Bipolaris infection presenting as granulomatous pleuritis and mediastinal mass in a young immunocompetent man: a case report

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ABSTRACT

Background: *Bipolaris* species are dematiaceous fungi that originally are plant pathogens but have been reported to cause a wide spectrum of diseases in both immunocompromised and immunocompetent human hosts.

Case Presentation: We report a case of a young immunocompetent man who presented with fever, dry cough, and malaise. He had unilateral pleural effusion with mediastinal mass. Histopathology of pleura and mediastinal mass revealed granulomatous inflammation with fungal pseudohyphae. Tissue cultures grew *Bipolaris* species. He is on itraconazole with significant clinical improvement.

Conclusion: This clinical presentation of *Bipolaris* infection has not been previously described. In Pakistan, where tuberculosis pleuritis is frequently encountered, this case highlights that other rare causes of granulomatous pleuritis can also present in a similar fashion.

Keywords: Case report, Pheohyphomycosis, granulomatous pleuritis, *Bipolaris* infection.

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Background

Bipolaris species are among the group of filamentous pigmented fungi containing melanin in their cell walls [1]. It is ubiquitous in the environment, and isolated from soil and decaying vegetation [1]. *Bipolaris* species were previously considered pathogenic in immunocompromised people only, but are being increasingly recognized to cause disease in immunocompetent individuals as well. The clinical spectrum is wide, ranging from allergic and chronic invasive sinusitis [2], keratitis, orbital cellulitis [3], endocarditis [4], meningoencephalitis [5], peritonitis, cutaneous infections, allergic bronchopulmonary disease [6], and systemic disease[7,8]. Pleurisy and empyema are rare manifestations of fungal diseases. We report a case of young immunocompetent patient who presented with mediastinal mass and granulomatous pleuritis secondary to *Bipolaris* species.

Case Report

A 32-year-old man visited our clinic with a 6-week history of low-grade fever, dry cough, mild dyspnea, and easy fatigability. He is a nonsmoker with no known comorbid illness. He is a security guard by profession. He denied any recent history of travel outside Karachi, Pakistan.

On examination, he was vitally stable. Chest examination was suggestive of right-sided pleural effusion, while the rest of the systemic examination was unremarkable.

Chest X-ray revealed moderate right-sided pleural effusion. On laboratory investigations, hemoglobin was 12.3 g/dl and white cell count was 14,000/ mm^3 (neutrophils: 42%, lymphocytes: 16%, and eosinophils: 23%) with normal liver and renal functions. Pleural fluid was lymphocytic exudate (pleural fluid protein: 6.9 g/dl, glucose: 95 mg/dl, and cell count: 80/mm^3 with 25% neutrophils and 75% lymphocytes). Pleural fluid Adenosine deaminase (ADA) levels were 35.3 U/l (normal: <33 U/l). Pleural fluid bacterial, fungal, and acid-fast bacilli (AFB) cultures, including Mycobacterium Tuberculosis (MTB) GeneXpert, were negative. Pleural fluid cytology did not show malignant cells. After therapeutic thoracentesis, a mediastinal mass became evident. A subsequent computed tomographic (CT) scan chest with contrast showed a large confluent lobulated soft tissue density mass of 13 × 10 cm, extending from anterior to posterior mediastinum. It was encasing the right main pulmonary artery and the right main bronchus and subsequent bronchi (Figure 1). At this point, we were considering the possibility of lymphoma.

