Prosthetic Mitral Valve Endocarditis caused by Aggregatibacteractinomycetemcomitanscomplicated by an acute episode of hepatitis

Abdul Rashid Sheikh[1]

[1]Department of Microbiology Al-Amiri Hospital ,Kuwait

ABSTRACT

Introduction: We describe a case of subacute endocarditis of prosthetic mitral valve due to Aggregatibacteractinomycetemcomitansin a 48 year old Moroccan patient.

Case Presentation: Blood cultures were positive for A. acinomycetemcomitans. Transesophageal echocardiography (TEE) showed small vegetation in prosthetic mitral valve. The patient responded well to initial ceftriaxone therapy but after 25 days developed acute episode of hepatitis. His antibiotic was changed to ciprofloxacin.

Conclusions:We hypothesized ceftriaxone as a probable cause of acute hepatitis. However, during this episode, patient's lab result showed positive reaction for Hepatitis E virus IgM. During the follow up of one and a half years in cardiac outpatient clinic, he had fully recovered without any recurrence.

Key words: Infective endocarditits, Aggregatibacteractinomycetemcomitans, ceftriaxone, hepatitis

Corresponding author address: Abdul Rashid Sheikh, Department of Microbiology Al-Amiri Hospital, Kuwait, **M**: +965-67074255 **E-mail:** rashidkwt74@gmail.com

Conflict of interest: No

Case report is Original: YES/NO

Whether case report publishes any where? YES/NO

INTRODUCTION

Aggregatibacter (Actinobacillus) actinomycetemcomitans belongs to the HACEK group of organisms, along with Haemophilus species, Cardiobacteriumhominis, Eikenellacorrodens and Kingella species and is a small gram negative coccobacillus facultative anaerobe, non-motile and grows slowly in blood and chocolate agars in presence of CO2 with visible colonies appearing after 48 to 72 hours of incubation. A. actinomycetemcomitans is part of the normal oral flora and is an important pathogen causing various invasive infections, particularly infective endocarditis (IE).1Individuals at highest risk are those who have prosthetic heart

valves, a previous history of endocarditis (even in the absence of other heart disease), complex cyanotic congenital heart disease, or surgically constructed systemic pulmonary shunts or conduits.2,3 Six weeks of treatment with amoxicillin if beta-lactamase negative or third generation cephalosporin e.g., ceftriaxone, is recommended in patients having prosthetic valve endocarditis (PVE) due to one of the HACEK group of organisms. 4 The need for extended anti-microbial administration might have some inherent problems e.g., adverse drug reaction or development of anti-microbial drug resistance. Previous studies have reported a few cases of elevations of liver enzymes along with cases of hepatitis caused by ceftriaxone 5,6,7,8 and there are a few reports of gall stones (cholelithiasis) or bile lumps caused by ceftriaxone.9

CASE REPORT

A 48 year old Moroccan male with mitral prosthetic valve was admitted to Al-Amiri hospital, Kuwait in July 2012 with two months history of recurrent episodes of bilateral pain and swellings of knee joints, treated with intermittent NSAID (ibuprofen). The patient admitted to a two month history of low grade intermittent fever, weight loss of 3-4 Kgs and loss of appetite.Patient had his mitral valve replaced with a Saint Jude Prosthesis in 2007. He was doing well all these years without any complications or any hospitalizations except several months previously when he had attended a dentist for the extraction of his two molar teeth. His medication comprised of Captopril (12.5 mg) and aspirin 81 mg. Patient is married with three offspring and works in a local supermarket as an accountant. He is a non-smoker, non-alcoholic and does not give any history suggestive of use of any recreational drugs.

At the time of admission he was conscious, well oriented and did not have any pain or distress.His vitals were stable with heart rate of 80/min and temperature of 36.70C. His blood pressure was 120/70 mmHg, respiratory rate of 20/min with oxygen saturation of 98% on room air. Examination of eyes revealed pallor but there was no yellowish discoloration of conjunctiva. His oral examination revealed poor dental hygiene with caries in his second molar tooth in left lower jaw.He had multiple light brownish macular lesions in both palms and soles. His lungs were clear and on auscultation of heart he had loud metallic S1 and normal S2 .There was no murmur.On abdominal palpation, liver or spleen was not enlarged. His CNS and musculoskeletal examinations were also normal.

