

CASE REPORT

Disseminated *Penicillium Marneffe* Infection

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SUMMARY

This is a case report of disseminated *Penicillium marneffe* infection in a patient with leprosy, responding to antifungal therapy. Radiologically there were nodules in the left lung, right pleural effusion, lymphadenopathy in neck, mediastinum and upper abdomen and abscesses in the liver and right parietal lobe. This case highlights a rare infection in a non-HIV related immunocompromised patient, and its non-specific radiologic manifestations.

KEY WORDS:

Penicillium marneffe, Penicilliosis, leprosy, Disseminated, Antifungal

INTRODUCTION

Penicillium marneffe infection, generally referred to as Penicilliosis is an AIDs defining disease with a mortality of 75% if left untreated. The peak incidence occurred in the period from the year 1996 to 2000, which was about 10 years after the first case of human HIV infection. Although the threat of this fungus has greatly diminished in the advent of multidrug antiviral regimen, the disease is now being recognized more and more among non-HIV related immunocompromised patients. We report a case of disseminated *Penicillium marneffe* infection in a patient suffering from lepromatous leprosy with cutaneous, lung, liver, spleen, brain and generalized lymph nodes involvement.

CASE PRESENTATION

A 57 year old construction labourer presented to our center with complaints of intermittent fever episodes and progressive abdominal distension for the past two months. During the same duration he loss of 4kg of his weight and had loss of appetite for the past two weeks. He was diagnosed to suffer from Hansen's disease four years ago which was complicated by erythema nodosum leprosum and dapson-resistant *Mycobacterium leprae*. He had no high risk behaviour nor did he smoke or consume alcohol. He was dyspneic and there was palpable hepatosplenomegaly with jaundiced sclera and abdominal ascites. Other than generalized skin hyperpigmentation and oral ulcers, there were scaly erythematous papules seen on the right thigh and around the umbilicus.

Routine blood investigations revealed deranged liver function with severe hypoalbuminemia of 17g/L and anemia of 61g/L. Inflammatory markers such as erythrocyte sedimentation rate (ESR), C-reactive protein and serum ferritin were marked raised. He tested negative for anti-HIV antibody, hepatitis B

surface antigen and anti-hepatitis C antibody. Other than a weakly positive antinuclear factor, the rest of the connective tissue disease screening tests came up negative. Serial blood, peritoneal fluid and skin culture failed to identify any incriminating pathogen.

A whole body contrast enhanced computed tomography (CECT) revealed a 1cm lung nodule in the left upper lobe, right pleural effusion with precarinal, bilateral cervical and supraclavicular lymphadenopathy [Figure 1]. In the abdomen, a well demarcated hypodense lesion with an enhancing rim was seen in the caudate lobe of the liver in keeping with an abscess. There were multiple enlarged lymph nodes with low attenuation center seen in the para-aortic, paracaval and porta hepatis regions [Figure 2]. Several non-specific cystic lesions were seen in the liver, spleen, left adrenal gland and kidneys.

During his stay in the ward, he developed left upper arm motor weakness and left wrist drop. A focal area of deep white matter hypodensity in the right centrum semiovale without any noticeable contrast enhancement was detected following an urgent CECT of the brain. Magnetic resonance imaging (MRI) of this lesion revealed a ring enhancing lesion with extensive surrounding vasogenic oedema [Figure 3]. A strong lactate peak was seen in the spectroscopy interrogation of this lesion. Diffusion weighted imaging along with apparent diffusion coefficient (ADC) mapping were supportive of a brain abscess.

He subsequently underwent ultrasound guided liver biopsy which showed multiple granuloma formation with central necrosis. Grocott's silver (GMS) stain showed a fungal organism but Ziehl Neelsen stain was negative for acid fast bacilli. Microscopic histopathological examination of subsequent skin biopsy described the presence of *Penicillium marneffe* infection. A second confirmatory evidence was garnered from a sessile colonic polyp during colonoscopy examination one week later.

Remarkably our patient made a complete recovery with resolution of the radiological findings [Figure 4] after two weeks of intravenous amphotericin B followed by ten weeks of oral itraconazole. Later immunological studies pointed to a low CD4 count of 216/uL with a CD4/CD8 ratio of only 0.36, suggestive of primary CD4 cell lymphopenic immunodeficiency disorder.

DISCUSSION

Penicillium marneffe is a dimorphic fungus endemic in the tropical Southeast Asia, not very dissimilar to *Histoplasmosis*

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Fig. 1: Axial computed tomography (CT) in lung window showing left upper lobe nodule (arrow A) and right pleural effusion (arrow B).



Fig. 2: CECT of the abdomen shown in axial plane at the level of the celiac trunk demonstrating a hypodense lesion in keeping with an abscess in the caudate lobe of the liver (arrow A) and enlarged necrotic lymph nodes in the porta hepatis around the pancreatic head (arrow B).



Fig. 3: Post gadolinium DTPA enhanced MRI of the brain showed a ring enhancing lesion (arrow A) with perilesional white matter oedema in the right parietal lobe typical of cerebral abscess.

