CASE REPORT

Invasive aspergillosis presenting as an intracardiac mass in an immunocompetent host

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SUMMARY

Invasive aspergillosis is a severe fungal infection that primarily affects immunocompromised patients. We report a case of invasive aspergillosis presenting as a febrile respiratory infection with a cardiac mass in an immunocompetent patient. Excision of the intracardiac mass followed by histopathological examination confirmed the diagnosis. The patient was managed with voriconazole, to which he responded well. Rare occurrence of an intracardiac mass with systemic aspergillosis in an immunocompetent host is discussed in this case report.

BACKGROUND

Aspergillus fumigatus is a common pathogen in human airways and causes various diseases ranging from mild hypersensitivity reactions to more severe invasive disease that is rapidly progressive and carries 50% mortality despite treatment.¹ Disease normally occurs in immunocompromised hosts, however, immunocompetent patients may, rarely, develop invasive aspergillosis.^{2–3} Cardiac involvement is seen in only 0.7–6% of high-risk patients with invasive aspergillosis and may have a variable clinical presentation.^{4–5–7} Invasive aspergillosis should be considered in the differential diagnosis of an otherwise undiagnosed culture-negative invasive febrile respiratory illness.¹ Histopathological examination along with microbiological confirmation remains the gold standard in diagnosis.¹ The fastidious nature of aspergillus may delay the diagnosis on culture, hence early attempts to establish a tissue diagnosis should be made. Assays estimating the components of the fungal cell wall may assist in establishing diagnosis of invasive aspergillosis.^{8–9} Appropriate antifungal therapy when administered early in the illness may cure the disease. We report a case of invasive aspergillosis presenting as a febrile respiratory infection with a cardiac mass in an immunocompetent patient.

CASE PRESENTATION

A 22-year-old man presented with a history of low-grade fever of 15 days duration associated with anorexia and weight loss of 5 kg over a period of 1 month. There was no history of pre-existing comorbidities. He denied a history of contact with patients having tuberculosis. He did not have any risk factors for HIV infection such as history of promiscuous behaviour or intravenous drug abuse. Clinical examination revealed a thin built male with a body mass index of 19 kg/m². There was neither pallor, icterus nor lymphadenopathy. There

were no stigmata to suggest tuberculosis or HIV infection. Systemic examination revealed a few scattered coarse crepitations in the right apical and interscapular regions with normal breath sounds. Examination of the other systems was unremarkable.

INVESTIGATIONS

Investigations revealed haemoglobin of 11.6 g/dL, total leucocyte count of 21 600/μL, with 30% eosinophils, and a total eosinophil count of 6500/μL. The biochemical profile was normal. Chest X-ray revealed non-homogenous opacity in the right upper zone. Ultrasound of the abdomen was normal. Blood, sputum and urine cultures were negative.

CT scan of the chest showed centrilobular nodules with a 'tree in bud' appearance along with septal thickening in the apical segment in right upper, middle and lower lobes. Sputum for acid fast bacillus (AFB) was negative. The patient was evaluated for eosinophilia. Peripheral blood smear did not show any abnormal cells. Stool test for the spores and ova of parasites was negative on multiple occasions. Bone marrow aspirate showed increased precursor cells and mature eosinophils, however, bone marrow biopsy was normal. PDGFRA gene rearrangement, performed to rule out hyper-eosinophilic syndrome, was negative. Bronchoalveolar lavage was negative for AFB, fungal hyphae and eosinophils. Transbronchial lung biopsy was carried out, which showed necrotic tissue and inflammatory exudates.

Echocardiography showed a large intracardiac mass measuring 3.38 cm² protruding from the left ventricular outflow tract (LVOT) into the aorta (figure 1). The mass was homogenous in echotexture, had smooth margins and was freely mobile. Overall biventricular function was normal with no regional wall motion abnormality. Right ventricular systolic pressure was 36 mm Hg+right atrial pressure. There was no vegetation noted in any of the cardiac valves.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis in a 22-year-old man who presents with fever and weight loss, and is detected to have eosinophilia along with centrilobular nodules on CT scan and cardiac mass on echocardiography, includes invasive aspergillosis, lymphoma and carcinoma lung. The differential diagnosis for eosinophilia includes parasitic infections, allergy, drug reactions, sarcoidosis, collagen vascular disorders, hypereosinophilic syndrome and eosinophilic leukaemia.

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Figure 1 Echocardiogram showing a mass lesion (white arrow) protruding into the left ventricular outflow tract in parasternal long axis view (A) and five chamber view (B).

TREATMENT

After detection of the cardiac mass on echocardiography, the patient was referred for surgical excision of the mass due to its high risk of embolisation. Intraoperative findings revealed a 2×2 cm firm friable lobulated mass in the LVOT, adherent to the interventricular septum, with an overlying thrombus. The aortic and mitral valves were normal. The mass was excised in totality and sent for histopathological examination, which revealed muscle fibres, fibrocollagenous tissue and foreign body giant cells along with numerous fungal hyphae. H&E and Grocott's stain highlighted these fungal hyphae, which were septate, and showed acute angle branching, suggestive of aspergillosis (figure 2).

