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AUTHORITY

BDRL D/A ltr, 22 Oct 1971

TRANSLATION NO. 631

DATE: 1 July 1968

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A Contribution to the Picture of the Pathomorphological Changes in Histoplasmosis.

The first cases of histoplasmosis observed in the Rumanian People's Republic.

by A. Mureshanu (Bucharest)

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Translated from Arkhiv Patologii (USSR), 18: 7: 84-92, 1956

Among the infrequently encountered infectious diseases is a severe disease that has been described by Darling - histoplasmosis, which is caused by a fungus; the latter was named Histoplasma capsulatum by the author.

After the discovery of the first cases of this disease in the Panama region, many cases of this illness have been described and substantiated in autopsies. These cases have been observed chiefly in the Mississippi River Basin and in tropical countries. To date the total number of cases published does not exceed 200. Of the 138 cases published prior to 1950 only 65 were substantiated by appropriate investigations after autopsy.

According to the data in the literature, to the present time five cases have been described in Europe. Of these, only one was observed in France, in a person who had not left Europe; consequently, this single case was of local origin. We did not find a description of this disease in the Soviet medical literature that we have at our disposal.

Histoplasmosis is considered as a severe lethal disease when dissemination of the fungus in the organism occurs. The parasite develops and reproduces in the organism of humans and animals (domestic and wild) in the reticulo- endothelial cells of the organs, but not on the surface of mucous and serous membranes as do the saprophytic or random fungi (as in oidiomycosis).

Darling believed that the parasite causing this disease belonged to the protozoa. It was later discovered that he was describing a fungus belonging to the group of false yeasts, because in an organism it develops in the form of spores resembling yeasts, but on nutrient media, at a certain stage of its development, the presence of threadlike mycelia are observed; they are pseudomycelia just as those of the Hyphomycetes. With material that was taken from

patient DeMonbreun succeeded in growing this fungus on nutrient media and discovering the different forms of its development. At present the growth of the fungus on nutrient media is the accepted method. The greatest number of histoplasmosis cases, however, were discovered only after autopsy of suspected cases, particularly in the regions where there had already been cases of the disease detected. In a few cases the diagnosis has been established during life, with a subsequent observation of the patient until his death.

The parasite Histoplasma capsulatum is believed to belong to the group of hyphomycetic yeasts, because in the human and animal organism it develops in the form of a yeast, but on nutrient media, in addition to spores, it also forms a mycelium, just as is observed in the threadlike fungi. In the literature that has been published to date on the problem of histoplasmosis it is known that this fungus does not produce a formation of the mycelian type in vivo. Only one author (Humphrey) discovered elements of a mycelium in the lungs, but he, himself, has doubts concerning this. The histological picture set forth in his work shows the margin of a lung-tissue cavity that is filled with necrotic material of a reddish-brown color. In scrutinizing this picture one finds that he makes reference to several pseudomycelia of some sort of fungus that reproduces by blastospores. These false mycelia lie freely on the edge of the cavity, surrounded by necrotic tissue, and at the same time they are not growing on the alveolar wall as is seen with histoplasmosis. We think that he is making reference to a saprophytic fungus, and by no means makes reference to the actual mycelium of Histoplasma capsulatum. On the other hand, the nodule in which the author detected this histological picture, differs sharply in appearance from the other segments of the lung, and differs also from the bronchopneumonic nodules that were encountered in this case. The mycologist, with whom Humphrey consulted, had this to say, "In view of inadequate smears we hesitated to call this stage of the growth a phase of the mycelium of the yeast form that was discovered in the tissues."

To establish a diagnosis while the patients are alive presents great difficulties because the clinical symptomatology of the illness is extremely varied; the illness frequently develops under the disguise of other syndromes that are connected or related to other diseases. Histoplasmosis is particularly confused with chronic malaria, kala-azar, lymphogranulomatosis, and the hyperplasias of the reticulo-endothelial system.

