5-year survival rate for patients with testicular cancer is 73%. In the treatment of testicular mesothelioma distinguish 3 main methods: 1) the operation, 2) radiation therapy, and 3) chemotherapy. Often, depending on the tumor stage is used combined (multimodal) treatment with two or all three methods, which is recommended, particularly, for the treatment of diffuse mesothelioma [109]. Approaches to treatment are being developed for neoadjuvant therapy with cytokines only in the early stages. Operation is possible only in the early stages of the disease [102]. Treatment is surgical of adenomatoid tumors, usually with a good prognosis. Radiation therapy is used mainly with palliative purpose. Radiation may be used if the patient's health cannot withstand a major operation. The treatment of the testicular tumors depends on several factors including the histological structure of the tumor, stage of disease, the presence of contralateral testicular damage and general state of the patient and his opinion. The main problem is the timeliness of treatment and the sequence of preoperative radiation execution, the remove of the primary tumor, the diagnostic and therapeutic lymphadenectomy and the chemotherapy effects in the cancer institutions [21, 98]. Malignant mesothelioma is difficult to treat, because it is not a centralized tumor mass [72]. Mesothelioma tends to spread along nerves, blood vessels, and surfaces. Because of this tendency to spread, multiple methods of treatment must be employed to fight the cancer, and treatment is often unsuccessful if the cancer is in a later stage.

The most common treatment option available for testicular mesothelioma is the removal of the testicles, or a portion of it [40]. If the cancer has advanced very high, it may be necessary to remove the entire testicles. Surgery can be performed to remove the cancer in addition to radiation and chemotherapy. These methods are usually used to relieve symptoms related to mesothelioma. Other treatment options available are chemotherapy or radiation therapy [41]. Chemotherapy or radiation may also be suggested following surgery to kill any cancerous cells that may remain. Radiation therapy will attempt to kill any cancerous cells

in the testicles via the help of a high beam razor that directly targets tumorous cells. As the successful schemes used chemotherapy for tumors of the testis recommend complex, involving the use of cisplatin, mitomycin, vinblastine, etoposide, doxorubicin, bleomycin, gemcitabine, and folic acid, which in combination are effective in 90% of cases [64].

If malignant mesothelioma is diagnosed in stage I of the disease, surgery is often used to remove tumor masses. If mesothelioma is diagnosed during the initial stage, surgery will usually be performed to remove the tumor. The use of chemotherapy and radiation after surgery is still being studied to determine a good course of action for mesothelioma treatment. In stages II and III, symptom relief is stressed because mesothelioma is often incurable at this level of development of the cancer. Surgery to remove as much of the cancer as possible is employed, as well as some chemotherapy and radiation. In stage IV, malignant mesothelioma spreads to organs distant from the original site of disease and becomes impossible to cure. A hospice or supportive care is usually the best option for this advanced form. The patient may also wish to try alternative methods of therapy for pain relief, including acupuncture. In addition, testicular mesothelioma tends to recur within a few years, even in cases where tumors are surgically removed [58]. It is also necessary to remember that 1-3% of patients with testicular cancer is the risk of cancer in the other testicle. Therefore, it is necessary to improve methods of treatment to reduce the frequency of relapses and worsening prognosis [88]. In this sense, periodic surveillance and screening are important in patients with testicular cancer. With a view to early detection of tumor recurrence must regularly determine the levels of tumor markers such as alpha-fetoprotein, human chorionic β-gonadotropin and lactate dehydrogenase. Moreover, it should be regularly assigned to X-rays of the chest and the appropriate methods of radiological investigations to detect recurrence, metastases or occurrence of multiple primary tumors.

It is always necessary to remember that in the course of treatment for testicular mesothelioma or after may occur the following complications [25]:

1. Practically in all patients with radio-and chemotherapy leads to oligospermia. Many observations of spermatogenesis recovered in 1-2 years and 2 years after chemotherapy with one testicle preserved the ability to fertilize are generally returned.
2. Chemo-and radiotherapy increase the risk of secondary leukemias. The greatest risk of leukemia (0.5% in 5 years) has been established for patients receiving etoposide.
3. Nephrotoxicity. During chemotherapy with platinum drugs may be a slight decrease in creatinine clearance - on average by 15%.
4. Ototoxicity. Decreases mainly the perception of sounds with a frequency of 4.8 kHz, ie not spoken frequency.
5. Retrograde ejaculation. Occurs as a complication of retroperitoneal lymphadenectomy due to standard intraoperative intersection of sympathetic pathways, providing a reflex contraction of the bladder neck during ejaculation.
6. The development of secondary tumors. Established higher incidence of stomach cancer, bladder and pancreas.

