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Disseminated bipolaris infection in an immunocompetent host: an atypical presentation

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Disseminated Bipolaris Infection in an Immunocompetent Host: An Atypical Presentation

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Introduction

Organisms of the genus Bipolaris are found in the soil and plant material. These fungi are known to be plant pathogens[1,2] and infection may result from either inoculation or inhalation of the organism[3-5]. Infections due to this genus are probably more comnuon than previously recognized[6] and have been increasingly reported in apparently imniunocornpetent hosts[7-10]. Currently, they should be included in the differential diagnosis of disseminated fungal disease. Genus Bipolaris have been associated with central nervous system infections, sinusitis, keratitis, peritonitis associated with continuous anibulatory peritoneal dialysis, orbitopathy[4] and allergic bronchopulmonary disease[6].
In addition to the ability of this genus to cause invasive as well as 'allergic' disease in humans, it is reported that a rnycotoxin produced by Bipolaris may induce lung and liver adenomas ill mice[11]. We report a case of disseminated Bipolaris infection in a previously healthy and irnmnucompetent patient with infection including the lungs, liver and lymph nodes.

Case Report

An otherwise healthy I 8-year-old girl, developed productive cough fever and weight loss for which she consulted a pulmonologist. Bilateral wheezes on chest examination were noted and laboratory investigations revealed a white blood cell count of 34.8x 1 0 9/L (eosinophils at 59%) and an ESR on 85 mm/hr. Filariasis was suspected and Diethyl carbamazine was prescribed, although her blood test for filiaria was negative. After noting no improvement in the next few weeks she presented to the Aga Khan Hospital.
On physical examination, the patient was ill looking and cachectic. Her pulse rate was 100/min and blood pressure 110/70 numHg. General physical examination revealed small discrete cervical lymph nodes which were moderately tender. Her head, eyes, ears, nose and throat were normal on examination. Respiratoly examination revealed diffuse bilateral wheezes along with crackles, predominantly in the mid-chest. Abdominal examination revealed a moderately enlarged non-tender liver and palpable spleen. Cardiovascular and nervous system examination were normal.
On laboratory investigaLion, ESR was 130 mm/hr, hemoglobin 10.1g/dl and serum glucose 96 mg/dl. The white blood cell count was 19.8x10 9/L (neutrophils 48% lymphocytes 14%, Eosinophils 38% and monocytes 1%)and ablood culture was negative as was the HIV test. Setrum immunoglobulin levels were lgA 2.60 g/L (normal range, 0.6-4.5 g/L), lgG 43.58 g/L (8-18.0 g/L) lgM 0.41/g/L (0.6-2.5 g/L). The result of serum Anti-DNA was 3.3 IU/ml (normal range 0-6 IU/ml). Autommune markers like A.N.A., A.S.M.AA., A.M.A were negtivr. A chest roentgenogram revealed bilateral pulmaonary infiltretes, mostly perihilar in distribution and more singnificant on the right lung. There was widening of the superior mediastinum with right paratracheal lymph adenoapathy (Figure 1).