The following have been described as the important clinical symptoms of histoplasmosis: a. an irregular fever, sometimes of the septic type with a subacute or chronic picture of development; b. an expressed anemia and leukopenia; c. a progressive enlargement of the spleen with the development of emaciation.

This symptomatological picture, however, can change depending on each case separately and in particular on the localization of the parasite in one of the organs, or in one of the systems. There are cases described in the literature about localized histoplasmosis of a comparatively benign nature, and even of complete cure, particularly in the event of lesions in the form of ulcerations on the cutaneous covering, or on the mucous membrane of the pharynx or mouth, and even with the presence of deep lesions in the pharynx and larynx, or in the intestines.

The localisation of the process in the lungs is frequently mistaken for "atypical" pneumonopathy, or for a suspected case of pulmonary tuberculosis. Cases of a disease that resembled pneumonia according to character have been noted in military camps; later, the presence of the fungus Histoplasma capsulatum was discovered in mycological investigations.

Sufficiently clear x-ray pictures, showing a diffuse fibrosis with small micronodular calcifications in the lungs, have been long recorded for histoplasmosis as well as for toxoplasmosis. It is just as well known that in some of the forms, when Koch's bacillus is not detected, the reaction to fungus extracts (histoplasmin) proves positive. Some of the cases of appendicitis and mesenteric adenopathy are considered to subclinical forms of an illness that is also caused by this fungus.

In a limited number of cases investigation of removed appendices has established the presence of this parasite with a subsequent growth of it on nutrient media.

In the forms where generalization of histoplasmosis is observed, one usually encounters the symptomatic picture described above, which is considered sufficiently characteristic. In many cases the presence of intercurrent diseases is noted, for example tuberculosis, lymphogranulomatosis, cancer, diabetes, suppuration in the lungs, cirrhosis of the liver, gastric ulcer, endocarditis, ulcerated enterocolitis, etc, which disguise the main disease. Some authors have discovered an etiological connection between the parasite and the ulcerated lesions of the digestive canal and even with some forms of endocarditis.

In spite of the fact that the development of the parasite occurs in the reticulo-endothelial cells, enlargement of the lymphatic nodes is observed in only one-third of the cases. Owing to the pseudotumoral hyperplasia of the lymphatic nodes and spleen, histoplasmosis is frequently confused with either lymphogranulomatosis or lymphoreticulosarcomatosis.

According to Meleny's findings, forms do exist in which the major symptoms listed above are foremost, and thus histoplasmosis presents itself as a common febrile disease accompanied by an enlargement of the spleen with leukopenia. Nevertheless, enlargement of the spleen and hyperplasia of the lymphatic nodes can predominate in other cases; owing to this the disease is confused with tumoral afflictions of the lymphatic system. The pulmonary forms with the fibrosis and calcifications should call the doctor's attention to the possibility of histoplasmosis, particularly where there is a positive reaction to histoplasmin and an absence of Koch's bacillus. In some cases ulcers of the skin or mucous integuments are accepted as common lesions, without consideration of a possible mycotic etiology (Histoplasma capsulatum). Symptoms that differ greatly from those described above are noted in many cases; these cases, evidently, remain without appropriate diagnosis and the observable symptoms are attributed to a different etiology.

The presence of the parasite in the cells is necessary for substantiation of a diagnosis of histoplasmosis. It is discovered in the form of minute bodies

(1-4 microns), which resemble a yeast and are situated intracellularly, extracellularly in rare instances, with a chromatic center surrounded by a clearly expressed clitellum enclosed by a capsule. The parasite can also be discovered in living patients in blood smears and bone marrow, ir impressions of ulcerations, in smears obtained by puncture from the liver and the lymphatic nodes, in smears from the sputum, etc. The parasite is stained without difficulty by the usual laboratory methods (Giemsa, Gram, etc). It should be noted, however, that the parasite is seldom detected in these materials, due to which the diagnosis is established with difficulty. Particularly recommended are biopsies of the lymphatic nodes and also puncture of the liver, by which it is possible to produce impressions, histological smears, and cultures on nutrient media; it is also possible to inoculate susceptible animals. Cases are published in the literature where, during the life of the patients, the fungus was expressed on nutrient media, the material for the seeding having been taken by punctures and also from the blood and bone marrow.