Thus, treatment in testicular tumors developed in some detail, but research in this area are continuing. The main areas of focus are to develop the optimal treatment strategy of residual retroperitoneal tumors after chemo- or radiation therapy, treatment of patients with bilateral tumors and cancer of the single testis, more efficient treatment of chemoresistant

cancer. Given the rarity of the disease, it is advisable to carry out the treatment in the specialized cancer institutions that have experience in treating such patients. For each method of treatment are possible complications that may persist for several months. Knowledge of therapy complications may help to fight them. Currently, there is intensive development of promising new methods of treatments, like gene therapy, photodynamic therapy and immunotherapy, which are the subject of clinical studies and that really can qualitatively change the suffering of the patients with testicular mesothelioma in the near future.

9. Prognosis

Testicular malignant mesothelioma is considered to be a very clinically aggressive form of cancer, spreading quickly [86, 103]. Because of this, the prognosis for a patient with this form of mesothelioma is often poor [73, 93]. However, the prognosis depends on factors such as age, macro-microscopic version, stage of disease, intercurrent illness. Severe intercurrent diseases, stage 3 and 4, diffuse form and sarcomatoid or biphasic types of testicular mesothelioma and advanced age are associated with a poor prognosis [38]. The median survival after diagnosis of testicular mesothelioma is 1 year and five-year survival is 10%. Most patients die within 2 years after their diagnosis. In the U.S., a 5-year survival rate for mesothelioma patients is 28%. In Russia the figure is 23%. Out of all types of testicular cancers, the survival rate after ten years is around 98%.

Thus, the prognosis for testicular mesothelioma in the light of certain factors set forth above are generally unfavorable, and the determination of histological variants of tumors has important prognostic value in relation to anything other than light microscopy in the diagnosis of mesothelioma are commonly used methods of immunohistochemistry and electron microscopy.

10. Conclusion

From this analytical review of the world literature implies that the testicular mesothelioma is a mysterious and rare tumor originating from mesotheliocytes, covering the serous membranes of the testis, epididymis and spermatic cord with an unknown etiology and pathogenesis, a poor clinic and prognosis, and as a rule, of the late diagnosis, in spite of intensive development and application of new methods of diagnosis and treatment in recent years. The speed of the correct diagnosis establishing, prevention and treatment of the testicular mesothelioma depend on the attention to the health of the patient's cancer, oncological vigilance and art of a doctor, from the provision of modern medical equipment, from a qualitative immunohistochemical, immunophenotypical and cytogenetic studies with the use of modern medical and computer technologies and techniques, as well as on the creation in all highly developed countries of the united, up-to-date, organizational, methodical, consultative, and statistical centres on studying human pathology at a qualitatively new level – the national centres of pathology, in which multiple studies on the etiology, patho-and morphogenesis of tumors, and in particular, mesothelioma testis, and also analysis of the intravital diagnosis of the character of pathological processes according to data of cytologic, biopsy and autopsy banks with the help of modern computer and telecommunication technologies would be carried out.

11. References

[1] Ahmed M, Chari R, Mufi GR, Azzopardi A. Malignant mesothelioma of the tunica vaginalis testis diagnosed by aspiration cytology – A case report with review literature. Int Urol Nephrol 1996; 28 (6): 793–796.

[2] Akyildiz EU, Oz B., Schitoglu I, Demir H. The diagnostic utility of maspin in the distinction between malignant mesothelioma and pulmonary adenocarcinoma. J Int Med Res 2010; 38 (3): 1070–1076.

[3] Alexandrov VP, Mikhailichenko VV. Urology and andrology. The modern guide for physicians. In: Diseases and injuries of the scrotum. Chapter 12; 414–440. Moscow: "AST"; St. Petersburg: "Sova" 2005; 576 p (in Russian).

