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Short Communication

Actinomycosis as a Neglected Diagnosis of Mediastinal Mass

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SUMMARY: Thoracic actinomycosis is a rare disease in children. Diagnosis is typically delayed, since the presentation can be very similar to that of malignant tumors, tuberculosis and fungal infections. We here present the case of a 9-year-old girl who was treated for tuberculosis at the first presentation, for non-Hodgkin's lymphoma at the second presentation, and for chronic granulomatous disease at the third presentation before actinomycosis was finally diagnosed by culture.

Mediastinal masses in pediatric-age patients have a wide range of differential diagnoses, including benign and malignant tumors and chronic infectious processes. Because the clinical and radiological findings may be very similar among these entities, most lesions require biopsy for a definite diagnosis. Here, we present the case of a 9-year-old girl with a mediastinal mass who was a diagnostic challenge in our center.

A 9-year-old girl who had experienced no major medical problems until age 7 presented at our institution with cough, fever, anorexia, weight loss, night sweating and left upper lobe consolidation on chest X-ray (CXR). Because tuberculosis (TB) seemed possible, isoniazid, rifampin and ethionamide were prescribed for 6 months by a local physician. When she failed to improve, a chest CT was performed and revealed an anterior mediastinal mass and a mass in the left upper lobe of the lung. Fine needle aspiration of the lung mass supported a diagnosis of lymphoma. Cerebrospinal fluid cytology, bone marrow aspiration and biopsy were negative for malignancy. Under the assumption of non-Hodgkin's lymphoma, a 1-year course of chemotherapy and radio-therapy was ordered by the oncologist, who then followed the patient monthly in the outpatient department. The size of the mediastinal and lung mass did not change significantly after 1 year. Thoracotomy was done and a hard solid mass in the anterior mediastinum with a part of the left upper lobe of the lung was excised. Histopathologic study showed a chronic granulomatous reaction with focal abscess formation without any evidence of malignancy. The patient was referred to the Infectious Department of our hospital. The results of a Mantoux test, gastric washing for acid fast staining (AFS) and TB culture were negative. Flow cytometry (CD4, CD8, CD19, CD22) and complement levels (C3, C4) were normal. Plasma levels of IgM, IgG and IgA were within normal ranges and the result of a nitroblue tetrazolium (NBT) test was 10%. With possibility of superimposed infection on the base of chronic granulomatous disease (CGD), intravenous clindamycine and co-trimoxazole were started, and 2 weeks later the patient was discharged with oral co-trimoxazole as a prophylaxis. One month later she was again referred to our hospital with fever, and bulging and pain in the left anterior chest wall with purulent discharge from the site of the previous chest tube. She was admitted again and aerobic, anaerobic, fungal and mycobacterium cultures and staining were done on the purulent discharges. All cultures and smears were negative. Due to periosteal elevation in the left upper ribs in CXR, bone scintigraphy using TC^{99} and chest CT were requested. The bone scan showed increased uptake in the six left upper anterior and posterior rib (Fig. 1), and chest CT revealed a left anterior chest wall abscess and collapse of the left upper lobe with fibrotic changes. The abscess was drained, the involved area of the chest wall was debrided, and pathological analysis indicated a chronic granuloma with focal abscess and fibrosis; the sample was negative for malignancy. The results of sulfur granule and AFS were also negative. The NBT test was repeated twice and yielded results of 80 and 60%, respectively, so CGD was ruled out and we assumed that the first abnormal NBT test had been due to chemotherapy (1). Because osteomyelitis remained possible, we continued intravenous clindamycin and ciprofloxacin for 4 weeks, and then the patient was discharged. Forty-five days later she presented with a painless hard mass in the right mandible. Bone scintigraphy was compatible for tumoral involvement of the right mandible and upper thoracic spines (Fig. 2). The biopsy of the mandibular mass indicated chronic granuloma with negative immunohistopathologic evidence for lymphoma. For the third time, she was admitted with a high grade fever (> 40°C orally), toxic appearance, severe chest and shoulder pain in the left side with a new draining sinus on the right mandible. Because of the possibility of actinomycosis, a culture and smear were requested and a high dose of penicillin (400,000 unit/kg/day) was started. Gram stain of the purulent discharge revealed irregular Gram-positive filamentous microorganisms in clusters with negative AFS. Chest CT showed a left anterior chest wall abscess and an abscess on the fourth thoracic vertebra. The mandibular mass and chest wall abscess were surgically excised and the tissue was sent for culture, gram stain and pathologic study, but there were no sulfur granules microscopically or macroscopically. The patient's condition became much better; her shoulder and chest pain disappeared, and her erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and white blood cells (WBC) count decreased gradually (ESR, 120→30 mm/h; CRP, 300 →40 mg/ml; WBC, 20,000→10,000/mm^3).