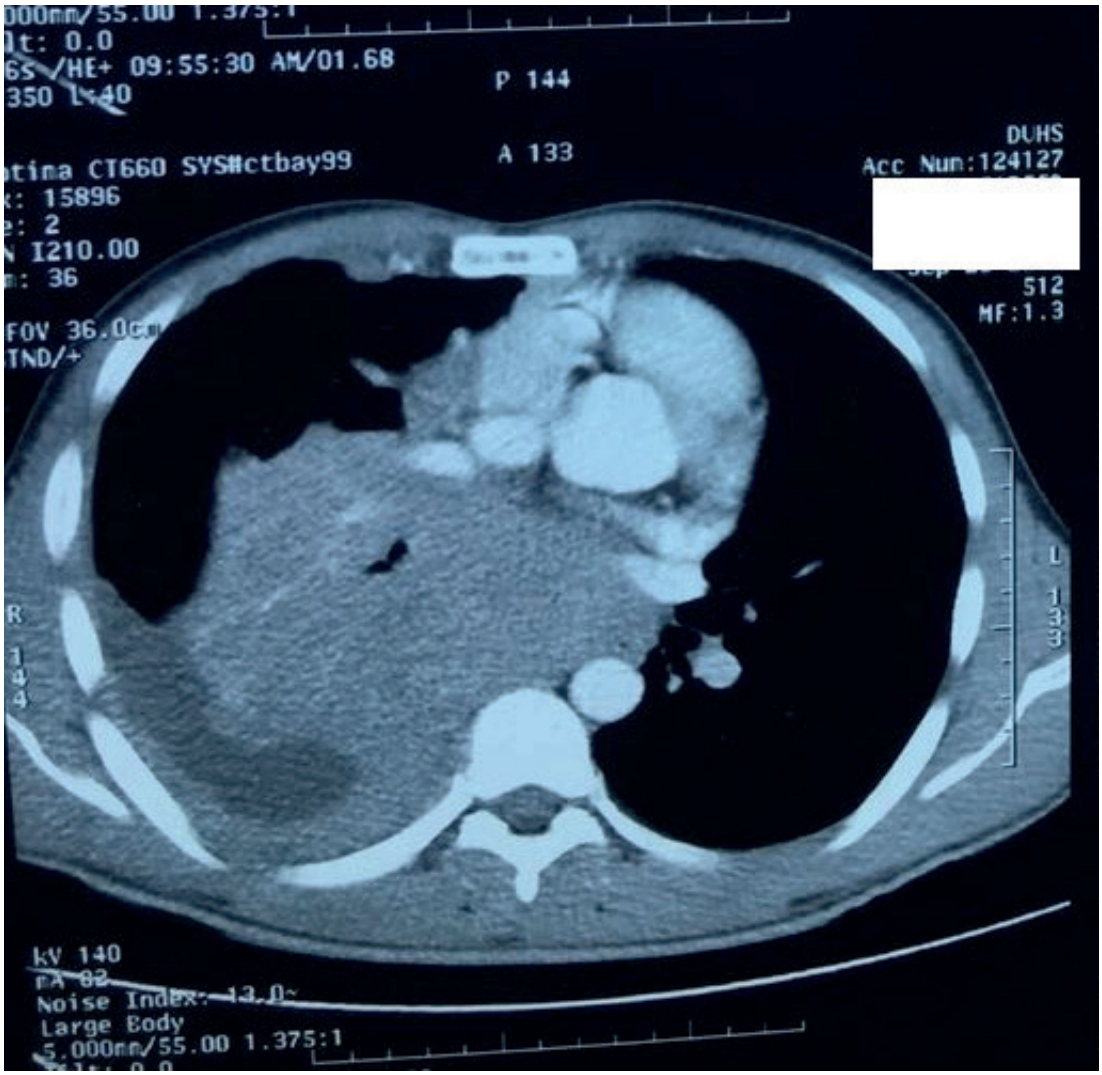

Figure 1. *Computed tomography of chest with contrast showing mediastinal mass encasing right lower lobe bronchus. The pleura is thickened and nodular.*

