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Case Report

Co-infection with bacterial and fungal endocarditis at scar tissue in an immunocompromised patient

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ABSTRACT

We present the case of a 65-year-old immunocompromised male with a history of kidney transplantation, diabetes, coronary artery bypass, and cardiac resynchronization therapy device implantation who was finally diagnosed with an unusual form of infective endocarditis due to co-infection of fungal and bacterial pathogens. He was afebrile at the time of admission and presented with decompensated heart failure and pneumonia. A spleen abscess was discovered incidentally and prompted us to search for a cardiac source of emboli. Culture of the suppurative fluid drained percutaneously from the abscess was positive for *Enterococcus* and *Aspergillus* species. Transthoracic and transesophageal echocardiography revealed a mobile vegetation attached to the scarred myocardium of anterior septum — an unusual location for intracardiac vegetations. With regard to the prohibitive risk for redo surgery, the patient was managed medically with broad spectrum antimicrobial therapy. Finally, the patient died with severe sepsis.

<**Learning objective:** Immunocompromised patients are at risk of opportunistic infections such as fungal endocarditis. Co-infection of fungal and bacterial pathogens is very rare. Early diagnosis of such infections needs a high level of clinical suspicion due to its non-specific presentations and culture negative essence. Many patients are afebrile during the disease course. Fungal endocarditis is characterized by large vegetations highly prone to systemic embolization even in the early stages of infection. Mortality is high despite optimal antimicrobial and timely surgery.>

Introduction

Infective endocarditis (IE) is a life-threatening infection involving the cardiovascular system. The numbers of immunocompromised patients especially organ-transplant recipients are rapidly rising. Diagnosis of IE in these patients may be challenging because they may be culture-negative and usually show unusual presentations of this disease. Herein we describe a case of fungal endocarditis (FE) with an unusual intracardiac location of the vegetation on scarred myocardial tissue that resulted in septic embolization to the spleen in an immunosuppressed patient who had received a kidney transplant recently before the presentation.

Case report

The patient was a 65-year-old diabetic male under insulin therapy with a history of coronary artery bypass (CABG) and cardiac resynchronization therapy with an implantable cardioverter defibrillator (CRT-D) 7 and 5 years ago, respectively. He underwent renal transplantation 4 months before presentation following a diagnosis of end-stage renal disease (ESRD) and he was under immunosuppressive therapy with mycophenolate, cyclosporine, and prednisolone. The patient presented with progressive dyspnea and lower limb edema accompanied with malaise. On physical examination, the patient appeared ill and pale. He was afebrile with stable vital signs. We noticed irregular heat sounds (due to atrial fibrillation) with no

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audible murmur, fine rales at the base of lungs with diminished breath sounds of the right lung, and 3+ pitting edema of lower extremities. He was admitted with the initial impression of decompensated heart failure (DHF) and pneumonia. The initial laboratory results showed a white blood cell count of 18×10^9/L and hemoglobin level of 9.8 g/dl. Chest computed tomography (CT) revealed a massive right-sided pleural effusion. By pleural tap, 400 cc exudative fluid was removed and was sent for smear, culture, and cytologic analysis which were all negative. Parenteral antibiotic therapy for treatment of pneumonia was started with ciprofloxacin, meropenem, and vancomycin. The control chest CT showed mild residual right-sided pleural effusion, paratracheal lymphadenopathy (Fig. 1A) a lobulated lung nodule in the pulmonary right upper lobe with air bronchogram compatible with pneumonia (Fig. 1B). Patchy consolidation opacities were detected in the right middle and lower lobes (Fig. 1C). An incidental finding in this CT was a fluid density cystic lesion noted in lower aspect of the spleen suggestive of abscess formation with perisplenic fluid collection (Fig. 1D). Due to poor clinical condition, the patient was not suitable for surgical splenectomy and alternatively he underwent ultrasound-guided percutaneous drainage of the spleen abscess and perisplenic collection. About 200 cc of a turbid suppurative fluid was drained and sent for smear and culture and grew *Aspergillus fumigatus* and vancomycin-resistant *Enterococcus* (Fig. 2). The blood culture simultaneously obtained was negative for any organism. Subsequently, the antibiotic regimen was changed to a combination of caspofungin, voriconazole, ampicillin-sulbactam, and linezolid. A transthoracic echocardiography was requested to explore a potential cardiac source of emboli which showed severe left ventricular enlargement and systolic dysfunction with left ventricular ejection fraction of 25–30%. Regional wall motion abnormality was detected in both anterior and posterior circulation territory with scar tissue in some segments. There was a moderate size (1×0.5 cm) tissue texture mobile mass with well-defined margins and a narrow stalk superimposed on the scar tissue of the mid portion of anterior septum which was suggestive of a vegetation based on the clinical data (Fig. 3A, Video 1). The mass was further appreciated with two- and three-dimensional transesophageal echocardiography (Fig. 3 B and C, Video 2 and 3). No valvular abnormality was detected. Based on modified Duke criteria [1], the patient had one major criterion (an oscillating intracardiac mass) and two minor criteria (predisposition, embolic splenic abscess formation) which gave rise to possible diagnosis of IE. Initially after changing the antibiotic regimen the patient experienced improved clinical status but thereafter the clinical course became complicated for development of severe sepsis, loss of consciousness, and progressive thrombocytopenia. Finally, the patient died one month after the admission date.

