CASE REPORT

Systemic aspergilloma post aortic root surgery following coronary artery stenting: diagnostic and management dilemma

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SUMMARY

Aspergillus infections such as *Aspergillus endocarditis* were once relatively rare occurrences, however, due to the increased use of intracardiac devices, the incidence has grown. With mortality rates close to 100%, in medically treated cases, it is paramount that early diagnosis and treatment are performed. An immunocompetent aviculturist presented 8 months post aortic root replacement for severe aortic regurgitation with a composite graft, with central crushing chest pain. Investigations confirmed ST elevation inferior myocardial infarction due to stenosis of the origin of the right coronary artery, which was stented. Echocardiogram demonstrated a mobile mass posterior to the left ventricular outflow tract. Following referral to our cardiothoracic surgeons, a polypoidal mass covering the right ostial button was noted along with systemic complications of the disease. Emergency redo aortic valve replacement with a homograft and coronary artery bypass was performed. Histological analysis confirmed *A. fumigatus* and the patient was started on intravenous voriconazole.

BACKGROUND

Although the incidence of *Aspergillus* infections is relatively rare in the literature, typical presenting features of infective endocarditis are well documented; however, this unique case demonstrates the vague nature of the disease's presentation, which can create a major challenge to clinicians.

Raising awareness of *Aspergillus endocarditis* (AE) is crucial as the effect of delaying medical and surgical management can have profound effects on patient morbidity and mortality. Therefore, it is important to note that AE should be a potential differential diagnosis in all patients who present with cardiac symptoms postcardiac surgery, in particular those patients with intracardiac devices.

A review of the literature on AE was performed to further delineate the presenting features and complications of the disease, and possible management options in these cases.

This unique case highlights the successful treatment of a patient with AE with both surgical and medical management, despite a delay in diagnosis. The need for a more accurate diagnostic test is required in order to reduce the severe complications of the disease, which were also noted in this case.

CASE PRESENTATION

An immunocompetent 34-year-old man, an aviculturist with a long history of poorly controlled hypertension, presented to our cardiology clinic with progressive dyspnoea and flu-like symptoms. Severe aortic regurgitation was incidentally found on examination and this, along with a dilated ascending aorta (4.8 cm), was confirmed on echocardiogram. Subsequently, the patient underwent an elective aortic root replacement with a composite graft. Despite the intraoperative complexities the patient made an excellent recovery without any cardiothoracic surgical complications.

Eight months postoperative, the patient was readmitted to hospital with central crushing chest pain and dyspnoea, which was eased with rest. ECG had ST elevation consistent with an inferior myocardial infarction. Transoesophageal echocardiogram revealed a tiny mobile mass posterior to the left ventricular outflow tract; however, no obvious vegetations were seen. Coronary angiogram demonstrated severe stenosis at the origin of the right coronary artery, which was subsequently stented. In spite of spiking temperatures, and a persistently raised white cell count and C reactive protein, blood cultures remained negative. Postangiogram, the patient developed left hemianopia and inattention deficit.

Further investigations, including a full body CT scan, showed a polypoidal mass growing intraluminally involving the right coronary ostial button along with multiple cerebral abscesses and a large splenic abscess. The patient resultantly had emergency redo aortic root replacement with a homograft and a coronary artery bypass graft ×1. Intraoperatively, it was noted that the right coronary ostial button was destroyed by the *Aspergillus* infection, therefore the artery was debrided to healthy tissue and bypass grafting using the right internal mammary artery was performed. The operation was surgically challenging, with dense adhesions of the pericardium and myocardium requiring extensive dissection. Additionally, substantial debridement of the aortic root and coronary ostia was also required, resulting in a total bypass time of 477 min and cross-clamp time of 263 min. Once dissected, the aorta was opened and the fungating mass from the origin of the right coronary artery was detached. The previous prosthetic valve was then explanted, after a thorough debridement and washout with normal saline, and a new homograft

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inserted with the distal end being anastomosed to the ascending aorta.

Postoperatively, the patient required a brief period of circulatory support in the form of intra-aortic balloon pump and inotropes for low cardiac output syndrome, however, they were successfully weaned off within 48 h.

Histological analysis confirmed that the mass contained *A. fumigatus*. The patient was started on intravenous voriconazole 400 mg two times per day to treat the systemic aspergillosis, which was changed to oral when tolerated.