Pieces of the organs taken in an autopsy of deceased patients are the most suitable material for the detection of the parasite. The material taken in an autopsy can be utilised for culturing nutrient media and for inoculating animals, if the dissection is accomplished no later than two hours after the death of the patient.

Domestic and wild animals and even insects are the sources of infection in the disease caused by Histoplasma capsulatum. Some authors believe that person to person inoculation is sometimes observed in the pulmonary forms. Cases have been described of laboratory infections in persons who were working with cultures of the parasite, or who participated in experiments on animals.

The routes of the infection's distribution have not as yet been precisely established. It is presumed that inoculation can occur by the air-borne and cutaneous routes and through the digestive tract.

The persons who have become ill are predominantly agricultural workers; to the present time the illness has been most frequently observed among the farmers of the U. S. A. In the U. S. A. a large number of cases of latent and asymptomatic forms have been registered; as a result of this, in several regions along the Mississippi River Basin the test with histoplasmin gives positive results in up to 60 % of the local population; numerous cases of the disease have been noted in children even less than a year old; whereupon it is believed that these cases result from contact with infected domestic animals.

The development of the illness is varied and depends on the character of the case and particularly on the localization of the parasite, from where sometimes occurs a dissemination of the fungus accompanied by a generalization of the process. In the majority of the cases that have been published the development of the disease occurred in a period of 1-3 months, evidently from the moment that the illness attained the generalization phase.

Histoplasmosis gives an acute picture of the disease in children: a febrile condition, disorders on the part of the the digestive organs, diarrhea, and loss of weight. Later, enlargement of the liver and spleen is noted, with anemia and leukopenia.

In adults the disease is chronic; the illness is frequently intercurrent with other diseases that disguise the histoplasmosis. Cases of papulo-ulcerative lesions of the integument accompanied by itching and enlargement of the local lymphatic nodes have been described.

Signs of empyema in the specific tissues, which are evident in the other mycoses, are lacking in histoplasmosis, unless, of course, a secondary infection caused by pus-forming bacteria is developed. This absence of empyema in the specific tissues is a characteristic peculiarity of the disease.

Darling, in his cases, described the presence of necrotic foci in the various organs, but these were without suppuration. Around these foci the parasites were situated intra and extracellularly (in macrophages). The presence of necrotic foci is noted also by other authors, but this manifestation was not invariable.

In spite of the use of all the medicaments that are presently known, the treatment of the generalised forms proves to be ineffective. Only complete removal of the foci of affliction and also radiation therapy can sometimes give good results. Cases have been described of recovery after removal of afflicted portions of the lung; in these cases the diagnosis was made by a histological study of the removed tissue after the operation.

Histoplasmosis has never before been described in the Rumanian People's Republic. Consequently the disease is ignored by the clinicians in establishing a differential diagnosis of febrile conditions.

In the "Kolentina" hospital (Bucharest), during the past two years, we have had the opportunity to observe and study three cases of histoplasmosis, and we assume that this disease is not just incidental, because this type of disease is frequently not even suspected.

We will now set forth a description of the cases observed, for the purpose of attracting the doctors' attention to this disease.

1. In May, 1953, Patient S., 35 years old, died in the infectious disease hospital "Kolentina". The disease began three weeks prior to the patient's coming to the hospital with an irregular fever, together with enlargement of the spleen, anemia and leukopenia. He was sent from the therapeutic section of the city hospital with a suspicion of having typhoid fever on the basis of his febrile condition, spleen enlargement, and leukopenia (2,000). The diagnosis of typhoid fever was not supported by the laboratory investigations made in the "Kolentina" hospital. Miliary tuberculosis was suspected on the basis of the febrile condition and the results of a roentgenological investigation (a diffuse micronodular infiltration of the lungs). After death the body was sent to the dissection room, which is under our supervision.