On fiberoptic bronchoscopy, the right bronchus intermedius was found to be externally compressed. We then took endobronchial biopsies. Histopathology showed granulomas with giant cells. On periodic acid-Schiff (PAS) stain, fungal pseudohyphae with thick-walled spores were seen at the center of the granulomas. Bronchoscopic lavage (BAL), AFB, and fungal and bacterial cultures were negative. Serum galactomannan was 0.19 Optical density index (ODI) (negative if <0.5) and β-d-Glucan was >523 pg/ml (positive if >80pg/ml): Considering the possibility of superficial endobronchial biopsies, he then underwent video-assisted thoracoscopic surgery (VATS) for further confirmation of fungal infection as BAL, and pleural fluid cultures did not grow any organism. Intraoperatively, the pleura was found to be thick and nodular with a large mediastinal lymph node mass. Pleural fluid was drained and biopsies were taken. The repeat histopathologies from pleura and nodal mass showed similar findings as before (Figures 2 and 3). The tissue fungal culture grew *Bipolaris* species. His HIV status was negative and immunoglobulin levels were normal.

He was started on itraconazole 200 mg twice daily after discussion with an infectious disease specialist. His fever and eosinophilia subsided within 20 days of treatment. A repeat CT chest at 6 months follow-up showed no recurrence of pleural fluid and a remarkable reduction in mass size to 4.4 × 2.9 cm. He is still on treatment and tolerating it well. There is a plan to repeat CT chest in 6 months' time to decide the total duration of treatment.

Discussion

Dematiaceous fungi are filamentous mold containing melanin in their walls, which is an important virulence factor in their pathogenesis [6]. In 1974, Ajello et al. [9] coined the term "Pheohyphomycosis" to describe infections caused by dematiaceous fungi. It is derived from the Greek word *phaios* meaning dark. This term is collectively used for heterogeneous superficial and systemic infections caused by the dematiaceous fungi. These molds are common in tropical and subtropical areas with multiple case reports from south Asia [6,7,10]. It is different from chromoblastomycosis and mycetoma which are characterized

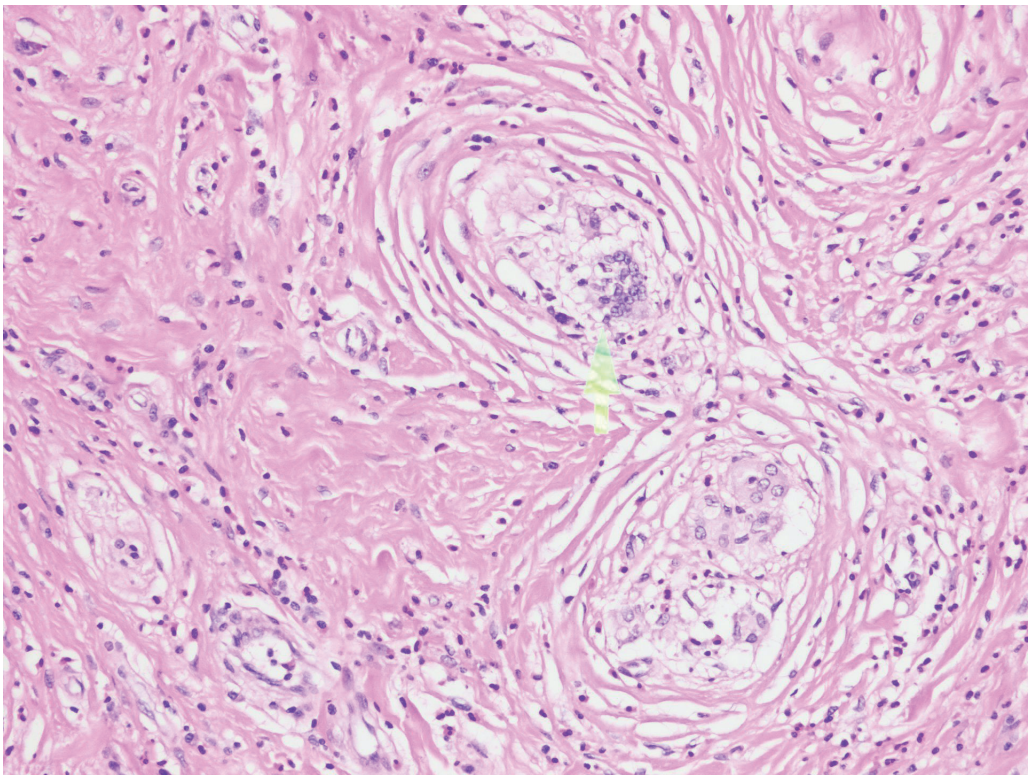

Figure 2. *Photomicrograph of mediastinal mass showing granulomas with giant cells (H&E stain, 20 × 10 magnification).*