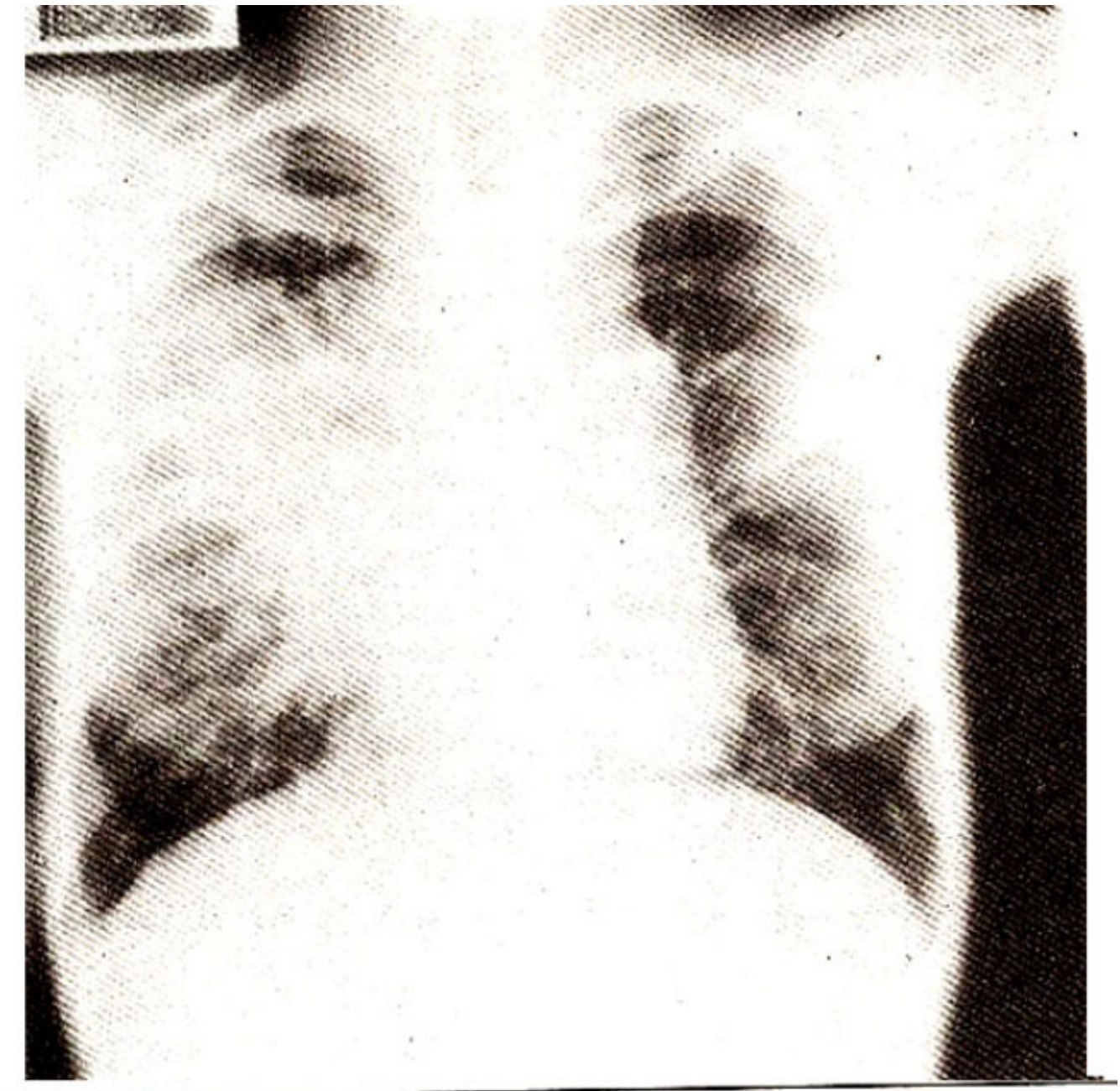

Figure 1 Chest X-ray showing bilateral peribilar infiltrates, more marked are right side alongwith right paratracheal lymphadenopathy

On abdominal sonography, the liver and spleen were moderately enlarged and numerous lymph nodes were visible near the porta hepatitis.

Sputum smears and cultures for both acid fast bacialli as well as for fungi were reported as negativee. A biopsy of the cervical lymph node (specimen analyzed at the Armed Forces Institute of Pathology, Washington D.C.) revealed an exauberant granulomatous response comprising of epotheloid cells, histiocytes, giant cells, and numerous eosinophils, lymphocytes and plasma cells loosely interspersed within a fibrous background, as there was little resudual lymphoid atissue present. The fibrosis extended into the perilymphatic fat and the tissue eosinophilia was strikinfg. Easily identified on the haemoatoxyalin and eosin (H and Ea) stained sections were numerous fungal elements, mostly hyphae. Gomori methenamine silver (GMS) and periodic acid-Schiff (PAS) staining revealed myriad hyphal forms throughout the

inflammation and within essentially at the giant cells (Figure 2).