[4] Al-Qahtani M, Morris B, Dawood S, Okerheim R. Malignant mesothelioma of the tunica vaginalis. Can J Urol 2007; 14 (2): 3514–3517.

[5] Al-Shukri SKh, Tkachuk VN. Tumors of the genitourinary organs. Guide for physicians. In: Testicular tumors. Chapter 8; 159–181; Tumors of the testicular epididymis. Chapter 9; 182–183; Tumors of the spermatic cord. Chapter 10; 184–187. St. Petersburg: "Piter" 2000; 320 p (in Russian).

[6] Andipa E, Liberopoulos K, Asvestis C. Magnetic resonance imaging and ultrasound evaluation of penile and testicular masses. World J Urol 2004; 22: 382–391.

[7] Attanoos RL, Gibbs AR. Primary malignant gonadal mesotheliomas and asbestos. Histopathology 2000; 37: 150–159.

[8] Avtandilov GG. Fundamentals of pathoanatomical practice. Leadership. Moscow: "RMAPO" 1994; 512 p (in Russian).

[9] Benchekroun A, Jira H, Ghadouane M, Kasmaoui EH, Marzouk M, Faik M. Paratesticular malignant mesothelioma. Report of a new case. Ann Urol (Paris) 2001; 35 (5): 293–295.

[10] Bianchi C, Brollo A, Ramani L and Bianchi T. Malignant mesothelioma in Europe. Int J Med Biol Environ 2000; 28 (2): 103–107.

[11] Bianchi C, Brollo A, Ramani L and Bianchi T. Malignant mesothelioma in Central and Eastern Europe. Acta med Croat 2000; 53 (4–5): 161–164.

[12] Bianchi C, Bianchi T. Amianto un secolo di sperimentazione sull'uomo. Trieste: Hammerle Editori 2002; 102 p.

[13] Bisceglia M, Dor DB, Carosi I, Vairo M, Pasquinelli G. Paratesticular mesothelioma. Report of a case with comprehensive review of literature. Adv Anat Pathol 2010; 17: 53–70.

[14] Blaivas M, Brannam L. Testicular ultrasound. Emerg Med Clin North Amer 2004; 22: 723–748.

[15] Butnor KJ, Sporn TA, Hammnar SP, Roggli VL. Well-differentiated papillary mesothelioma. Am J Surg Pathol 2001; 25: 1304–1309.

[16] Cabay RJ, Siddiqui NH, Alam Sh. Paratesticular papillary mesothelioma: A case with borderline features. Arch Pathol Lab Med 2006; 130 (1): 90–92.

[17] Carbone M. Simian virus 40 and human tumors: It is time to study mechanisms. J Cell Biochem 1999; 76 (2): 189–193.

[18] Carbone M, Barbanti-Brodano G. Viral Carcinogenesis. Chapter 17; 214–232. In: Section Two. Translational Basic Science / Oncology. An Evidence-Based Approach Edited by Alfred E Chang, Patricia A Ganz, Daniel F Hayes, Timothy J Kinsellla, Harvey I Pass, Joan H Schiller, Richard M Stone, Victor J Strecher. New York: Springer 2006; 2022 p.

[19] Carbone M, Bedrossian CW. The pathogenesis of mesothelioma. Semin Diagn Pathol 2006; 23 (1): 56–60.