Even in the macroscopic investigation we rejected the diagnosis of tuberculosis on the basis of the general appearance of the lesions, because appropriate foci could not be detected. One of the major afflictions was

the enlargement of the spleen and liver (the spleen weighed 1500 grams, the liver 2200 grams), with a picture of a diffuse micronodular infiltration of these organs that resembled the infiltration in the leukoses (leukemic and aleukemic). Exactly the same type of infiltration, but less expressed, was noted in the lungs and kidneys. In the spleen, portions of irregular form were discovered that resembled fresh and old infarcts. On the basis of the appearance of these lesions we presumed the presence of leukosis.

At the same time, a manifestation was observed in this case that had never been observed before, namely: during palpation in the parenchyma of the lungs and kidneys we discovered a large number of rough indurations, which were as though comprised of grains of sand; they could be seen on the surface of a section of the kidney by the unaided eye.

During microscopic investigation of this patient's organs we noted a reticular and myeloid hyperplasia in the liver, spleen, kidneys and lymphatic nodes, with infrequent cells in the process of mitosis; we considered all of these afflictions as a myeloid reaction within the framework of an aleukemic condition. A series of minute calcified sections were detected in the kidneys. In the lungs, in addition to lesions of a serofibrinous and phagocytic (macrophagal) type of alveolitis, we detected sections that had been strongly stained with the hematoxylin in the region of the alveolar partitions and around the vessels (fig 1), whereupon, in our first investigation we considered this as a result of dystrophic calcification.

In the microscopic preparations taken from the patient's organs, Academician K. Ionesku-Mikhaesht' discovered that we were contending with histoplasmosis, having noted the presence of yeast-like bodies in the pulmonary parenchyma (fig 2a) and in the other organs. This conclusion forced us to turn our attention to the possibility of an occurrence of this type of disease.

2. After several months (in August, 1953) the body of a woman, 20 years old, with a clinical diagnosis of septicemia, was delivered from the "Kolentina" hospital to the dissection room for autopsy. According to the casehistory the patient had a febrile condition of the septicemic type, a leukopenia (2,200), and an enlargement of the spleen. The patient had been in the hospital only four days. At first she was presumed to have typhoid fever, but the laboratory tests proved negative. The blood culture also gave no indication of a presence of any sort of bacterial flora. The diagnosis was not determined until near the patient's death.

In the autopsy we noted that the afflictions were similar to the changes detected in the preceding case: enlarged spleen (600 grams), liver somewhat enlarged, and a picture of a diffuse micronodular "leukemic" infiltration in the spleen, liver and kidneys. Besides these changes we detected ulcerous necrotic and hemorrhagic foci on the mucous membrane of the gingiva (and also minor ones on the mucous membrane of the stomach) - a picture that is encountered rather frequently in leukemic conditions, particularly in the acute form.

In the macroscopic examination of the lungs we detected only a picture of congestion, but at the same time in palpation we felt the presence of small

sand-like protuberances along the length of the whole parenchyma as in the preceding case. The same minute whitish nodules were noted in the kidneys.

A reticular and myeloid proliferation was discovered in the spleen, liver, kidneys, and lymphatic nodes in the microscopic sections; also detected were many minute necrotic foci with granulation tissue, surrounded by epithelian and macrophagal elements, and here and there containing giant cells of the Langhan's type. On the basis of this microscopic picture we hesitated between a diagnosis of tuberculosis or brucellosis.

Having renewed our study of these microscopic sections after the establishment of a diagnosis in Case #3, and, also, on the basis of data in the literature, we concluded that these necrotic foci are characteristic for some forms of histoplasmosis. In our case numerous parasitic bodies of Histoplasma capsulatum were discovered within the macrophages and extracellularly (fig 2b) around the necrotic foci.