Discussion

We report a complicated case of FE with septic embolization to the spleen in an immunosuppressed 65-year-old diabetic male with a recent history of successful renal transplantation. His medical history was also remarkable for previous CABG and CRT implantation. Special aspects of this case were as follows:

1. The nonspecific presentation of the patient which could not point to a specific diagnosis of IE: He was afebrile at the time of admission and throughout the hospital stay. He was admitted with an initial diagnosis of DHF and pneumonia. The spleen

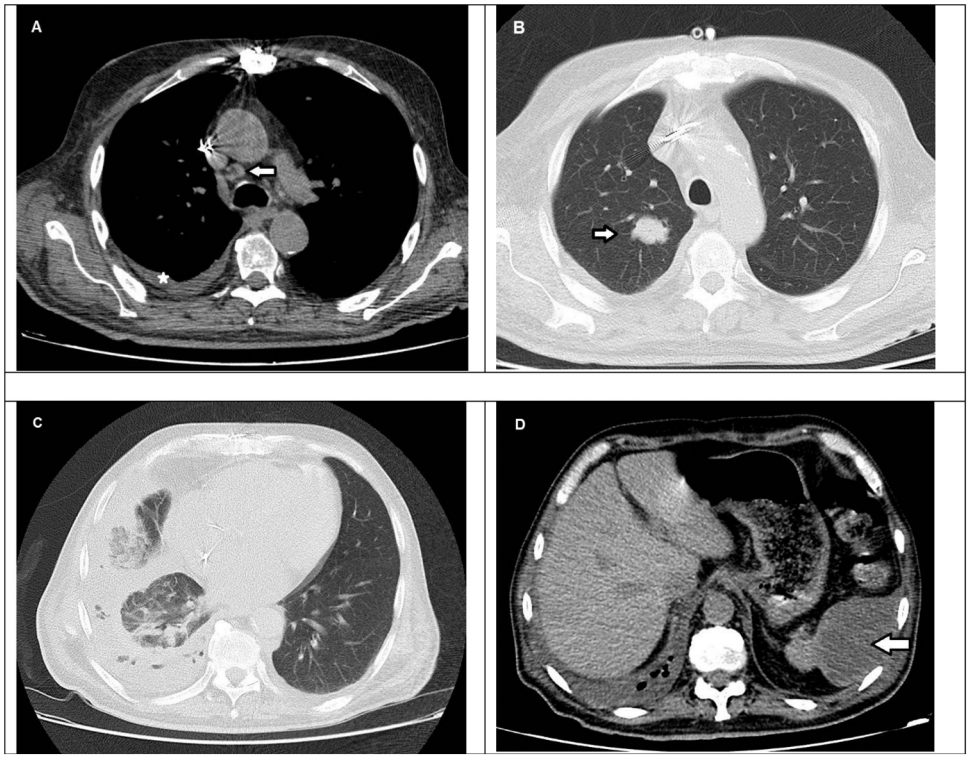

Fig. 1. (A) Computed tomography mediastinal window of thorax shows an enlarged lymph node in pretracheal region (arrow). Also effects of previous sternotomy and pace leads are visible. Mild pleural effusion is seen in right side (star). (B) An approximately 25-mm lobulated nodule in pulmonary right upper lobe (arrow). It has a few internal air bubbles (not shown) suggestive of air bronchogram of an air space nodule. (C) In lower thoracic sections hydropneumothorax is seen in right side with extension to the major fissure. Ground glass and patchy consolidation opacities are present in the right middle and lower lobes. (D) In upper abdominal sections a fluid density cystic lesion is noted in lower aspect of spleen (arrow) which proved to be an abscess after aspiration of its contents. Right side hydropneumothorax is also visible.