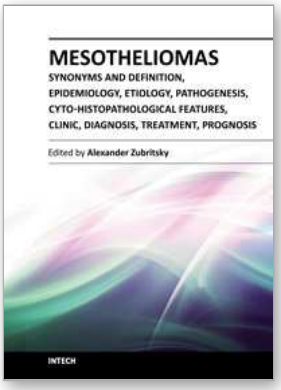
[20] Carbone M, Fisher S, Powers A, Pass HI, Rizzo P. New molecular and epidemiological issues in mesothelioma: Role of SV 40. J Cell Physiol 1999; 180(2): 167–172.
[21] Castillo OA, Alvarez JM, Vitagliano G, Ramirez D, Diaz M, Sanchez-Salas R. Limfadenectomia retroperitoneal laparoscopia en cancer de testiculo no seminoma estadio. Arch esp urol 2007; 60 (1): 59–66.
[22] Churg A. Chrysolite, trenolite, and malignant mesothelioma in man. Chest 1988; 93 (3): 621–628.
[23] Churg A, Colby TV, Cagle P, et al. The separation of benign and malignant mesothelial proliferations. Am J Surg Pathol. 2000; 24: 1183-2000.
[24] Ekman S, Eriksson P, Bergstrom S, Johansson P, Goike H, Gulleo J, Henriksson R, Larsson A, Berqovist M. Clinical value of using serological cytokeratins as therapeutic markers in thoracic malignancies. Anticancer Res 2007; 27 (5B): 3545–3554.
[25] Fedorov VD, Pikunov MYu, Shchegolev AI, Dubova EA, Kamalov AA, Nikushina AA. Tumors of testicle. Khirurgiya. Zhurnal imeni NI Pirogova 2007; (5): 68–74 (in Russian).
[26] Foot N. Identification of Tumors. Philadelphia, London, Montreal: J.B.Lippincott Co 1948; 397 p.
[27] Foot N. Identification of Tumors. Translated from English V.B.Freiman / Prof. Ya.L.Rapoport (Ed). Moscow: Foreign Literature Publishing House 1951; P.41–42; P.140 (in Russian).
[28] Fujii Y, Masuda M, Hirokawa M, Matsushita K, Asakura S. A case of benign mesothelioma of the tunica vaginalis testis. Hinyokika Kiyo 1993; 39 (1); 89–92.
[29] García de Jalón A, Gil P, Azúa-Romeo J, Borque A, Sancho C, Rioja LA. Malignant mesothelioma of the tunica vaginalis. Report of a case without risk factors and review of the literature. Int Urol Nephrol 2003; 35: 59–62.
[30] Gibbs GW, Berry G. Mesothelioma and asbestos. Regul Toxicol Pharmacol 2008; 52: S223–31.
[31] Gilligan T, Kantoff PW. Testis Cancer. Chapter 49; 844–873. In: Section Five. Solid Tumors / Oncology. An Evidence-Based Approach Edited by Alfred E Chang, Patricia A Ganz, Daniel F Hayes, Timothy J Kinsellla, Harvey I Pass, Joan H Schiller, Richard M Stone, Victor J Strecher. New York: Springer 2006; 2022 p.
[32] Goel A, Agrawal A, Gupta R, Hari S, Dey AB. Malignant mesothelioma of the tunica vaginalis of the testis without exposure to asbestos. Cases J 2008; 1:310.
[33] Goldberg S, Rey G, Luce D, Ilg AGS, Rolland P, Brochard P, Imbernon E, Goldberg M. Possible effect of environmental exposure to asbestos on geographical variation in mesothelioma rates. Occup Environ Med 2010; 67 (6): 417–421.
[34] Golovin DI. Atlas of human tumours. Leningrad: Publishing House "Meditsina" 1975; P.201–205 ; P.306–309 (in Russian).
[35] Golovin DI. Errors and difficulties in histological diagnosis of tumors: (a guide for physicians). Leningrad: «Meditsina» 1982; 304 p (in Russian).
[36] Gorini G, Pinelli M, Sforza V, Simi U, Rinnovati A, Zocchi G. Mesothelioma of the tunica vaginalis testis: reported of 2 cases with asbestos occupational exposure. Int J Surg Pathol 2005; 13 (2): 211–214.
[37] Grove A, Jensen ML, Donna A. Mesotheliomas of the tunica vaginalis testis and hernial sacs. Virchows Archiv 1989; 415: 283–292.
[38] Guney N, Basaran M, Karayigit E, Muslumanoglu A, Guney S, Kilicaslan I, Gulbarut S. Malignant mesothelioma of the tunica vaginalis testis: a case report and review of the literature. Med Oncol 2007; 24 (4): 449–452.

