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Case report

Primary Pulmonary Botryomycosis: Case Report

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A B S T R A C T

A case is presented of pulmonary botryomycosis in a 61-year-old man with a massive right-side pulmonary infiltrate which looked like a tumor (on X-ray). Microscopic examination of a transbronchial biopsy specimen revealed chronic suppurative inflammation, which did not regress despite intensive antibiotic therapy for a period of two months. Histological analysis of specimens taken during surgery for hemoptysis revealed pulmonary botryomycosis. The disease was diagnosed on the basis of characteristic eosinophilic granules in which the bacteria are surrounded by protein material (Splendore-Hoeppli phenomenon). Pulmonary actinomycosis was excluded. The case demonstrates that pulmonary botryomycosis can have the appearance of a mass which resembles pulmonary carcinoma on X-ray, and may also be mistaken for pulmonary actinomycosis. For this reason, pulmonary botryomycosis, although rare, should be excluded during differential diagnosis of hemoptysis or pulmonary infiltrates.

***Key words**: pulmonary botryomycosis, hemoptysis, pulmonary infiltrates*

Introduction

Botryomycosis is a rare, chronic, suppurative, occasionally granulomatous bacterial infection of the skin, soft tissue or internal organs[1]. The characteristic histological finding is eosinophilic granular, fungus-like »clubbing« material, containing the causative bacteria in a suppurative focus, known as the Splendore-Hoeppli phenomenon[2]. This phenomenon is not unique for botryomycosis and can also be seen in actinomycosis, mycetoma, nasofacial subacute phycomycosis, coccidiomycosis and sporotrychosis. Characteristic, fungus-like granules of botryomycosis were first discovered in the pul- monary node of a horse in 1870[3], and the term botryomycosis (Greek: botrys, a bunch of grapes) was proposed by Rivolta in 1887[1],

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who considered that the causative agent came from the group of Actinomycetes. Up until 1913, when Opie[4] presented the case of a patient with hepatic botryomycosis, it was believed that the disease only occurred in animals. In 1919, Magrou experimentally demonstrated the bacterial etiology of the disease by isolating *Staphylococcus aureus* from an equine lesion and reproduced the disease in a guinea pig[5]. Since then numerous bacteria have been identified as causative agents[6].

Approximately 90 cases of botryomycosis have so far been reported in humans, of which around 75% were botryomycosis of the skin and underlying tissue, while primary involvement of internal organs is rare, with only a few cases reported in the literature[7,8.]

Case presentation

A 61-year-old patient, Z.Š., a shopkeeper, cigarette smoker, was admitted to the Hospital with right-side pleuropneumonia. He had previously been treated in the county hospital, where pleural puncture had been performed and a bloody exudate obtained. The patient was treated with amoxicycline with klavulonic acid, ampicillin, gentamicin and metronidazole.

On admission the patient's general condition was good, he was afebrile and complained of pleural pain and effort dyspnea. A physical chest examination showed percutanous muffled sounds over the lower half of the right chest and extremely weak respiration. The chest X-ray showed an extensive infiltrate of the middle lobe, with expansive secondary carina and slight pleural exudation (Figure 1). Small bloody pleural extravasation was obtained by pleural puncture, in which neutrophils and lymphocytes were found. Bacteriological cultures were negative.

The laboratory findings showed raised erythrocyte sedimentation (103 mm/h), leukocytosis (13.2×10^9/L) and hypergammaglobulinemia (26 g/L).

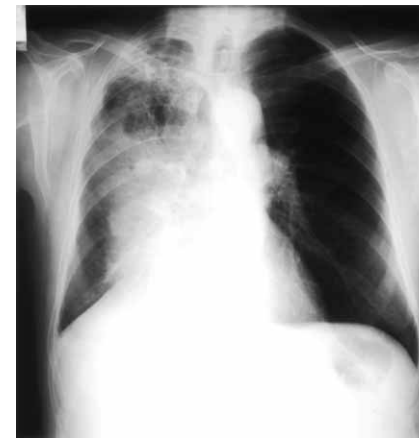

Fig. 1. Posteroanterior chest X- ray showing an extensive infiltrate of the middle lobe with small pleural exudation.

Although the patient had no respiratory disturbances during hospitalization, a control chest X-ray showed marked progress of the middle lobe infiltration.

Computed tomography of the chest showed an inhomogeneous infiltration of the middle pulmonary lobe, which looked like a tumor, extending up to the mediastinum and pericardium. Enlarged lymph nodes of the mediastinum could also be seen[9–11].

As pulmonary carcinoma was suspected, percutaneous needle aspiration puncture of the middle lobe infiltration was performed. Cytological examination of the puncture showed erythrocytes, neutrophilic granulocytes, necrotic detritus and macrophages.

Transthoracic puncture was negative for acidoresistant bacilli, and bacteriological cultures were sterile.

Fibrobronchoscopy was performed on four occasions and showed extramural

compression of the bronchial ostium of the middle lobe and infiltrated mucous membrane of the same ostium.