Galactomannan assay performed for confirmation of diagnosis of aspergillosis was positive. On the basis of the histopathological findings, the patient was started on intravenous voriconazole at a dosage of 6 mg/kg twice daily on day 1 followed by 4 mg/kg/day. After 7 days, he was switched over to oral voriconazole 200 mg twice daily.

OUTCOME AND FOLLOW-UP

The patient recovered well after the surgery. He became afebrile within 2 weeks of starting treatment with voriconazole. He has completed 3 months of voriconazole and is planned for a total

of 6 months of therapy. He has gained 10 kg weight in the past 3 months. Review at 3 months revealed normal echocardiography with no evidence of a mass lesion in the LVOT. A repeat CT scan has shown regression of the previously recorded lesions.

DISCUSSION

A high index of suspicion in otherwise undiagnosed culture-negative invasive febrile respiratory illness with eosinophilia led to the diagnosis of invasive aspergillosis in this case, which was confirmed by histopathological examination. Aspergillosis in immunocompetent patients is rare. However, these patients may, as in the present case, following massive exposure to spores, develop invasive pulmonary aspergillosis leading to eosinophilia along with suppurative necrotising granulomas mimicking tuberculosis.^{1–3}

Only 0.7–6% of patients with invasive aspergillosis have cardiac involvement.^{4–6} Risk factors for developing fungal (including aspergillus species) endocarditis include prior cardiac valve surgery, antibiotic use, major non-cardiac surgery and rheumatic heart disease,⁶ while 2% of patients may not have any identifiable risk factors.⁶ Patients with aspergillus endocarditis present with a variety of signs and symptoms, most commonly fever, changing or new heart murmurs, peripheral

Figure 2 Histopathology of the left ventricular mass stained with H&E stain showing necrotic tissue (white arrow), fungal hyphae (black arrow) and giant cell reaction to fungus (yellow arrow) at low power (A) and high power (B and C). Grocott's methenamine silver stain of the mass showing fungal hyphae in black with septae and acute angle branching (black arrow) (D).

embolisation, focal or generalised neurological signs, heart failure and dyspnoea. Classic signs of infective endocarditis, such as splinter haemorrhages or Osler's nodes, are rarely noted.⁶

Histopathological examination with microbiological confirmation remains the gold standard for diagnosis.¹ Blood culture for aspergillus is rarely positive, and sputum culture is of limited value due to lack of sensitivity and a prolonged incubation period; especially in the setting of an immunocompetent host.^{1–3} Diagnosis, as in our case, rests mainly on histopathological findings of characteristic septated hyaline hyphae with acute angle (45°) dichotomous branching visible with H&E or Grocott's methenamine silver staining.⁹ In some cases where it is not feasible to obtain a biopsy specimen, assays to detect components of the fungal cell wall (galactomannan (GMA) and β -(1,3)-d-glucan (BDG)) may be of help.⁹ These assays carry a sensitivity of 71% and specificity of 89%. The sensitivity of GMA is very low in immunocompetent patients or in non-invasive aspergillus infection.^{2–9} In our case, although aspergillus invaded the blood vessel and the disease was progressive, GMA was negative probably due to low sensitivity of the test and normal host immunity.

Treatment of invasive aspergillosis requires early initiation of antifungal therapy. Primary treatment with antifungal therapy is recommended with voriconazole in a dose of 4 mg/kg.^{1–3} Liposomal amphotericin is considered as an alternative to voriconazole.

Other agents, such as itraconazole, caspofungin, posaconazole and micafungin, can be considered for salvage therapy. Combination therapy is used in patients not responding to single drug therapy. Surgical resection of aspergillus-infected tissue is useful for lesions that are contiguous to great vessels or pericardium. Rapid aggressive medical and surgical intervention is recommended in patients with cardiac involvement in invasive aspergillosis.^{4–6} Duration of antifungal therapy is highly variable and should be individualised as per the clinical scenario, lasting from 3 months to 1 year. Our case was treated as per current guidelines with voriconazole. Surgical excision of the mass was considered mandatory as it was a large mobile mass in the LVOT, with high risk of systemic embolisation.

High index of clinical suspicion coupled with steps to establish tissue diagnosis leads to prompt diagnosis of invasive aspergillosis. Timely institution of appropriate antifungal therapy may cure the disease.

Contributors NB and DC were involved in the diagnosis and management of the patient. DC, PH and HSA assisted in management of the patient and manuscript preparation.

Competing interests None declared.

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Learning points

- Invasive aspergillosis should be considered in the differential diagnosis of an otherwise undiagnosed culture-negative invasive febrile illness.
- Echocardiography may be a useful tool to pick up cardiac mass lesions in patients with undiagnosed febrile illness involving the respiratory tract.
- The fastidious nature of aspergillus may delay the diagnosis on culture, hence early attempts to establish a tissue diagnosis should be made and appropriate antifungal therapy administered early in the illness.
- Medical therapy with antifungal drugs remains the mainstay of treatment, however, a surgical option needs to be exercised in a few cases.

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