[39] Gupta NP, Agrawal AK, Sood S, Hemal AK, Nair M. Malignant mesothelioma of the tunica vaginalis testis: a report of two cases and review of literature. J Surg Oncol 1999; 70: 251-254.
[40] Gupta NP, Kumar R. Malignant gonadal mesothelioma. Curr Treat Opt Oncol 2002; 3 (5): 363–367.
[41] Hamm M, Rupp C, Rottger P, Rathert P. Malignant mesothelioma of the tunica vaginalis testis. Chirurg 1999; 70 (3): 302–305.
[42] Hassan R, Alexander R. Nonpleural mesotheliomas: mesothelioma of the peritoneum, tunica vaginalis, and pericardium. Hematol Oncol Clin North Am. 2005; 19: 1067–1087.
[43] Hatzinger M, Hacker A, Langbein S, Grobholz R, Alken P. Malignant mesothelioma of the testes. Aktualle Urol 2006; 37 (4): 281–283.
[44] Hodgson JT, McElvenny DM, Darnton AJ, Price MJ, Peto J. The expected burden of mesothelioma mortality in Great Britain from 2002 to 2050. Br J Cancer 2005; 92: 587–593.
[45] Hyland RA, Ware S, Johnson AR, Yates DH. Incidence trends and gender differences in malignant mesothelioma in New South Wales, Australia. Scand J Work Environ Health 2007; 33 (4): 286–292.
[46] International Histological Classification of Tumours N 3. Histological Typing of Soft Tissue Tumours / FM Enzinger, R Lattes, H Torloni (Eds). World Health Organization. Geneva, 1969.
[47] International Histological Classification of Tumors N 3. Histological Typing of Soft Tissue Tumors / FM Enzinger, R Lattes, H Torloni (Eds). World Health Organization. Geneva, 1974; P.23–24 (in Russian).
[48] International Histological Classification of Tumours N 16. Histological Typing of Testis Tumours / FK Mostofi, LH Sobin, et al (Eds). World Health Organization. Geneva, 1977.
[49] International Histological Classification of Tumours N 16. Histological Typing of Testis Tumours / FK Mostofi, LH Sobin, et al (Eds). World Health Organization. Geneva, 1981; P.16; P.36 (in Russian).
[50] Jones MA, Young RH, Scully RE. Malignant mesothelioma of the tunica vaginalis. A clinicopathologic analysis of 11 cases with review of the literature. Am J Surg Pathol 1995; 19: 815-825.
[51] Kashansky SV. Mesothelioma in Russia: systematic review of 3576 published cases from occupational medicine viewpoint. Occupational medicine and industrial ecology 2008; (3):15–21 (in Russian).
[52] Kimura N, Dota K, Araya Y, Ishidate T, Ishizaka M. Scoring system for differential diagnosis of malignant mesothelioma and reactive mesothelial cells on cytology specimens. Diagn Cytopathol 2009 ; 37 (12): 885–890.
[53] Klaassen Z, Lehrhoff BJ. Malignant Mesothelioma of the Tunica Vaginalis Testis: A Rare, Enigmatic Tumor. UroToday Int J 2010; 3(6).
[54] Klimanova Z F. Tumor processes of the serous membranes (for exudates of the serous cavities). In: A guide to the cytological diagnosis of human tumors / AS Petrova, MP Ptokhov (Eds). Moscow: Publishing House "Meditsina" 1976; 279–301 (in Russian).
[55] Kroczynska B, Cutrone R, Boccheta M, Yang H, Elmishad AG, Vacek P, Ramos-Nino M, Mossman BT, Pass HI, Carbone M. Crocidolite asbestos and SV40 are cocarcinogens in human mesothelial cells and in causing mesothelioma in hamsters. Proc Natl Acad Sci USA 2006; 103: 14128-14133.
[56] Kuzaka B, Biernacka-Wawrzonek D, Szymanska K, et al. Adenomatoid tumors of the testis and epididymis. Przegl Lek 2004 ; 61: 531–534.
[57] Lee SC, Lee JK. A case of primary malignant mesothelioma of tunica vaginalis testis. Korean J Urol. 1991; 32: 843–845.

