Coccidioidomycosis in Hungary

The first imported case

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A case of an isolated subcutaneous coccidioidomycosis in a 61-year-old man is presented. The patient has lived and worked in Arizona for 3 years previously but developed no apparent clinical signs of the disease. The painless, cavitating, tumor-like mass was surgically excised and the diagnosis was established by histological demonstration of the fungi and confirmed by serum counterimmuno-electrophoresis. This represents the first imported case of coccidioidomycosis in Hungary. (Pathology Oncology Research Vol 4, No 2, 147-151, 1998)

Key words: coccidioidomycosis, skin, pathology, human

Introduction

Coccidioidomycosis is a systemic fungal disease endemic in the southwestern USA, Mexico, Central and South America. It is very rarely seen in Europe, because the climatic conditions do not favor the life cycle of the organism. Sporadic cases have been reported from England,32 Belgium,43 Norway,28 the former Soviet Union,30 Finland,3 Switzerland,8,12 France,14 Czechoslovakia,42 Romania1 and Sweden,29 most of these were imported. A relatively larger number of patients was diagnosed in Germany,5,18,25,36,37; these were members of the armed forces who had previously been trained in the endemic areas of the USA. Actually, a positive skin test was demonstrated in 3.7 % of them.41 In Hungary a case was diagnosed 40 years ago:12 this was a 22-year-old woman who had generalized synovitis for 2 years before the diagnosis was established by histological and mycological methods and confirmed by inoculation into mice. This patient was a native of Hungary who never traveled to endemic areas and the source of her infection remained unclear.

Because of its low incidence in our regions, European pathologists are not familiar with this disease. However, coccidioidomycosis can be expected to become more prevalent. The case reported here represents a typical example of this fungal disease with emphasis on its pathological characteristics.

Case report

A 61-year-old white immunocompetent male, a US citizen, presented with a painless bump which had appeared two weeks previously in his chest wall. He had lived in Arizona and worked in the desert region between 1993 and 1996. Subsequently he accepted a teaching position and arrived in Hungary shortly thereafter. The past medical history was unremarkable. On physical examination, in the anterior thoracic wall, on the right side of the sternum, above the sternocostal junction of the 4th-5th ribs a 6 x 6 cm immobile but well-defined mass was seen; there were no signs of an accompanying inflammation. Computed tomography described this mass as a 4 x 4.5 x 3 cm, mainly subcutaneous lesion with central necrosis. The lesion was hypodense (12-15 HU) and did not accumulate contrast material. Physical examination did not reveal any other significant findings, except inguinal intertrigo and pytiriasis versicolor on the skin of his chest and abdomen. Neurologic examination was negative. Laboratory parameters (ESR, WBC, RBC, hematocrit, hemoglobin, glucose,
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BUN, creatinin, bilirubin, albumin, alkaline phosphatase, GGT, LDH, AST, ALT, uric acid) were all within the normal limits. Chest X-ray and abdominal ultrasound examinations were negative; the bones were normal.

Fine needle aspiration biopsy of this lesion yielded thick, gray-pink pus; no causative organism was identified in it. Aerobic and anaerobic cultures proved to be sterile. The lesion was regarded to be a tumor of indeterminate origin with central cavitation and suppuration, and the subcutaneous mass was surgically removed.

Grossly, the specimen consisted of multiple friable, pea-sized pieces of tissue measuring 4 x 2 x 1 cm in aggregate, in which irregular, grayish-red, hemorrhagic, and soft, yellowish areas were unevenly present. Histologically, no neoplastic proliferation was observed. Instead, a suppurative granuloma was seen with large areas of hemorrhage and caseating necrosis. No foci of calcification were notable. Multiple microabscesses were surrounded by a zone of pale, sometimes palisading epithelioid cells and some multinucleated, Langhans-type giant cells. Around these cells, a large infiltrate of lymphocytes and plasma cells was observed (Figure 1a). Throughout the specimen, randomly distributed spherules were present exhibiting all stages of maturation (Figure 1b-e). The spherules were located partlly in the cytoplasm of the giant cells, but not infrequently they were lying freely in the necrotic debris. The diameter of the spherules varied between 30 and 80 μm, their wall exhibited a double contour, and some of them contained numerous endospores. No budding phenomenon could be seen. The fungi gave a strongly positive PAS reaction, their wall showed no birefringence under polarized light.