Cytological finding of the bronchoscopic material (catheter aspirate and brush swab) included neutrophylic granulocytes, detritus, clusters of lymphocytes, plasma cells and an occasional fibrocyte, indicating possible chronic inflammation.

The histopathologic finding of the excised bronchial mucous membrane for the middle lobe revealed beneath normal respiratory epithelium, connective tissue densely infiltrated with granulocytes, lymphocytes, plasma cells, and histiocytes. Cytological examination of the expectorate revealed frequent detritus and neutrophilic granulocytes. On several occasions bacteriological culture of sputum and bronchoscopic material showed normal flora.

Although the etiology of the pulmonary infiltrate had not been resolved the patient refused further treatment and left the Hospital.

After two and a half months the patient was again hospitalized because of further radiographic progression of an infiltrate in all three lobes of the right lung, and because lung cancer was suspected. The patient was still in good general condition, with no discomfort. Laboratory findings still showed marked raised sedimentation of erythrocytes (109 mm/h), leukocytosis (15.8×10^9/L), hyperglycemia (7.1 mmol/L) and hypergammaglobulinemia (31.44 g/L). Liver and renal functions were normal and HIV was negative.

Fibrobronchoscopy with transbronchial biopsy of the right lower lobe was again performed. Histopathological finding showed chronic inflammation, characterized by clusters of neutrophils, suppurative bodies and actinomyces.

However actinomyces could not be isolated in the cultures of bronchoscopic material or from the sputum. Other tests for actimomyces (staining of the preparations of the involved pulmonary tissue by periodic acid-Schiff and methenamine silver) were not performed. Nevertheless, β-hemolytic streptococci of the F group were isolated from the bronchoscopic material and expectorate. They were proven sensitive to benzylpenicillin, amoxyciclin and clavulonic acid, azythromycin, ceftriaxone and vancomycin. High doses of benzylpenicillin were prescribed (up to 24 million i.u. daily) for one month. However, the patient's condition continued to deteriorate and he began to cough up a suppurative, putrid expectorate.

As the X-ray finding indicated tumor etiology of the pulmonary infiltrate, thoracoscopy was planned in order to obtain bioptic material. However, due to severe hemoptysis, surgery was urgently performed. On surgery complete hepatization of the right pulmonary branch was found and a mass of tissue protruded from the lung, during manipulation, resembling a necrotic mass. The infiltrate of the right lower lobe looked like tumor tissue, which extended up to, and infiltrated, the diaphragm. Because of the above finding and copious hemoptysis, right-sided pulmonectomy, mediastinal lymphadenectomy and partial diaphragmatic resection were performed.

Histopathological finding of the lung tissue revealed sacculated bronchiectasis, chronic pneumonia (macrophages in the alveoli, suppurative bodies). On this occasion tests for actimomyces were performed (staining of the preparation by periodic acid-Schiff and methenamine silver) which excluded pulmonary actimomyces and established the diagnosis of pulmonary botrymycosis (Figure 2). Histopathological finding of the mediastinal lymph nodes showed chronic inflammatory changes. Histopathological finding of the diaphragmatic infiltrate showed bronchopneumonia with abscess formation.

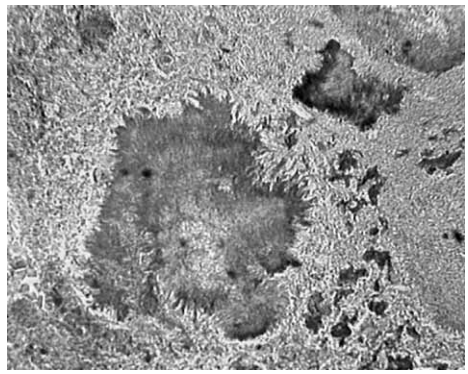

Fig. 2. Surgical specimen from the lung middle lobe demonstrates a bunch of bacteria within an abscess (hemalaun eosin – magnification × 200).

Following the operation, antibiotic therapy was continued (amoxicycline and clavulonic acid 3 × 1.2 gr. i.u.) and the patient's condition stabilized. However, on the third post-operational day his condition deteriorated and he developed respiratory acidosis. The patient was put on a respirator, but despite intensive therapy he died due to acute respiratory insufficiency. Post-mortem histopathological examination of the remaining pulmonary branch confirmed the diagnosis of primary pulmonary botryiomycosis.

Discussion

We present a case of a 61-year-old man with a mass detected on a chest X-ray. It was initially thought to be bronchial carcinoma, but after lung surgery pulmonary botrymycosis was diagnosed. Primary pulmonary botrymycosis is frequently mistaken for actinomycosis[12]. During the second lung biopsy we had the same dilemma about the diagnosis of our patient. Pathohistologically botrymycosis and actinomycosis both indicate Splendore-Hoeppli phenomenon[2], and so they are readily confused. In the patient described, gram-positive cocci seen on the Gram-stained lung tissue and the absence of branching hyphae, when periodic acid-Schiff and methanamine silver stains were used, helped in the differential diagnosis of botryomycosis.