OUTCOME AND FOLLOW-UP

Postoperative, the patient underwent procedures to address the systemic complications of the fungal infection, such as a splenectomy for the splenic abscess (figures 1 and 2) and required renal replacement therapy with dialysis for acute renal failure. Furthermore, the patient reported painful loss of vision in the right eye, which was diagnosed as severe aspergilloma endophthalmitis. In spite of conservative measures to treat the inflammation, the patient ultimately requested an evisceration.

With reference to our intriguing case, it is important to recognise that our patient was immunocompetent and initially presented with symptoms that would not necessarily indicate a diagnosis of infective endocarditis, let alone AE. In spite of thorough clinical examination and several investigations, it was still increasingly difficult to make the diagnosis of AE, which led to a delay in management. Major septic emboli were evident in our case, with the patient suffering multiple end-organ damage, leading to significant effects on the patient's morbidity. In retrospect, after clinically evaluating the case, it is believed that some of these major embolic events may have been secondary to the coronary artery angiography and stenting that was initially undertaken. Perhaps an improved strategy would involve performing the full body CT scan first and proceeding directly to emergency aortic root surgery instead of coronary angiography, potentially reducing the systemic complications in this case.

However, in spite of these complications, the patient was successfully treated for the infection and remained in remission on oral voriconazole 200 mg two times per day and erythromycin 250 mg three times per day for 1 year postoperative.

Lifelong antifungal prophylaxis was considered in this patient to prevent further long-term complications, however, after 1 year of treatment it was decided not to continue with

Figure 1 Histological specimen of the patient's spleen following splenectomy, demonstrating an area of acute inflammation and necrosis with fungal hyphae (H&E stain, ×200).

Figure 2 Grocott stain of splenic tissue showing the *Aspergillus*-type fungal hyphae (×400).

prophylaxis. Seven and a half years of follow-up have shown no signs of progression of the cerebral emboli or neurological deficit. There have since been no further cardiac complications to the disease.

DISCUSSION

For many years, *Aspergillus* infections were a relatively uncommon phenomena, but they are now becoming a regular occurrence in the hospital setting.¹ First described by Micheli in 1729, the *Aspergillus*, found in soil, is a universal airborne saprophytic fungus the conidia of which are inhaled by humans and animals. Usually, these spores are efficiently removed by the innate immune system, but they can potentially be sources of morbidity to select patients.² This fungus has the ability to create severe invasive infections in most body systems, as demonstrated in our unique case.³ With mortality rates close to 100% in medically treated cases, the diagnosis and prompt treatment of these patients is critical.¹

The increased incidence of *Aspergillus* infections, particularly AE, is primarily due to the increasing use of intracardiac devices.^{1 3} Fungal endocarditis occurs in approximately 0.1% of prosthetic devices, with *Aspergillus* contributing to approximately 20–30% of these cases, as *Candida* remains the most common cause with a ratio of 1:2.^{1 3 4} Of the *Aspergillus* spp, the majority of cases are due to *A. fumigatus* (60–90%) followed by *A. terreus* (5–20%), with *A. niger*, *A. flavus* and *A. nidus* contributing in much smaller proportions.¹

Multiple risk factors increase the likelihood of developing AE in patients with intracardiac devices. The most significant is being an immunocompromised patient, however, it is important to recognise that the infection can also occur in immunocompetent patients, such as in our case. Previous valvular surgery is another major risk factor and is consistent with up to 50% of reported cases. Additional risk factors include being male in the third and fourth decade of life, valvular abnormalities, history of intravenous drug use, prolonged central venous catheters and previous cardiac surgery.^{1 5}

Once a susceptible host has been exposed to *Aspergillus*, usually intraoperatively, the organism binds to the damaged/prosthetic valve via seeding of the airborne conidia. *A. fumigatus* is the predominant species, as it has a tendency to bind more efficiently than the others.⁶ Moreover, these species are particularly unique, having their own defensive mechanisms to protect themselves from phagocytosis by secreting toxic

metabolites.⁷ Although operative theatres are vigorously cleansed, the airborne nature of the species makes it increasingly difficult to prevent patient exposure during cardiac surgery. Many new and existing cardiac theatres contain high efficiency particulate air filtration systems with laminar flow designed to reduce the number of particles circulating intraoperatively, which has had a significant reduction on incidence, particularly in epidemic regions.⁸

Clinical presentation for AE can be quite nebulous due to a large variety of presenting features. Typically, infective endocarditis presents with fever, changing heart murmurs and stigmata of major emboli, which are also the most common presenting features of AE. Additionally, the period between the time of valve replacement and infection is extremely variable (1–24 years), therefore making diagnosis increasingly difficult.¹ In our case, the patient reported chest pain and dyspnoea 8 months postoperative, which are relatively rare initial presenting features. These symptoms are attributed to the unique growth of the mass leading to severe stenosis at the origin of the right coronary artery, precipitating the patient's presentation. It is also important to note that fever was not an initial symptom in this case. In a literature review on presenting features of 60 patients with AE, only 10% of patients presented with chest pain, demonstrating the subtlety of the infection.³ Therefore, thorough history taking and examination are paramount in suspicious cases.