The patient’s serum was investigated by counterimmuno-electrophoresis for specific IgG against Coccidioides immitis (Coccidioides Immunodiffusion Antigen, Immuno-Mycologics Inc., Norman, Oklahoma, USA). Two antigen concentrations (10x, 100x dilution) and a blank control were applied to agarose slides. After 180 min running time the slides were washed with 0.9% NaCl for 4 hours, dried and stained with Amidoblack. A positive reaction could be observed in the 10-fold dilution confirming the diagnosis of coccidioidomycosis.

The patient has been treated with a 400 mg daily dose of ketoconazol for 4 months and he is now symptomless.

Discussion

Coccidioidomycosis is primarily a respiratory disease; the patients are infected by inhalation of the Coccidioides immitis arthroconidia which normally live in dry soil. Once in the lung, the organism remodels into a 30–60 μm, thick, double-walled spherule containing thousands of endospores. Although the pulmonary infection is usually self-limited, in 0.1-0.5% of the cases hematogeneous dissemination may occur: the skin, lymph nodes, bones and meninges are the most frequently affected organs.6,31 However, any organ can be involved, including unusual sites such as the hypophysis,15 eye,16,27 larynx,4 thyroid,26 breast,3 adrenal glands,26 uterus,31 epididymis or prostate.9,10

The majority of the infected persons are asymptomatic or have flue like symptoms. The disease may affect immunocompetent as well as immunocompromised individuals, but the course is more aggressive in the latter. Immunosuppressed patients after transplantation and HIV-infected persons are at an increased risk, and have an exceedingly high mortality (up to 63%).11,32,33,39 The host factors facilitating the dissemination of the fungus in immunocompetent patients are poorly understood.

Individuals in certain occupations are more frequently exposed to the contaminated soil (dust) and therefore are more likely to be infected by C. immitis. Among them agricultural and construction workers or military personnel, geologists, archeologists, etc. are most frequently affected, but practically anyone who visits endemic areas is at risk. It is well known that the fungus poses a health hazard to hospital and medical laboratory workers even outside the endemic regions.39 Kohn et al. have reported a fatal case of a veterinarian who had performed an autopsy on a horse with disseminated coccidioidomycosis.24 The mode of infection was inhalation of the aerosolized endospores. Exceptionally, primary cutaneous inoculation also may occur.

Animals living in endemic areas may also be affected: horses,48 cats,13 dogs,7 and rarely other species like swine,30 tapir,13 or Bengal tigers,48 can also be infected.

The fungus evokes a suppurative-granulomatous tissue reaction. The spherules attract the macrophages, lead to formation of multinucleated giant cells of the Langhans or foreign-body type, accompanied by a collection of lymphocytes and large number of plasma cells, while the purulent component is a reaction to the released endospores.

The pathological diagnosis is based on the direct identification of the fungus. Fine needle aspiration biopsy permits early recognition of this disease,21,31,38 however, a negative result could be attributed to sampling error. Rarely, the bone marrow smear may contain the diagnostic fungi.44 Additional methods like immunohistochemistry, counterimmuno-electrophoresis, delayed-type hy-

Figure. 1. Histologic picture of coccidioidomycosis displaying the different stages of maturation. a.) Overview of the suppurative granuloma. On the left there is caseous necrosis, in the center a large multinucleated giant cell containing a mature spherule with endospores, and this cell is surrounded by epithelial cells and plasma cells. x450; b.) early tissue phase of the fungus. x1200; c.) a fungus phagocyotosed by a giant cell exhibiting cleavage lines. x1200; d.) mature spherule with endospores. x1200; e.) the wall of the spherule is disrupted and PMNs invade the released endospores. x1200.

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persensitivity skin tests, complement fixation procedure, ELISA all can be helpful in the confirmation of the diagnosis. Histologically, coccidioidomycosis must be distinguished from cryptococcosis, paracoccidioidomycosis or blastomycosis, because these fungi also produce suppurative granulomas. Cryptococcus neoformans rarely exceeds 15 μm in diameter and, characteristically, the round to oval organisms lack an internal structure. The Blastomyces and Paracoccidioides species are 8–15 μm (max. 30 μm) in diameter, and typically display budding, a phenomenon never seen in coccidioidomycosis.

In Hungary, coccidioidomycosis is practically non-existent. To the best of our knowledge, this case represents the first imported case. The origin of this patient’s subcutaneous coccidioidomycosis is unknown. Although primary cutaneous coccidioidomycosis does occur, most cases are due to dissemination from the primary pulmonary infection. Here we can not exclude or confirm either possibility.

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References


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