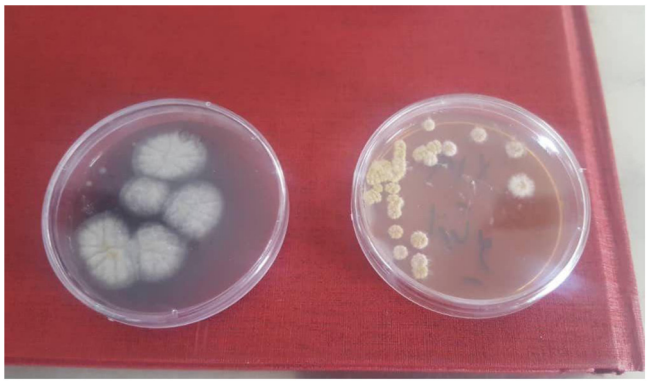

Fig. 2. Cultures of the fluid drained from the spleen abscess showed growth of two different organisms: the left culture positive for *Aspergillus* and the right one positive for *Enterococci*.

abscess was discovered incidentally and eventually changed the diagnostic pathway.
2. The unusual location of the intracardiac vegetation.
3. The co-infection of *A. fumigatus* and *Enterococcus.*

In the modern era of clinical practice, IE has become a great challenge given to the older and sicker patients involved [1]. Although being rare, its presentations and clinical course are highly variable resulting in difficulties for diagnosis and treatment. A broad spectrum of bacterial and fungal organism can be causative for IE. Notwithstanding the changes that have occurred in the epidemiology of IE in developed countries [2], the overall distribution of infective pathogens has remained constant and Gram-positive cocci lead the major proportion of IE cases [1]. The most important predisposing factor of IE is structural abnormalities of the heart such as valvular and congenital heart lesions. The unusual predisposing structural abnormality in our patient seems to be the scar tissue in the septal myocardium. To our knowledge, this was the first report of IE in which a scar tissue functions as a nidus for the developing vegetation. Other