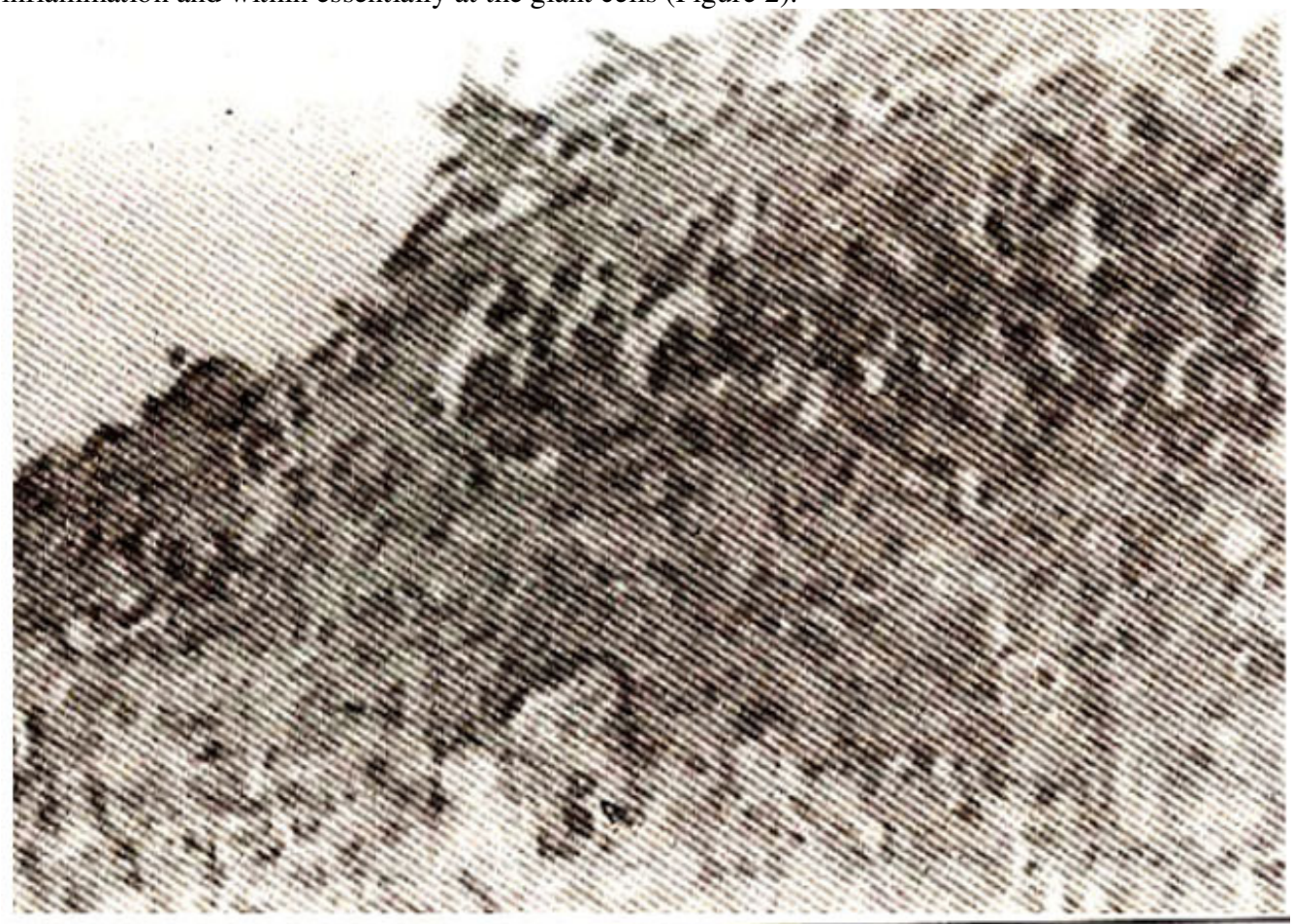

Figure 2. Photomicrographs of lymphnode showing granunomatous inflammation with budding fungal spores (arrow) (PAS stain Mag X 200).

At bronchoscopy, the right intermediate and middle lobe bronchus was found to be edematous and inflamed: Bronchial lavage was negative for acid fast bacilli smear and culture. A biopsy taken from the right middle bronchus showed presence of chronic granulomatous inflammation along with evidence of fungal infection (Figure 3).

