**Infective Endocarditis – A Tale of Two Cases and the Lessons (re)learned**

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**Abstract**

Infective endocarditis due to uncommon organisms or at uncommon sites presents a diagnostic challenge. Because signs and symptoms can be nonspecific and vary greatly, a high index of suspicion is necessary. We have recently treated two such cases, one due to HACEK organism (Eikenella corrodens) in a patient with established valvular heart disease and other of right sided endocarditis due to Pseudomonas aeruginosa. This report describes the diagnostic difficulties faced.

**Introduction**

The clinical syndrome of infective endocarditis (IE) spans a continuum between acute and subacute presentations. The classic nonsuppurative peripheral manifestations of SIE like glomerulonephritis, Osler’s nodes, Roth’s spots, and rheumatoid factor are related to the duration of infection1. These pose a diagnostic challenge by mimicking systemic vasculitis, drug reaction, malignancy, etc.

We report two cases of IE. The first a case of left- sided IE caused by Eikenella corrodens, a rare cause of IE, and highlight the importance of proper culture methods in the diagnosis of this infection. The second, a case of right- sided IE caused by Pseudomonas aeruginosa, highlights the fact that right- sided endocarditis is not limited to injection drug abusers, and how modern imaging techniques like PET scanning, are helpful in localizing the focus of infection in a patient with unexplained bacteremia.

**Case 1**

A 35 years old male a known case of rheumatic heart disease with atrial fibrillation on penicillin prophylaxis till about 6 months prior to the onset of the present illness, consulted us on 26/11/07. He had undergone mitral valvuloplasty and aortic valve replacement (metallic valve), in the year 1999 and, was on regular oral anticoagulation (acitrom) with INR maintained between 2 to 3.

In July’2007, he started having episodes of extremely painful and tender erythematous lesions, mostly on pulps of fingers and toes (figure 1). These would resolve spontaneously in 2-3 days without scarring. The frequency had increased lately with virtually no symptom-free periods. The lesions were associated with marked constitutional symptoms, pain, and disability.

Two months later, he developed high grade fever (upto 39.5° C) and was admitted at another hospital. Investigations showed HB=10.3 g/dl, TLC=9090 cells/mm³ (P, L, M.), platelets=2, 93,000 / mm³, ESR=55 mm 1st hour. Results of urine routine, creatinine, SGOT, SGPT, alkaline phosphatase, GGT, random blood sugar, calcium, LDH, and TSH were normal. Tests for HIV, HBsAg and HCV were negative. Trans-thoracic and trans-esophageal echocardiograms were normal. Multiple blood cultures were negative. Lower limb color doppler was normal. Protein C, protein S, antithrombin III, factor V Leiden, and vWF levels were within normal limits. ANA 1:80 positive, RF 1:2 positive, ANCA (c and p) negative, cryoglobulins and anticardiolipin antibodies absent.

CT of the chest and abdomen showed ill-defined, patchy ground glass nodular low density lesions in both lower lobes interpreted as either subacute hypersensitivity pneumonitis, or diffuse alveolar hemorrhage, and an old splenic infarct. During this period, patient’s appetite was low and he lost about 8 kg weight. No definite diagnosis was arrived at. He was discharged...
on indomethacin and clopidogrel, and felt better.

One week after discharge, the patient developed generalized tonic-clonic convulsions and was readmitted to the same hospital. INR was 4.7. CT brain showed hemorrhagic subcortical lesion. Indomethacin and clopidogrel were discontinued. Anticoagulation was restarted before discharge. Systemic vasculitis was suspected and was advised steroids.

A full-thickness surgical biopsy from a fresh lesion showed septal panniculitis without vasculitis - erythema nodosum (EN). Due to an oversight, the specimen was not sent for microbiological studies.

The case history was reviewed and even though multiple blood cultures were negative, the clinical picture was highly suggestive of infective endocarditis, and a possibility of IE caused by fastidious organisms was considered. Blood culture was repeated with proper precautions and instructions to hold the culture for at least 6 weeks. After 3 weeks, gram negative cocci were grown and identified as Eikenella corrodens, a HACEK group of organisms susceptible to all the commonly used antibiotics. The diagnosis of IE caused by Eikenella corrodens was confirmed. He was treated with intravenous ceftriaxone 2g twice a day and amikacin 60 mg daily. Within one week, the skin lesions stopped completely and he felt better. Inj amikacin was stopped after 2 weeks and inj ceftriaxone was given for a total of 6 weeks. Blood cultures repeated twice at intervals of 4 weeks were negative. On telephonic follow-up on 1st January' 2009, he was completely free of symptoms and leading a normal active life.