Botryomycosis is a very rare disease in man. It mainly involves the skin[12], and very rarely occurs in organs such as the liver, kidneys, brain, prostate, tongue, ear, orbit, lungs and trachea[13]. To date 16 cases of pulmonary and/or visceral botryomycosis have been reported in the literature, primarily in persons with underlying diseases, and in a few cases in patients without underlying diseases. According to the literature predisposing diseases are cystic fibrosis, AIDS[6], diabetes mellitus, chronic granulomatous diseases[8], asthma[7] and pulmonary sequestration. Our patient had diabetes mellitus type II.

In our patient, group F *Streptococcus* was isolated from the expectorate and bronchoscopic material (catheter aspirate from the middle lobe) as was isolated in a case reported in the literature[14]. Group F *Streptococcus* is gram positive and usually β-hemolytic. Botryomycosis can be caused by a number of different bacteria and the most common agent is *S. aureus*. Other bacteria, such as *Pseudomonas auroginosa, Escherichia colli, Peptostreptococcus species, Streptococcus sanguis* and *Serratia marcescens* are also associated with botryomycosis.

As only a few cases of botryomycosis have been reported the guidelines for medical treatment are still insufficient to accurately suggest the correct duration of the antibiotic therapy for such patients. The treatment of patients with botryomycosis consists of targeted antibiotic therapy, depending on the isolated causative agent and, according to the literature[14], in the majority of patients, surgical procedure together with antibiotic therapy[7]. Antibiotic therapy is carried out for a minimum of two weeks and for a maxi-

mum of 6 months, with good results[14]. Our patient was empirically treated with various antibiotics for one month and after the isolation of group F *Streptococcus* from the expectorate, high doses of benzyl penicillin were administered the following month. In spite of the antibiotic therapy the clinical condition of our patient worsened and radiological examinations indicated bronchial carcinoma. At the onset of the disease the patient had refused the recommended operation.

It is still not known why some bacteria cause the botryomycotic type lesion, although it is believed that both bacteria and host factors contribute[15]. Investigations have suggested that the size of the inoculum[5], virulence of the bacteria and presence of specific bacteriophages condition the formation of granules by the bacteria. Some cases of botryomycosis suggest that the presence of a foreign body in human organs contributes to the formation of botryomycosis granules[16,17]. No foreign body was found in the lungs of our patient either during bronchoscopy or during the operation.

Of the host factors immunosuppression as in the case of diabetes mellitus, chronic granulomatous diseases[8], HIV infections[6], and long-term corticosteroid therapy[15]. Our patient had type II diabetes, well regulated by diet, hypergammaglobulinemia (predominantly increased IgG fraction) and anergy demonstrated by skin PPD test of cellular immunity.

Clinical symptoms are non-specific and in case presentations are described as mild, as in our patient at the onset of the disease. With regard to respiratory disturbances patients complain of dyspnea, pleural pain, cough and hemoptysis[18]. Our patient complained of occasional pleural pain, cough and hemoptysis, although he did not have loss of body weight. Chest X-rays often reveal affection of the upper lung lobes, either as diffuse infiltrates, homogenic mass, or with cavitation. In our patient the right middle and right lower pulmonary lobe was involved in the form of a large, inhomogenous infiltration, which resembled a tumor.

In a number of cases secondary involvement of the hilar lymph nodes, pleura, ribs and spine has been reported. In our patient the hilar lymph nodes and diaphragm were involved, which made us suspect lung carcinoma, as in other reported cases[17,18]. Thoracoscopy was planned and surgery performed after four transbronchial biopsies had been repeated in our patient.

In all cases reported diagnosis was based on the histological and microbiological findings of the bioptic material or from a surgical specimen, as in our patient, or during autopsy.

The case presented illustrates how pulmonary botryomycosis can mimic lung cancer and actinomycosis and therefore, although rare, it should be considered during differential diagnosis of these diseases.

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PRIMARNA PLUĆNA BOTRIOMIKOZA

S A Ž E T A K

Prikazan je slučaj plućne botriomikoze u 61-godišnjaka s masivnim desnostranim plućnim infiltratom nalik tumoru. Mikroskopski pregled plućnog uzorka dobivenog transbronhalnom biopsijom pokazuje kroničnu gnojnu upalu, koja ne regredira unatoč intezivnoj antibiotskoj terapiji tijekom dva mjeseca. Histološka analiza plućnog uzorka dobivenog operacijom pluća zbog jakih hemoptiza ukazuje na plućnu botriomikozu. Dijagnoza je postavljena temeljem karakterističnih eozinofilnih granula u kojima su bakterije okružene proteinskim materijalom (*Splendore-Hoeppli phenomenon*), nakon što je prethodno isključena dijagnoza plućne aktinomikoze. Ovaj slučaj pokazuje da plućna botriomikoza na radiogramu pluća može izgledati kao infiltrat nalik plućnom karcinomu, a može se također zamijeniti s plućnom aktinomikozom. Stoga, iako je rijetka, plućnu botriomikozu treba isključiti tijekom diferencijalne dijagnoze hemoptiza ili plućnih infiltrata.