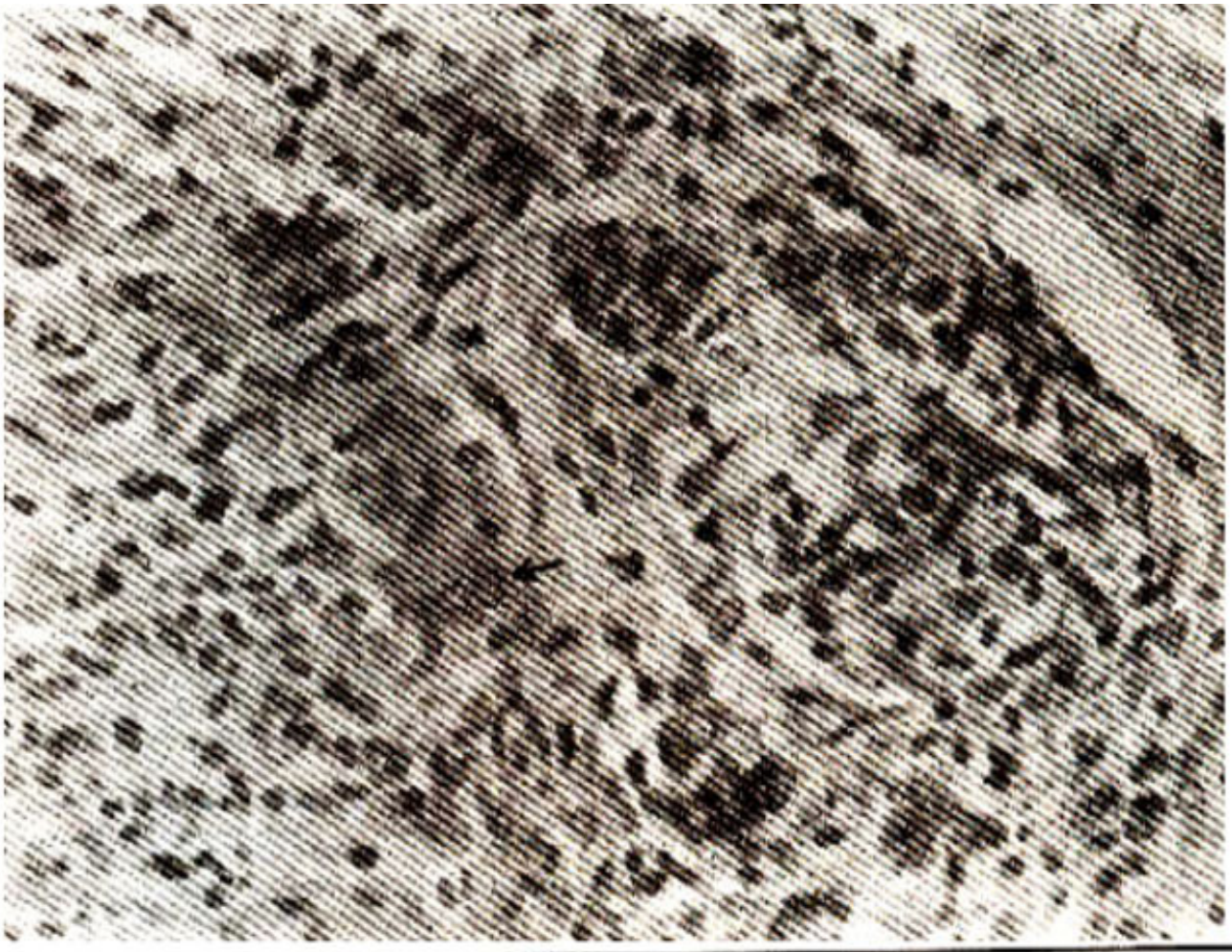

Figure 3. Photomicrograph of bronchial mucous showing fungal spores (arrow) (PAS Mag X 200)

The fungal culture (confirmed at the Mayo Clinics, Minnesota) was positive for Bipolaris spiciferal species. After reviewing the reports of the lymph node analysis, the patient was started on oral itraconazole 200 mg twice daily. Within a week on starting treatment, the patient's fever began to settle. Her cough decreased and she gained weight. Her white blood cell count decreased to 7.6x10 9/L (neutrophils 62%, lymphocytes 33% and eosinophils at 4%). Her ESR dropped to 60 mm/hr and hemoglobin increased to 11 .6 g/dl within 3 months of therapy. A repeat chest roentgenogram showed significant improvement. There was minimal residual scarring in the right mid zone (Figure 4).