3. Patient - Doctor I., 45 years of age, worked in one of the scientific research institutes where experiments were conducted on animals. For many years this doctor had an asthenic appearance, pale face, and frequently suffered cold miseries. He did not, however, interrupt his work. The first signs of the disease noted during the 3-4 months prior to his admittance to the hospital were: a febrile condition, an expressed asthenia, an enlarged spleen, and some degree of anemia and leukopenia (2,000). At the beginning of the disease the patient was sent to an infectious disease hospital with the suspicion that he had typhoid fever, but this diagnosis was not substantiated. Progressive enlargement of the spleen and liver, anemia and leukopenia were noted. Upon slight exertion, very difficult breathing was noted. The lymphatic nodes were slightly enlarged. The presence of reticular hyperplasia was detected by a sternal puncture.

A biopsy of the lymphatic nodes was not made for fear of affecting the patient's psychic condition. The febrile condition persisted the whole time spent in the hospital; the anemia and leukopenia progressed to such a degree that on some days the number of leukocytes dropped to 800 per cubic millimeter. During the last days of the patient's life there was a hemorrhage from the digestive tract.

The clinicians proposed a diagnosis of lymphogranulomatosis or reticulosarcomatosis on the basis of the general symptomatological picture. In addition to the symptomatic treatment specific preparations were prescribed for the patient (for example nitrous yperite, which, however, the patient could not bear). The use of ACTH gave a temporary improvement. After a short time the patient died with strongly expressed asthenia, cachexia, spleno-hepatomegaly, anemia, and leukopenia.

In autopsy (4 June 1955) the following were discovered: hemorrhage into the chest cavity (three liters of blood and clots) caused by the bursting of the spleen's capsule in its lower portion; the spleen (weight - four kilograms) was of an extremely fragile consistency with a violet-red shade in section. The liver was enlarged (weight - about two kilograms), a picture of

nodular cirrhosis in section; the portal vein and the mesenteric vessels are free. The suprarenal glands and kidneys with an eroded structure. The lymphatic nodes of the chest cavity were not enlarged. Changes were not detected in the gastro-intestinal tract.

The lungs were pneumatic, but rather solid to the touch. In cross sections we observed a large number of white nodules, which here and there had the appearance of fascicles; as a result the clinicians, who were in attendance at the autopsy, expressed the possibility of a tuberculous process. In a careful palpation of the lungs we noted that it were as if grains of sand were in the parenchyma of the lungs and extended along their full length, which reminded us of the picture observed in the preceding two cases.

On the basis of the enlargement of the spleen and liver, the micronodular infiltration in the lungs, and also the dense nodules in the lungs, we expressed a supposition of the presence of either toxoplasmosis or histoplasmosis.

The microscopic investigation substantiated this supposition: lesions that are characteristic for histoplasmosis were discovered, particularly in the lungs, where the cells of the alveolar partitions proved to be crowded with parasitic bodies (figs 2b and 3); in the other organs (the spleen, liver, kidneys and suprarenal glands) the parasite's spores seemed to be less numerous, but here, too, they were situated in the cytoplasm of the reticular cells. In the lungs we discovered a picture of a proliferative chronic alveolitis and also many portions that were strongly stained by hematoxylin; these portions corresponded to the alveolar partitions (fig 4). As in the first case, there was a great quantity of the parasites in these portions.

In the liver, kidneys and suprarenal glands we discovered a diffuse infiltration by reticulohistiocytary and myeloid elements in the form of belts or nodules.

Not in a single organ did we find appearances to substantiate the clinically proposed diagnosis of reticulosis; nor were any inflammatory manifestations of a suppurative nature detected.