[58] Liguori G, Garaffa G, Trombetta C, Bussani R, Bucci S, Belgrano E. Inguinal recurrence of malignant mesothelioma of the tunica vaginalis: one case report with delayed recurrence and review of the literature. Asian J Androl 2007; 9 (6): 859–860.
[59] Likhachev YuP, Shtern RD. Tumors of the testis, seminal vesicles and penis. In: A guide to the pathoanatomical diagnosis of human tumors /NA Kraevsky, A.V Smoliyannikov (Eds). Moscow: "Meditsina", 1971; 258–277 (in Russian).
[60] Livingstone RR, Sarembock LA. Testicular tumours in children. S Afr Med J 1986; 70 (3): 168–169.
[61] Mak CW, Cheng TC, Chuang SS, Wu RH, Chou CK, Chang JM. Malignant mesothelioma of the tunica vaginalis testis. Br J Radiol 2004; 77: 780–781.
[62] Malignant mesothelioma edited by Andrea Tannapfel. Springer-Verlag 2011 ; 193 p.
[63] Malignant mesothelioma: advances in pathogenesis, diagnosis, and translational therapies edited by Harvey I Pass, Nicholas J Vogelzang, and Michele Carbone. New York, NY: Springer 2005; 854 p.
[64] Manual of Urology: In three volumes. Vol. 3. In: Testicular tumors. Chapter 23; 317–348; Tumors of the testicular epididymis. Chapter 24; 349–350; Tumors of the spermatic cord. Chapter 25; 351–353 / Prof. NA.Lopatkin (Ed). Moscow: Publishing House "Meditsina" 1998; 672 p (in Russian).
[65] Marchevsky AM. Application of immunohistochemistry to the diagnosis of malignant mesothelioma. Arch Pathol Lab Med 2008; 132: 397–401.
[66] Marinbakh EB. Malignant tumors of the testis (clinic, diagnosis and treatment): Abstract of thesis. … Doctor of Medical Sciences. Moscow 1970; 25 p (in Russian).
[67] Marinbakh EB. Tumors of the testis and its epididymis. Moscow: Publishing House "Meditsina" 1972; 216 p (in Russian).
[68] Masson P. Tumeurs Humaines. Histologie Diagnostics et Techniques. Paris: Librairie Maloine 1956.
[69] Masson P. Tumeurs Humaines. Histologie Diagnostics et Techniques. Translated from the French Prof. SA Vinogradova / AI Strukov (Ed). Moscow: Publishing House "Meditsina" 1965; 108–110; 308 (in Russian).
[70] Matsuzaki K, Nakajima T, Katoh T, Kitoh H, Mizoguchi K, Akahara K, Inone T. Malignant mesothelioma of the tunica vaginalis : a case report. Hinyokika Kiyo 2008; 54 (9): 629–631.
[71] McElvenny DM, Darnton AJ, Price MJ, Hodgson JT. Mesothelioma mortality in Great Britain from 1968 to 2001. Occup Med (Lond) 2005; 55: 79–87.
[72] Melloni G, Puglisi A, Ferraroli GM, Carretta A, et al. Il trattamento del mesotelioma pleurico maligno. Minerva chir 2001; 56 (3):243–250.
[73] Mesothelioma edited by Bruce WS Robinson and A Philippe Chahinian. London: Martin Dunitz 2002; 366 p.
[74] Mikuz G, Hopfel-Kreiner I. Papillary mesothelioma of the tunica vaginalis propria testis. Virchows Archiv 1982; 396 (2): 231–238.
[75] Moore AJ, Parker RJ, Wiggins J. Malignant mesothelioma. Orphanet J Rare Dis. 2008; 3: 34.
[76] Morikawa Y, Ishihara Y, Yanase Y, et al. Malignant mesothelioma of tunica vaginalis with squamous differentiation. J Urol Pathol 1994; 2: 95–102.
[77] Mossman BT, Gruenert DC. SV 40, growth factors, and mesothelioma; another piece of the puzzle. Am J Respir Cell Mol Biol 2002 ; 26 (2): 167–170.
[78] Murai Y. Malignant mesothelioma in Japan : analysis of registered autopsy cases. Arch Environ Health 2001; 56: 84–88.