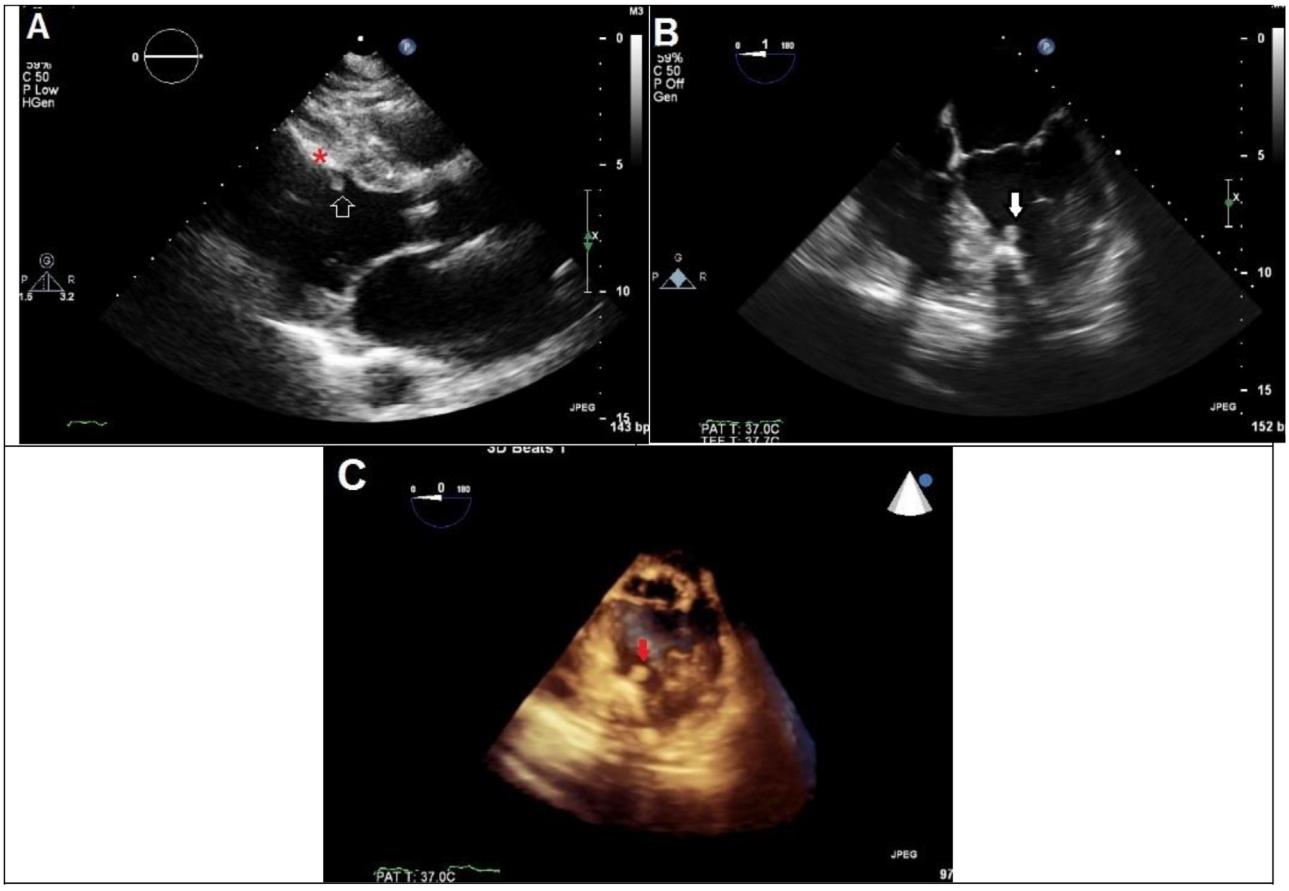

Fig. 3. (A) Parasternal long-axis transthoracic view showing a moderate size tissue texture mobile mass with well-defined margins and a narrow stalk superimposed on the scar tissue (star) of the mid-portion of anterior septum suggestive of a vegetation based on the clinical data, (B) the four chamber transesophageal two-dimensional and (C) real-time three-dimensional views showing the vegetation (arrows).

contributing conditions include intravenous drug abuse, indwelling catheters and devices, and also general medical conditions such as diabetes, ESRD, and chronic immunosuppressive therapy [3]. Accordingly, multiple factors predisposed our patients to IE.

FE is rare and fatal [1]. In recent decades, the incidence of FE has raised significantly especially in immunocompromised hosts [4]. The most common fungal organisms causing FE are *Candida* and *Aspergillus* species [1]. Predisposing risk factors for FE include immunosuppression, underlying cardiac abnormalities, previous cardiovascular surgery, and indwelling central venous catheters [5].

Co-infection of fungal pathogens with bacteria in IE is extremely rare and to our knowledge, this is the second reported case in immunocompromised adult patients. The previous case reported by Simon et al. was a histopathology-proved IE with *Staphylococcus epidermidis* and *Rhodotorula mucilaginous* in an ESRD patient with a prosthetic aortic valve. They described *Rhodotorula* as an opportunistic fungal pathogen which rarely causes IE [6].

FE is characterized by large vegetations highly prone to systemic embolization even in the early stages of infection with special tendency to prosthetic valves and high mortality despite full medical and surgical treatment [7]. Our case had clear indication for surgical treatment (a large mobile fungal vegetation in the left heart that had already embolized to the spleen) but given the advanced heart failure, the history of previous CABG, and accompanying comorbidities, we predicted a prohibitive risk for redo surgery. Prompt antibiotic treatment was started accordingly.

Invasive aspergillosis is extremely rare in immunocompetent individuals [8]. The lungs and/or sinus are usually affected first, then the fungus spreads hematogenously to other organs; however cardiac involvement is rare [9]. *Aspergillus* accounts for 24–28% of all cases of FE [10]. The clinical diagnosis of *Aspergillus* endocarditis (AE) is usually challenging due to its non-specific presentations and because it is rarely isolated from blood cultures and a high level of clinical suspicion is needed for early diagnosis [7].

In a recent study by Meshaal et al. aiming to identify clinical predictors of AE, 374 patients with IE were investigated in an 11-year-period [10]. Of the total study population, 37.7% were culture/serology negative, 11.5% had FE, of which *Aspergillus* was the most common pathogen (8.3% of the total population). *Staphylococcus* was the most common bacterium in the non-FE patients (42.1%). Clinical and echocardiographic characteristics of the AE patients were compared with the non-FE patients. Lack of fever and acute limb ischemia at presentation were significantly associated with AE. The only significant risk factors associated with AE by univariate analysis was health-care associated IE (87.1% of AE patients). The most common culprit procedure in patients with health-care associated AE was cardiac surgery. By multivariate regression analysis, health-care associated IE was the most powerful predictor of AE, followed by absence of fever, aortic abscess/pseudoaneurysm, and prosthetic valve IE. The majority of patients with AE underwent surgery (87.1%). Regarding patient outcomes, they reported a non-significant trend toward higher incidence of severe sepsis and mortality in AE compared to non-FE patients. The rate of mortality in AE patients was 42%. Significant predictors of mortality included: prosthetic valve IE, single antifungal therapy, severe heart failure, and severe sepsis.

Conclusion

In summary we reported a rare case of FE with bacterial co-infection in an immunocompromised male with history of kidney transplantation, diabetes, CABG, and CRT implantation, with an unusual site of vegetation on scarred myocardium. An incidentally detected spleen abscess led to the diagnosis of culture-proven FE. Unfortunately, the patient died due to severe sepsis despite broad-spectrum anti-fungal and anti-bacterial therapy.

Conflict of interests

The authors declare that they have no competing interests.

Acknowledgment

None.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.jccase.2018.11.004.

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