Summary

From the description of the clinical and pathomorphological findings in our cases it is possible to draw the conclusion that they completely correspond to Darling's clinico-anatomic picture of histoplasmosis. The clinical symptomatology of these three cases are very similar, the symptoms observed in all the patients are considered characteristic for the generalized forms: an irregular type of fever lasting from three weeks to 3-4 months, an enlargement of the spleen, anemia and leukopenia. The febrile condition did not terminate after the usual drug therapy. On the basis of the spleen enlargement and the leukopenia the clinicians suspected in all cases the beginning of typhoid fever, and the enlargement of the spleen in case #3 led to a tentative diagnosis of reticulosis. One should note that in cases No. 1 and 3, symptoms occurred on the part of the respiratory organs, and in the first case miliary tuberculosis was presumed on the basis of the diffuse fibrous process in the lung and the presence of the nodular infiltrates.

In spite of a disease picture that is sufficiently characteristic for histoplasmosis the clinicians never suspected its presence, evidently because this disease had never been encountered in Southeastern Europe until this time.

Among the pathomorphologic al changes in our cases, one should first of all note the presence of the enlarged spleen and the hyperplasia of the reticulo-endothelial elements in the majority of the organs, and particularly in the spleen and liver. The participation of the lymphatic nodes in this process was not expressed, but, still, the presence of the parasitic bodies is detected in them upon microscopic investigation. The hyperplasia of the reticulo-endothelial system forced us to suspect the presence of a malignant tumor in one case (No. 3).

The reticulo-endothelial hyperplasia, which appeared in the organs as a micronodular infiltration, created a picture that is usually encountered in the leukoses, which forced us, in the autopsy of the first two bodies (where we did not consider the presence of histoplasmosis), to presume that death occurred as a result of a leukemic (or aleukemic) condition. The reticular and myeloid elements diffusively perforated the organs, and only the presence of the parasite in some of the reticular cell indicated the infectious origin of this hyperplasia. In histoplasmosis the hyperplasia of the reticulo-endothelial system sometimes gives a picture of pseudoneoplasia, and thus histoplasmosis is confused with diseases of this category. It is extremely probable that a portion of the cases that until the present time have been considered as reticulosis, reticulendotheliosis, and aleukemic conditions were actually histoplasmosis, the presence of which was not suspected.

Also important in all three of our cases was the discovery of minute indurations in the lungs and kidneys that are not encountered in other diseases. These indurations can lead to a correct diagnosis upon autopsy of the body; they are detected by the unaided eye and are the basis of the roentgen picture of the lungs that is sufficiently characteristic both for histoplasmosis and for toxoplasmosis.

One should also note the presence (Case #2) of the minute necrotic foci in the liver, spleen, kidneys, and lymphatic nodes, which also can be detected by the unaided eye. Because of the partial necrosis and the presence of Langhan's type of giant and epithelioid elements we hesitated between tuberculosis and brucellosis in our diagnosis, and only after having become acquainted with the literature about histoplasmosis did we direct our attention to the mycotic nature of these elements (see fig 2b). The histological changes of the lungs that were noted in the microscopic study of our cases were so characteristic that with their presence in the lung it is possible to substantiate a diagnosis of histoplasmosis even in those questionable cases where infrequent parasites of an uncharacteristic appearance are discovered in the other organs.

In two of our cases (1 and 3), by means of a simple staining with hematoxylin-eosin, we noted an extreme selective staining of some of the alveolar partitions by the hematoxylin (see fig 4), which was in contrast with the remaining portion of the organ. This extreme staining was observed even in the

most minor enlargement, and in a great enlargement, and with immersion it was discovered that in these portions were situated the largest number of the reticular cells containing the spores of Histoplasmosis capsulatum, whereupon some of the cells were solidly crammed with these bodies (see figs 2a and b, and fig 3).