Laboratory investigations showed normal white blood cell (WBC) count of 8.0×10^9 /L with neutrophils of 72%.He had moderate anemia with hemoglobin of 96 g/L and was microcytic hypochromic type. His red blood cell (RBC) count was also low, 3.81×1012 /L.His erythrocyte sedimentation rate (ESR) was significantly raised with value of 120 mm/hour and C reactive protein of 128 mg/dl.Routine urine examination revealed microscopic hematuria with RBCs of 6-8/HPF.Clinical chemistry with Glucose, BUN, Creatinine, Sodium and Potassium were all within normal limits. His LFT was (AST-24 IU/L, ALT-19 IU/L, Alkaline phosphatase- 93 IU/L , GGT- 35 IU/L) normal on admission. Transesophageal

echocardiography (TEE) showed small vegetation of 2 mm × 2 mm attached to atrial side of the posterior suture line in prosthetic mitral valve [Figure 1].

Three sets of blood cultures were drawn from peripheral sites with more than six hours between them and sent to the microbiology lab. After 72 hours of incubation, five bottles signaled positive for small gram negative bacilli in clumps. VITEK-2 (BioMérieux Marcy l'Etoile, France) identified these gram negative coccobacilli as A. acinomycetemcomitans. Subsequently E-test (BioMérieux Marcy l'Etoile, France) was done on the isolate which showed MIC of the following antibiotics: penicillin (3.0 µg/ml), ceftriaxone (0.032 µg/ml), ciprofloxacin (0.012 µg/ml) and chloramphenicol (0.25 µg/ml). Diagnosis of IE by one of the HACEKgroup organisms was made on the basis of Duke's two major criteria; positive blood culture for IE and evidence of endocardial involvement by echocardiography.

The patient was put on ceftriaxone 2 g OD I/V on the basis of BSAC guidelines of NOV 2011 for the PVE by one of the HACEK organism. After 25 days on ceftriaxone, patient developed right upper quadrant pain and laboratory examination showed elevation of liver enzymes, as shown in figure 2. USG of hepato-biliary system showed multiple gall stones with normal wall thickness and normal common bile duct. Hepatitis B surface antigen, anti-hepatitis B core Ig M, anti-hepatitis C virus, anti-hepatitis A virus Ig M, cytomegalovirus Ig M, Ig G and Epstein-Barr virus Ig G and Ig M were negative but anti-hepatitis E virus Ig M was positive. His serology for liver kidney microsomal antibody, anti-mitochondrial antibody, anti-smooth muscle antibody, anti-nuclear antibody, anti-cyclic citrullinated peptide antibodies, and anti-neutrophil cytoplasmic antibody were all negative. Ceftriaxone was replaced with ciprofloxacin and his pain subsided within few days with normalisation of liver enzymes within 10 days. This is shown in figure 2 where the peak of transaminases gradually recedes after the cessation of ceftriaxone therapy. He completed a total of 6 weeks of antimicrobial therapy and his inflammatory markers (CRP, ESR) had decreased markedly with significant improvement in clinical symptoms and signs; and was discharged after six weeks in the hospital.

Figure 1.Transesophageal echocardiogram showing small vegetation of 2 mm × 2 mm.