**Case 2**

A 43 years old male a known case of diabetes mellitus (DM) since 16 years, and hypertension (HTN) since 2 years consulted us on 7th May' 2008. He had undergone balloon angioplasty in October’ 2005 and percutaneous transluminal coronary angioplasty (PTCA) with stenting in July’ 2007 and in December’ 2007 (involving different arteries). There was no history of IV drug abuse. Time course of events prior to consultation with us was as follows:

- 15–1–08 – Fever. Treated with ofloxacin x 5d. Responded
- 30–1–08 – Fever recurred. Pseudomonas grown on blood culture. Treatment - Ceftriaxone + amikacin x 5 d followed by ofloxacin x 3 weeks (until 24.2.08)
- 25-02-08 – Fever recurred
- 03-03-08 – Serology for Brucella abortus and Brucella melitensis +ve. Treated with Inj. Streptomycin and doxycycline – no response
- 30-03-08 – Blood culture grew Pseudomonas aeruginosa – Treated with Piperacillin/Tazobactam x 3 weeks
- 25-04-08 – Fever persistent. Blood culture positive for Pseudomonas aeruginosa

He was extensively investigated during this period. This is summarized.

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<th>15.01.08</th>
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<td>Urine (R)</td>
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<td>8.10 PC/HPF</td>
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CRP - 10.7 mg/dl 153 mg/dl
Creatinine - 1.2 mg/dl
S. Iron - 6 mg/ml
TIBC - 186 mg/ml
Transferrin saturation - 3.2%

**Other Investigations**

- HBs Ag, HIV –ve, Widal –ve, ANA, ANA –ve
- USG abdomen (30.01.08 and 25.03.08) moderate hepatomegaly, and moderate enlargement of left kidney
- CT paranasal sinuses – no significant abnormality
- CT abdomen (25.03.08) – bulky spleen, and left kidney
- X-ray chest and CT chest (3.3.08) segmental consolidation of right middle lobe and areas of patchy consolidation in both lungs
- 2D Echo (trans- esophageal) – normal

![Fig. 3 : HRCT chest showing a wedge-shaped infarct in the lower part of left lobe](image)

He consulted us on 7-5-08. On examination he was febrile, with pulse rate 111/min, BP 130/90 mmHg. No clubbing or signs of peripheral embolization. To localize the persistent source of Pseudomonas bacteremia a PET scan and DMSA scan were performed.

PET scan was advised. It (Figure 2) revealed multiple bilateral lung lesions of abnormal metabolic activity with abnormally high uptake in the lower lobe of left lung; marrow and spleen showed increased activity, possibly due to anemia; kidneys showed normal physiologic uptake. HRCT chest (Figure 3) showed a wedge-shaped infarct in the lower lobe of left lung, correlating with the area of abnormally high uptake on PET scan, and scattered lesions in varying stages of healing.

These findings suggested right-sided IE. A transthoracic 2-D echocardiogram showed vegetations on the anterior leaflet of tricuspid valve. Based on blood culture report meropenem was started. He underwent another facility. Vegetations were removed from the tricuspid valve. The stent was not infected.
Blood cultures became sterile and the patient was afebrile two weeks post-operatively. After 6 weeks, meropenem was stopped and the patient has remained afebrile till to date, has regained weight and is fully active (last seen 20.7.09).

Discussion

Case 1

HACEK group of organisms are part of normal human oropharyngeal or urogenital flora and primarily cause endocarditis. The IE caused by these organisms is typically subacute, with an insidious onset and indolent progression, associated with the classic nonsuppurative peripheral manifestations.

Five to 15% of patients with endocarditis have negative blood cultures; in one-third to one-half of these cases, cultures are negative because of prior antibiotic exposure. The remainder of these is due to fastidious organisms, such as nutritionally variant organisms (now designated Granulicatella and Abiotrophia species), HACEK organisms, and Bartonella species. When the diagnosis of IE is strongly suspected, it is important to inform the microbiologist of the suspected diagnosis, and to hold the blood cultures for at least 6 weeks. Many organisms are known to cause erythema nodosum. Eikenella corrodens could possibly be added to that list.

Case 2

In a retrospective study of right-sided IE in India Bahl et al. and Grover et al concluded that the clinical spectrum differs from that in the West in frequent presence of underlying congenital heart disease, rarity of IV drug abuse, equal involvement of tricuspid and pulmonary valves and a greater incidence of congestive heart failure. IE due to P. aeruginosa is seen mainly in IV drug users whose native valves are involved. Apart from suffering from DM, our patient did not have any traditional risk factors known to predispose to right-sided IE. PTCA with stenting, which the patient underwent approximately 3 weeks prior to the onset of illness, was possibly responsible. PTCA is not associated with bacteremia and routine procedural antibiotic prophylaxis against IE is not indicated.

Faced with problem of bacteremia due to an unidentifiable focus radionuclide scanning using technetium (Tc) 99m sulfur colloid, gallium (Ga) 67 citrate, or indium (In) 111-labeled leukocytes is useful localize the focus. However, false-positive and false-negative findings are common. PET scanning provides quicker results (hours vs. days); and may be more sensitive and specific.

Lessons learnt

1. Faced with a problem of elusive diagnosis, it is necessary to repeat studies or use different diagnostic techniques or strategy to avoid cognitive error of blind obedience (authors word).

2. IE is an important cause of unexplained fever and bacteremia. Right sided endocarditis can occur in non IV drug abusers.

References