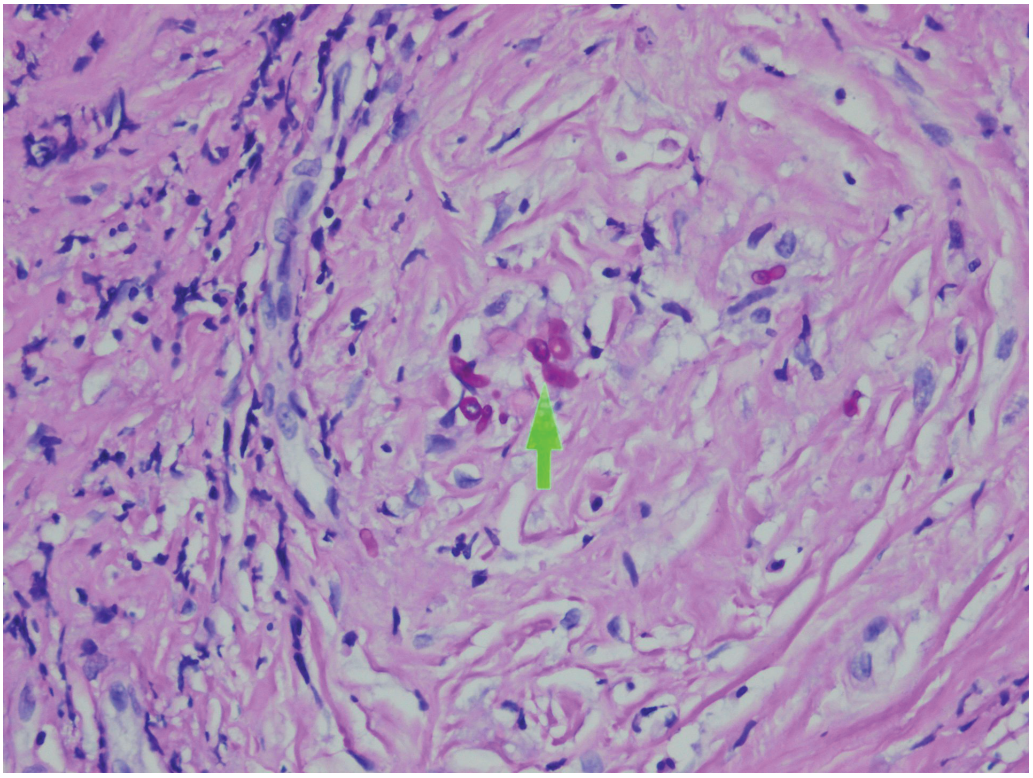

Figure 3. *Photomicrograph of mediastinal mass showing dark pink fungal organisms in the center of granulomas (PAS stain at 40 × 10 magnification).*

by sclerotic bodies in tissue and mycotic granules, respectively [11]. The dematiaceous fungi are known to cause localized and disseminated infections in immunocompromised and immunocompetent hosts [1-7]. In terms of pulmonary involvement, these molds are known to cause allergic fungal rhinosinusitis, bronchial asthma, hypersensitivity pneumonitis, allergic bronchopulmonary mycosis, and invasive pulmonary fungal disease [12].

Bipolaris is one of the genera of dematiaceous fungi with more than 45 species, and is generally a plant pathogen, but has been increasingly recognized to cause diseases in humans and animals [13]. It has fast-growing blackish-brown colonies with pseudo-septate, curved to canoe-shaped conidia, which germinate only from ends, hence named *Bipolaris* [13]. Previously, it was classified under *Drechslera* or *Helminthosporium* [1].