[79] Olkhovskaya IG. Tumors of the testis, seminal vesicles and penis. In: Pathoanatomical diagnosis of human tumors. Handbook / NA Kraevsky, AV Smoliyannikov, DS Sarkisov (Eds). - 3rd Edition. Moscow: "Meditsina" 1982; 296–312 (in Russian).
[80] Park HM, Kim JH, Bae SG, Kwon TK, Chung SK. A case of malignant mesothelioma of tunica vaginalis. Korean J Urol. 1997; 38: 1132–1134.
[81] Park YJ, Kong HJ, Jang HC, Shin HS, Oh HK, Park JS. Malignant mesothelioma of the spermatic cord. Kor J Urol 2011; 52 (3): 225–229.
[82] Pathology of malignant mesothelioma edited by Francoise Galateau-Salle. Springer-Verlag London 2010; 198 p.
[83] Perez-Ordonez B, Srigley JR. Mesothelial lesions of the paratesticular region. Semin Diagn Pathol 2000 ; 17: 294–306.
[84] Peto J, Decarli A, Vecchia CLa, Levi F, Negri E. The European mesothelioma epidemic. Br J Cancer 1999; 79 (3–4): 666–672.
[85] Peto J, Hodgson JT, Matthews FE, Jones JR. Continuing increase in mesothelioma mortality in Britain. Lancet 1995; 345: 535–539.
[86] Plas E, Riedl CR, Pflüger H. Malignant mesothelioma of the tunica vaginalis testis: review of the literature and assessment of prognostic parameters. Cancer. 1998;83:2437–2446.
[87] Reynards JM, Hasan N, Baithun SI, Neuman L, Lord MG. Malignant mesothelioma of the tunica vaginalis testis. Br J Urol 1994; 74: 389-390.
[88] Rekhi B, Pathuthara S, Ajit D, Kake SV. «Signet-ring» cells – A caveat in the diagnosis of a diffuse peritoneal mesothelioma occuring in a lady presenting with recurrent ascites: An unusual case report. Diagn Cytopathol 2010; 38 (6): 435–439.
[89] Roggli VL, Pratt PC, Brody AR. Asbestos fiber type in malignant mesothelioma : an analytical scanning electron microscopic study of 94 cases. Am J Ind Med 1993 ; 23 (4): 605–614.
[90] Roggli VL, Vollmer RT, Butnor KJ, Sporn TA. Tremolite and mesothelioma. Ann Occup Hyg 2002 ; 46 (5): 447–453.
[91] Sabo-Attwood T, Ramos-Nino M, Mossman BT. Environmental Carcinogenesis. Chapter 18; P.233–243 In: Section Two Translational Basic Science / Oncology. An Evidence-Based Approach Edited by Alfred E.Chang, Patricia A.Ganz, Daniel F.Hayes, Timothy J.Kinsellla, Harvey I.Pass, Joan H.Schiller, Richard M.Stone, Victor J.Strecher. New York: Springer, 2006; 2022 p.
[92] *Sawada K, Inoue K, Ishihara T, Kurabayashi A, Moriki T, Shuin T. Multicystic malignant mesothelioma of the tunica vaginalis with an unusually indolent clinical course. Hinyokika Kiyo 2004; 50 (7): 511–513.
[93] *Schure PJ, van Dalen KC, Ruitenberg HM, van Dalen T. Mesothelioma of the tunica vaginalis testis: a rare malignancy mimicking more common inguino-scrotal masses. J Surg Oncol 2006; 94 (2): 162–164.
[94] Shimada S, Ono K, Suzuki Y, Mori N. Malignant mesothelioma of the tunica vaginalis testis: a case with a predominant sarcomatous component. Pathol Int 2004; 54 (12): 930–934.
[95] Shin TK, Lee TY, Park MH. Mesothelioma of the tunica vaginalis of the spermatic cord with coincidental finding renal cell carcinoma. Korean J Urol. 1995; 36: 1142–1146.
[96] Smoliyannikov AV. Tumors of serous membranes. In: A guide to the pathoanatomical diagnosis of human tumors /NA Kraevsky, A.V Smoliyannikov (Eds). Moscow: "Meditsina" 1971; 77–79 (in Russian).
[97] Spiess PE, Tuziak T, Kassouf W, Grossman HB, Czerniak B. Malignant mesothelioma of the tunica vaginalis. Urology 2005; 66: 397–401.