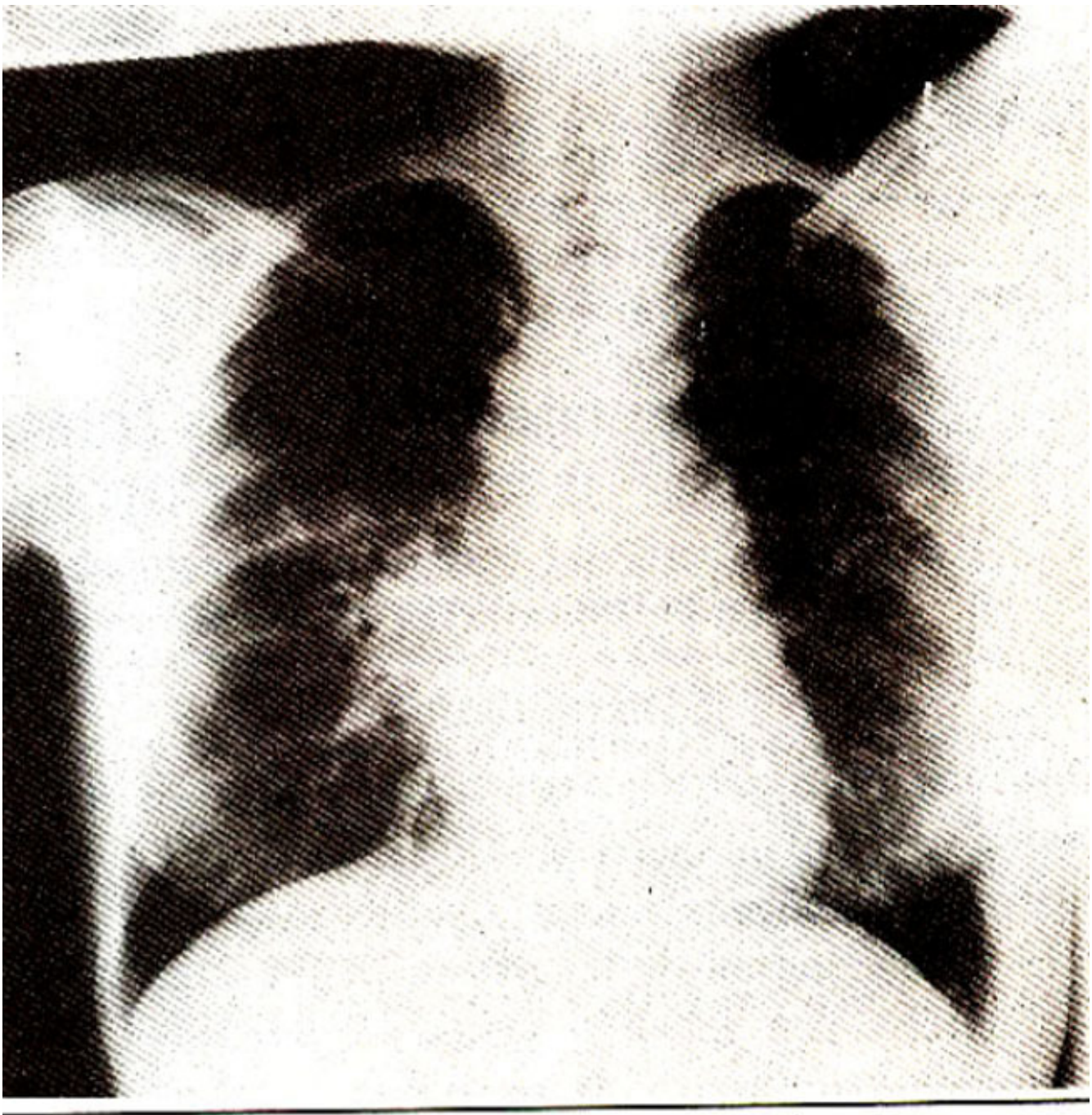

Figure 4. Chest X-ray after 3 months showing significant improvement

In 6 months of treatment, she gained five kilograms of weight and her fever resolved. Her lymphadenopathy subsided completely and the liver and spleen were no longer palpable. After 12 months of Itraconazole at 200 nìg twice daily, dose was reduced to 100 mg twice daily and continued for another 6 months. A bone marrow biopsy showed no evidence of granulomas and the aspirate sent for fungal culture was negative. An analysis of her T-cell function showed a reversed T-helper (CD4) to T-supression ratio (CD8) at 1:2 with CD4 count of around 500/mi. The proportion of Natural Killer Cells was increased. She was asymptomatic 6 months after stopping Itraconazole therapy when reviewed in July 1998.

Discussion

The discovery of Bipolaris species and related fungi in cultures in the recent past was initially believed to be contamination and confusion has encompassed the taxonomy of the genera Bipolaris, Dreshlera and Exserohilum[12]. These fungi are widespread in the environment, especially on commodities for consumption, such as rice[13] and have remained rare pathogens. The recent increase in reported cases of infection due to these fungi suggests that this infection ma)[14] have been missed in the community. Also, in the majority, sinusitis is the initial presentation[4,6], particularly in atopic individuals. In our patient. there was no sinusitis and she did not have any history of atopy. Another case of disseminated Bipolaris infection was reported from The Aga Khan University Hospital in 1993 in which the patient presented with pneumonia and addisonian crisis: however, the patient was atopic and an asthmatic on steroids[14]. After review of the available literature, we believe this is the 2nd report of an immunocompetent non atopic patient with disseminated Bipolaris infection.

Elevation of lgG and Igh specific to Bipolaris, Aspergillus or Curvularia. has been described in several cases of allergic or invasive fungal infection, suggesting a similar pathogenesis[4,14,15]. In our patient, lgG was elevated. it is important to note that the previously reported case of disseminated Bipolaris infection had a history of steroid consumption which has been noted as a significant risk factor for invasive fungal disease[16]. However, immunocompetent hosts with no history of corticosteroid use have recently been reported to develop invasive aspergillosis[17]. it is unclear