After 4 weeks, microorganisms grown on anaerobic culture media and biochemical testing confirmed *Actinomyces israelii* (positive glucose, mannitol and sucrose fermentation but negative hemolysis, catalase, starch hydrolysis, DNase, indole and urease), but an antimicrobial susceptibility test was not done.

The patient had significant clinical and radiological

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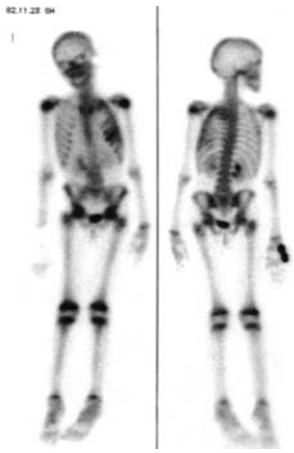

Fig. 1. Bone scintigraphy using TC^{99} showed increased uptake in the six left upper anterior and posterior ribs.

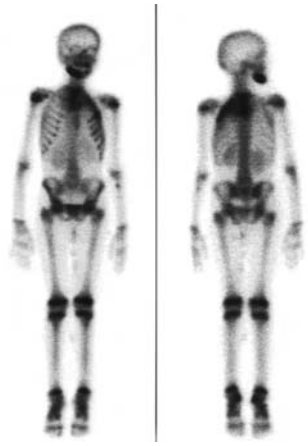

Fig. 2. Bone scintigraphy revealed high uptake in the right side of the mandible, the upper part of the hemithorax, and the first to sixth thoracic spines.

improvement after 6 weeks intravenous penicillin therapy and was discharged with oral penicillin V (200 mg/kg/q6h) for 12 months. She had excellent response to this treatment.

Thoracic actinomycosis is a rare disease in childhood. Only 46 cases have been reported in the last 25 years in the English literature (2). It usually occurs after inhalation or aspiration of the microorganism, penetration of colonized foreign bodies to the chest or local spread from the abdomen or cervicofacial infections, but it rarely occurs hematogenously. Thoracic actinomycosis usually presents as a mass (inflammatory pseudotumor) in the mediastinum or lung, but it can also present as a diffuse or local pneumonia, pleural empyema or endobronchial mass (3).

Rib involvement is common in pulmonary actinomycosis. It can also invade the sternum or vertebra, as in the present case. Most patients present with cough, chest wall pain, weight loss, fever and finally empyema necessitans if untreated. Less commonly the patients may have hemoptysis (4) or present with superior vena cava syndrome (5). Delayed diagnosis is common; because there is no specific clinical or radiological finding and the disease closely mimics TB, lung abscess, tumor, fungal infections and pulmonary infarctions, both clinically and radiologically (6). Our patient was treated for TB at the first presentation, for lymphoma at the second presention, and for CGD at the third presentation.

Diagnosis of actinomycosis is very difficult because the microorganism can not be detected in most instances (3), so the diagnosis is sometimes based only on clinical findings and the response to antibiotics. Treatment of actinomycosis includes both prolonged antibiotic therapy and surgical debridement. The drug of choice is penicillin. The duration of therapy depends on the patient's condition, but most authorities recommend 4 - 6 weeks by an intravenous route, followed by 6 - 12 months of oral antibiotic.

Relapse is a problem in treatment of actinomycosis, and can be due to:

1. An inadequate dose of antibiotics or inadequate duration of treatment.
2. Co-infection with other microorganisms (especially *Actinobacillus actinomycetemcomitance*, which is present in 30% of cases). For this reason, it is recommended that all critically ill patients be treated for this microorganism (7).

In conclusion:

1. Clinical and radiological findings of thoracic actinomycosis can closely mimic a malignant tumor, fungal disease, pulmonary emboli, pneumonia or TB, so tissue biopsy (not fine needle aspiration) is usually necessary for a definite diagnosis.
2. If the pathologic findings of a mass are in favor of granulomatous inflammatory process or micro-abscess formation, and if the workup for TB, fungal infections or CGD are negative, the physician should keep actinomycosis in mind as a possible diagnosis and perform the appropriate investigation.
3. Clinical findings may be the only key for diagnosis, because some cases of actinomycosis neither have sulfur granules nor positive culture or gram stain in their tissue specimen.

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