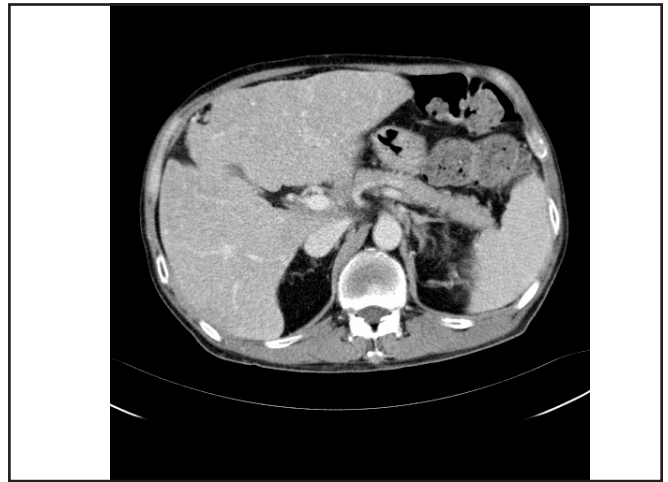


Fig. 4: CECT showed resolution of the liver abscess, lymphadenopathy and right pleural effusion.

capsulatum which is commonly found in the temperate climate. It is closely related to the bamboo rat and has been isolated from tissue specimens and also from the soil taken from the rat's burrow. The potential of this fungus to cause systemic mycosis or penicilliosis was first recognized in 1973 and has been described mainly among the immunocompromised, the vast majority of which are comprised of AIDS patients. In fact, the prevalence of penicilliosis follows closely the rise and fall of the Human Immunodeficiency Virus (HIV) transmission rate. Other associated predisposing conditions include Hodgkin's disease, leukemia, systemic lupus erythromatosis (SLE), corticosteroid or immunosuppressive therapy. The discovery of CD4 lymphopenia in our patient would most likely explain why he had contracted the *Mycobacterium leprae* and subsequently developed the disseminated form of this opportunistic infection.

The clinical signs and symptoms of our patient, i.e. prolonged fever, lost of weight and appetite, jaundice, skin lesions, abdominal lymphadenopathy, anemia, hepatosplenomegaly, pleural effusion and ascites secondary to hypoalbuminemia, although widely described in many case series, are nonspecific for penicilliosis. The most common infection to resemble this clinical picture is none other than histoplasmosis¹. Abdominal pain and hyperbilirubinemia is reported to be more common in penicilliosis whereas lymphadenopathy and hypotension in histoplasmosis. Although umbilicated papules are regarded to be characteristic of the former and erythematous plaques in the latter, none is pathognomonic. Bone and joint involvement have also been reported but these were not present in our patient. tuberculosis, cryptococcosis and blastomycosis are other possible but less likely candidates.

Chest radiographs can be normal in 78% of patient with penicilliosis. The most common findings are non-specific interstitial infiltration followed by pleural effusion and alveolar or interstitial infiltration seen as reticulonodular shadowing or frank consolidation. Cavitations and miliary disease are uncommon². Solitary lung nodules and lung masses mimicking carcinoma have also been reported. Common chest symptoms reflecting such findings are coughing and shortness of breath. Nevertheless we have to recognize that these symptoms can be caused by superimposed or co-infection. *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, *Mycobacterium tuberculosis*, *Cryptococcus neoformans*, and *Strongyloides stercoralis* have all been previously cultured from sputum or bronchoalveolar lavage. Multiple tissue organ involvement is well known in disseminated form of penicilliosis. In the event that tissue biopsy is not obtainable, empirical response to anti-fungal therapy would have strongly exclude malignancy as is the case in our patient.

Systemic infections among HIV positive patients in endemic areas of Northeastern India and Thailand did not demonstrate predilection for central nervous system (CNS). Involvement of the CNS is rare and often herald grave prognosis. Hematogenous route is the commonest method of spread. Out of the previously reported four cases of dissemination to the brain, the only one who survived had direct extension from a primary orbital-sinus infection³. These patients usually have focal neurological deficits depending on the region of the brain that is affected. Our patient had a stroke-like motor deficit of the left upper limb. Some may present with aphasia or hemiparesis. Surprisingly these CNS disseminations occurred in patients who had tested negative for HIV such as in our patient.

CONCLUSION

Clinical presentation of *Penicilliosis marneffeii* is remarkably similar to infection caused by *Histoplasma capsulatum* as well as their radiological features. These patients would usually be put through all kinds of tests and investigations before a diagnosis is reached. More often than not, the correct identification of the offending microorganism cannot be ascertained. *Penicillium marneffeii* is mainly differentiated from *Histoplasma capsulatum* by histopathological examination and culture. Immunological tests are still not widely used and the cost of PCR is prohibitive especially in developing countries. Dissemination to the CNS in the form of brain abscesses posts a real danger to HIV-negative immunocompromised patients. Although previous treatment result has been daunting, our case report demonstrated that early clinical and radiological diagnosis coupled with timely anti-fungal therapy can prove to be lifesaving.

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