if the patients reversed CD4: CD8 ratio was present prior to infection and contributed to her disease. Of interest is the finding of marked peripheral and tissue eosinophilia in our patient. Ihis finding, along with elevated IgE levels has been reported in cases of invasive pulmonary aspergillosis, making it difficult to distinguish this entity from allergic bronchopulnionary aspergillosis[18]. Data examined from a review of the literature suggest that hypersensitivity pneumonitis and invasive pulmonary disease encompass a spectrum of pathology[19].

The taxonomy and nomenclature of the pathogenic Bipolaris and Exerohilum species that cause phaeohyphomycosis (infection due to dematiaceous or darkly pigmented fungi) have been clarified[12]. McGinnis[20] emphasized that only the genera Bipotaris and Exserohilum contain well-documented etiologic agents of phaeohyphomycosis and described superficial, cutaneous, corneal, subcutaneous and systemic presentations of the infection. Pathological exam mat ion demonstrates granulomas with giant cells, yeast forms and pseudohyphae or hyphae. McGinnis et al.[12] described 52 cases caused by species of Bipolaris where involvement of the sinuses, brain, lung as welt as subcutaneous tissue was observed. In no case were the liyer or spleen affected and there was no mention of heavy tissue eosinophilia as reported in this case.

There have been two prey iotis cases of disseminated Bipolaris infection involving the lungs which have been successfully treated with ltraconazole[21]. The first patient had asthma and consumed marijuana B. specifera) having tried ketoconazole and failed. The second patient had no predisposing risk factors (B. hawaiiensis) hut required partial surgical resection of the lungs prior to therapy. Both patients received 200 nig twice daily for at least 4 months prior to improvement and later stabilization. In our patient, similar dosing was adequate enough for successful therapy. As in patients, residual involvement remained on the chest roentgenogram. In the previously mentioned series, successful outcome with Itraconazole was seen in 65% of patients treated, of which 60% had already failed to respond to amphotericin B. Therefore, it may be reasonable to consider Itraconazole as effective if not superior to amphotericin B. Also, oral azole therapy offers significant advantages in lowered toxicity and greater ease of administration than with amphotericin B.

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