Major septic emboli are the most significant complication in AE and can also be the initial presenting feature in vague cases. Embolisation can occur to any part of the body, such as the limbs, brain, lung, spleen, eyes and kidneys, thus increasing the chances of the disease mimicking other pathological conditions.¹ Generally, patients present with evidence of multiple septic emboli, such as in our case, leading to significant effects to patient morbidity. Ocular complications such as *Aspergillus* endophthalmitis can be highly debilitating to patients, leading to sudden visual loss, such as in this case.⁹

Diagnosis of AE presents a major challenge to clinicians. As portrayed earlier, the disease can present in multiple formats and at different time periods postoperative. Therefore, the diagnosis is primarily based on high clinical suspicion based on thorough history taking and examination.³ The gold standard in the diagnosis of infective endocarditis is by histological examination of the embolic tissue; however, this is extremely invasive and impractical in formulating a diagnosis.¹⁰ The modified Duke criteria presents a useful tool in diagnosing bacterial endocarditis, but has a heavy influence on microbiological indices. In AE, cultures are nearly always negative, with figures above 90%, therefore, this decreases the criteria's reliability.^{1 3 10} In spite of the negative blood cultures, our patient demonstrated one major and two minor criteria, suggesting that infective endocarditis was likely to be present. Unfortunately, this is not always evident with AE, leading to delays in diagnosis and potentially increasing morbidity/mortality to patients.

It is clear that a more accurate serological test is required in the diagnosis of AE. Non-invasive methods have been attempted, ranging from immunohistological techniques to molecular techniques such as the use of PCR.¹⁰ Although these techniques are not yet widely used, it is believed that they are more sensitive than traditional microbiological methods and are potentially the optimal solution for this diagnostic dilemma.¹¹

Management has always proved to be extremely challenging due to the precarious nature of the infection and its complications. Medical treatment alone has dismal results with mortality rates over 95%. Traditionally, the disease has been treated with

a combination of medical and surgical management, but mortality rates still remain very high.^{1 3 12} The British Society of Antimicrobial Chemotherapy's guidelines on AE recommend that initial treatment should be with voriconazole, a broad-spectrum tri-azole antifungal agent. It is obligatory that this is followed by radical surgical debridement of the necrotic tissue and vegetative mass with homograft valve replacement.¹²

While on voriconazole, it is essential that confirmation of the susceptibility of the agent and therapeutic drug monitoring is performed.¹² Research suggests that optimal plasma concentrations of voriconazole are required to treat the fungus, prevent resistance, and reduce drug-related side effects such as toxic epidermal necrolysis and photosensitivity.^{12 13} Regardless of neoadjuvant treatment, surgical procedures remain high risk with poor outcomes. Usually, once patients reach this stage they have advanced disease with major embolic complications. Prognosis is poor, as the reoccurrence rate of AE remains high regardless of long-term antifungal prophylaxis, with some papers suggesting intermediate mortality rates of 50%.¹² However, this number may be due to the immunocompromised nature of the host, thus increasing risk of mortality regardless of the AE complications.³

For those experiencing similar diagnostic dilemmas, it is paramount to consider the diagnosis of AE in patients with vague clinical features and negative blood cultures who have a history of cardiac operations. As demonstrated in our case, time is of the essence, therefore, in these individuals, radiological and cardiac investigations are required. Early cardiothoracic input should be obtained, as this may potentially reduce the risk of systemic complications. Additionally, it is important to be aware that coronary angiography can in fact exacerbate the embolic events, as was exhibited in our case.

Learning points

- ▶ Owing to the nebulous nature of its presentation, it is important to suspect *Aspergillus endocarditis* (AE) in immunosuppressed and immunocompetent patients with evidence of fever and vegetations on echocardiogram, in spite of negative blood cultures. This should be suspected more so in operated cardiac patients.
- ▶ There is a need for further research into non-invasive diagnostic techniques such as PCR, as it will inevitably assist with an early diagnosis of AE and its subsequent management.
- ▶ AE is usually associated with a poor prognosis, but this can be reduced with early detection and prompt medical and surgical treatment followed by antifungal prophylaxis.

Competing interests None declared.

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