Moreover, in these sections between the reticulo-endothelial cells, which were filled with the parasite's spores, we also noted numerous typical thread-like mycelia (see figs 1 and 6) with linear enlargements and pseudomycelia of a linear form. Both of these categories of mycelia are situated around the capillaries of the alveolar walls, and also around the larger vessels, penetrating between the connective-tissue cells. In some sections we noted the reproduction processes of the parasite in the form of a pseudomycelian fission into blastospores or arthrospores (fig 6).

The threadlike mycelia that were observed in two of our cases indicate, in our opinion, that Histoplasma capsulatum belongs to the group of false yeasts (the incomplete, fungoid forms).

It was discovered in our cases that the largest number of bodies and mycelia are detected chiefly in the lungs. We presume that this development of the fungus in the lungs is related to the parasite's requirement for oxygen; in addition the lungs are the portals for the fungus's penetration into the animal or human organism; by this it is possible to explain the genesis of epidemics among agricultural workers and also some of the laboratory illnesses.

In the majority of cases, evidently, the disease at first is in the pulmonary localized form that subsequently causes the generalization of the process that then leads to lethal termination. Thus we can explain some of the pulmonary forms that are considered as completely healed as the result of lobectomy (after 2-3 years).

In our cases the microscopic picture of the affliction, particularly the changes of the lungs and the mycological properties of the parasite in this organ, presents a peculiar appearance as compared to those which have been published to date. As a result it is possible to assume the existence of geographical variations of this illness in relation to the variety of Histoplasma capsulatum. The presence of the parasite should be determined by means of cultures on nutrient media and by inoculating susceptible animals.

On the basis of our observations we can assert that this illness is encountered in the Rumanian People's Republic and it is probable that many cases of this disease were formerly not exposed. The problem of histoplasmosis is extremely important from the prophylactic point of view.

Conclusions

1. In three cases of histoplasmosis detected in Bucharest the clinical and pathomorphological pictures fully correspond to the picture of this disease.

2. In regards to the clinical symptomatology there were observed in all three cases a febrile condition that lasted from three weeks to four months with an enlargement of the spleen and anemia with leukopenia, whereupon the lethal termination occurred in a condition of emaciation. These clinical symptoms are considered typical for the severe disease in question.

3. The diagnosis of histoplasmosis was established microscopically as a result of discovering yeast-like bodies and also Histoplasma capsulatum in the reticulo-endothelial cells of the tissues, particularly in the lungs where we detected the processes of the parasite's maximum development.

4. In the lung tissue, in addition to fungus spores, we detected the presence of numerous threadlike mycelia, and also the pseudomycelia of this fungus with manifestations of the division of these formations and the formation of blastospores (or arthrospores), which, evidently, is the first time this is noted in the literature.

5. It is possible to express a supposition concerning the existence of a local variant of Histoplasma capsulatum with a characteristic pathomorphological picture.

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Illustrations

Suitable illustrations are not available for reproduction - Translator's note.

Fig. 1 - Case 1. Multiple threadlike fragmented linear mycelia around the pulmonary alveoli and vessels (450x)

Fig. 2 - Yeast-like bodies of Histoplasma capsulatum in the cytoplasm of reticular cells: a. in the lungs (case 1); b. In the granulation tissue around the necrotic portions of the kidney (case 2); c. in the wall of the pulmonary alveolus(case 3). (1500x)

Fig.3 - Case 3. The pulmonary alveolus in the presence of swelled, partially desquamated cells; in the numerous alveolar cells the cytoplasm is filled with the yeast-like bodies (900 x)

Fig. 4 - The selectively extreme staining of the yeast-like bodies and mycelian threads of Histoplasma capsulatum by hematoxylin in the interalveolar partitions (100x).

Fig. 5 - Case 3. Reticulo-endothelial and myeloid hyperplasia with proliferation of Kupffer's cells in the liver (450x).

Fig. 6 - Case 3. Threadlike mycelia in the partitions of the pulmonary alveoli; part of the mycelium in the stage of separation (the formation of blastospores or arthrospores); the presence of free spores between the connective cells (900x).