[98] Stathopoulos J, Antoniou D, Stathopoulos GP, Rigatos SK, Dimitroulis J, Koutandos J, Michalopolou P, Athanasiades A, Veslemes M. Mesothelioma: Treatment and survival of a patient population and review of the literature. Anticancer Res 2005; 25 (5): 3671–3676.
[99] *Strukov AI, Serov VV. Pathological anatomy. Textbook. Moscow: Publishing House "Meditsina" 1979; 188–189 (in Russian).
[100] Thomas C, Hansen T, Thuroff JW. Malignant mesothelioma of the tunica vaginalis testis. Urologe A 2007; 46 (5): 538–540.
[101] Tolhurst SR, Lotan T, Rapp DE, Lyon MB, Orvieto MA, Gerber GS, Sokoloff MH. Well-differentiated papillary mesothelioma occurring in the tunica vaginalis of the testis with contralateral atypical mesothelial hyperplasia. Urol Oncol: Semin Orig Invest 2006; 24 (1): 36–39.
[102] Torbati PM, Parvin M, Ziaee SA. Malignant Mesothelioma of the Spermatic Cord: Case Report and Review of the Literature. Urol J 2005; 2: 115–117.
[103] Tuttle Jr JP, Rous SN, Harrold MW. Mesotheliomas of spermatic cord. Urology 1977; 10: 466–468.
[104] Urology: Textbook / Prof. NA Lopatkin (Ed). Fifth Edition, revised and enlarged. Moscow: GEOTAR-MED, 2002; 520 p (in Russian).
[105] van Poppel H, van Renterghem K, Claes H, et al. Benign Mesothelioma of the Epididymis: Case Report. Urol Int 1988; 43: 370–371.
[106] World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of the Lung, Pleura, Thymus and Heart / WD Travis, E Brambilla, HK Muller-Hermelink, CC Harris (Eds). International Agency for Research on Cancer Press. Lyon, 2004 ; 344 p.
[107] World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs / John N Eble, Guido Sauter, Jonathan I Epstein, Isabell A Sesterhenn (Eds). International Agency for Research on Cancer Press. Lyon, 2004; 359 p.
[108] Xiao SY, Rizzo P, Carbone M. Benign papillary mesothelioma of the tunica vaginalis testis. Arch Pathol Lab Med 2000; 124: 143-147.
[109] Ya TD, Welch L, Black D, Sugarbaker PH. A systemic review on the efficacy of cytoreductive surgery combined with perioperative intraperitoneal chemotherapy for diffuse malignancy peritoneal mesothelioma. Ann Oncol 2007; 18 (5): 827–834.
[110] Zaridze DG. Cancer prevention. Guide for physicians. Moscow: IMA-PRESS 2009; 224 p.
[111] Zerbino DD, Dmitruk IM. Aetiology, pathogenesis and clinico- morphological peculiarities of mesothelioma: A review of the literature. Vrach Delo 1984; (10): 4–8 (in Russian).
[112] Zervos MD, Bizekis C, Pass HI. Malignant mesothelioma 2008. Curr Opin Pulm Med 2008; 14: 303–309.
[113] Zubritsky AN. Mesothelioma. Principal bibliographic index of Russian and foreign literature. Moscow: Meditsina Publishers, 2004; 64 p (in Russian).
[114] Zubritsky AN. Mesothelioma revisited. Acta Medica Bulgarica 2008; 35(2): 31–34.
[115] Zubritsky AN. Mesothelioma (a review of the literature). Present Interests of Pathological Anatomy: Proceedings. The 3rd Congress of Russian Society of Pathologists, Samara, May 26–30, 2009 / Phedorina TA (Ed). Samara, 2009; 2: 604–605 (in Russian).
[116] Zubritsky AN. Multiple primary tumours. Bibliographical index of Russian and foreign literature. Moscow: “Kalina” 2010; 112 p (in Russian).



Mesotheliomas - Synonyms and Definition, Epidemiology, Etiology, Pathogenesis, Cyto-Histopathological Features, Clinic, Diagnosis, Treatment, Prognosis

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Mesotheliomas are mysterious mesothelial tumors in that they are relatively rare, difficult to diagnose, with a large number of synonyms, and the etiology and pathogenesis of the disease are still not fully disclosed. This problem attracts the attention of various specialists in the field of medicine and biology every year. In recent years there has been a significant increase of mesothelioma morbidity in most of the countries, due to the further industrialization of society. In this regard, this book has been published with the participation of an international group of experts with rich experience from around the world . The book consists of 14 chapters containing the most advanced achievements of all aspects of the various types of mesotheliomas, both in humans and domestic animals, at a high methodological level. This book is intended for biologists and all health care workers, mostly oncologists of different profiles, as well as students of medical educational institutions engaged or even just interested in the problems of mesotheliomas.

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