Fuste et al. [5] reported the first case of meningoencephalitis by *Bipolaris* in 1973. Subsequently, in 1982, Drouhet et al. [4] reported *Bipolaris* as a cause of Spondylodiscitis and prosthesis endocarditis. Over the years, there were multiple case reports of disseminated *Bipolaris* infection involving pulmonary and extrapulmonary sites in immunocompromised patients, but in 1993, Karim et al. [10] reported the first case of disseminated *Bipolaris* infection in an immunocompetent host, although he was on high doses of steroids for his asthma management, likely making him immunocompromised.

Our patient has no known immunodeficiency state with negative HIV serologies, normal immunoglobulin levels, and no prior use of immunomodulatory therapy for any indication. He had no extrathoracic involvement, but had an extensive thoracic disease with mediastinal lymphadenopathy, lung mass, and pleural involvement. To the best of our knowledge, there are no previous case reports of *Bipolaris* infection presenting as granulomatous pleuritis. Radiologically, there was thickened costal, diaphragmatic, and mediastinal pleura with lymphocytic exudative pleural effusion and negative pleural cultures. Histopathology showed granulomas with fungal elements. Granulomatous fungal pleuritis is rare and has been reported with histoplasmosis [14]. Worldwide, the most common cause of granulomatous pleuritis is tuberculosis (TB). In the case reported by Karim et al. [10], their patient had lung consolidation with exudative pleural fluid where sputum and pleural cultures later grew *Bipolaris*, making it a case of *Bipolaris* pneumonia and empyema.

Like other fungal infections, dematiaceous fungi have been reported to cause eosinophilia [10,15]. In our patient, the absolute eosinophil count was 3,200/mm^3, which responded to the treatment.

The clinical experience of treatment of these dematiaceous fungi including *Bipolaris* is based on case reports and case series. The European Society of Clinical Microbiology and Infectious Diseases Fungal Infection Study Group recommends treatment with amphotericin B or an azole. Posaconazole, itraconazole, and voriconazole have shown good treatment responses against *Bipolaris* species [1]. As adjunctive therapy, surgical intervention may be needed in some patients like in cases with endocarditis where prosthetic valve replacement is needed as a part of therapy [1]. In our case, at the time of VATS, the possibility of lymphoma was high, so no surgical debridement was attempted. Treatment outcomes are better in immunocompetent patients than patients with any form of immunodeficiency [15]. So far, our patient is responding well to itraconazole.

Conclusion

In a TB endemic country like ours where it is a common practice in rural settings to treat young immunocompetent patients of lymphocytic exudative pleural effusion as TB pleuritis without further investigations, this case highlights the rare cause of granulomatous pleuritis secondary to fungal infection in an immunocompetent host. It also emphasizes the growing evidence of infections by dematiaceous fungi in this population. Every possible effort should be made to reach the definitive diagnosis with appropriate investigations as early diagnosis and management lead to a good outcome.

What is new?

Bipolaris is a plant pathogen which is being increasingly recognized to cause disease in human hosts as well. Granulomatous pleuritis secondary to *Bipolaris* species has never been reported.

List of Abbreviations

ADA	Adenosine deaminase
AFB	acid-fast bacilli
BAL	Bronchoscopic lavage
HIV	Human immunodeficiency virus
MTB	Mycobacterium tuberculosis
ODI	Optical density index
PAS	Periodic acid Schiff
TB	Tuberculosis
VATS	video-assisted thoracoscopic surgery

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this case report.

Funding

None.

Consent for publication

Written informed consent of the patient was taken where he agreed to publish clinical details and was ensured complete anonymity.

Ethical approval

Ethical approval is not required at our institute for publication of an anonymous case report.

Author details

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Summary of the case

1	**Patient (gender, age)**	M, 32-year-old
2	**Final diagnosis**	
3	**Symptoms**	Low-grade fever, dry cough, mild dyspnea, and easy fatigability
4	**Medications**	Itraconazole
5	**Clinical procedure**	
6	**Specialty**	Infectious Diseases