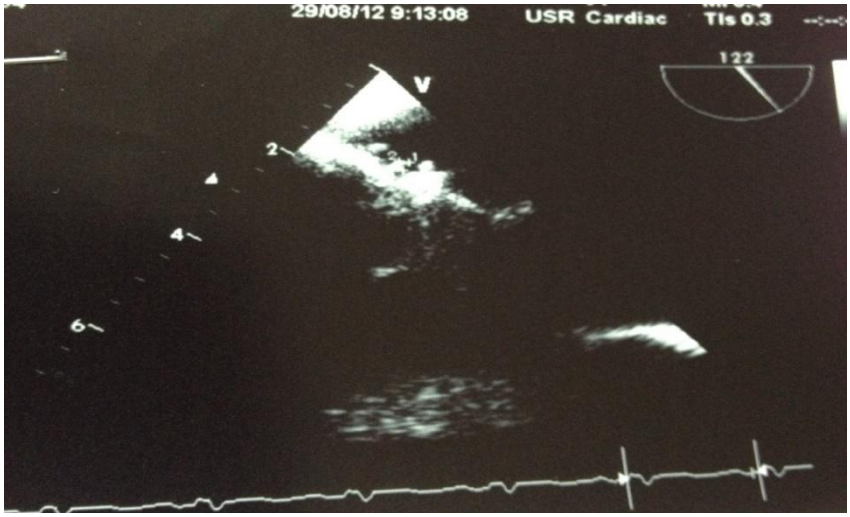
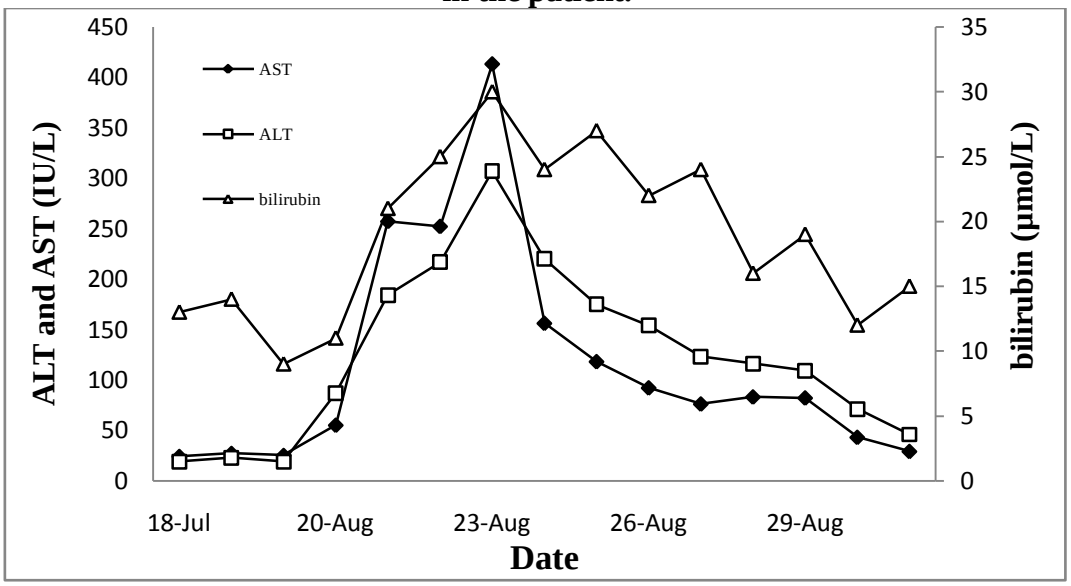

29/08/12 9:13:08
USR Cardiac
TIs 0.3
122
V
2
4
6

Figure 2.Progressive normalization of liver enzymes after ceftriaxone administration in the patient.



DISCUSSION

Aggregatibacter actinomycetemcomitans is part of the normal oral flora and is found in dental plaque, periodontal pockets, and buccal mucosa in up to 36% of the normal population.10 The organism may gain entry from these sites via dental infection, dental treatment procedures, or spontaneous random bactaeremias resulting from oral hygiene procedures or mastication11, to cause severe infections throughout the human body such as endocarditis and brain abscesses.10 It therefore appears more conceivable that the episode of endocarditis in present case could have resulted from a dental infection or dental treatment procedure and furthermore the patient had evidence of poor oral hygiene at the time of admission.A. actinomycetemcomitansendocarditis is a subacute or chronic illness with a prolonged symptomatic period before diagnosis and the onset of disease is very insidious and intermittent.11 In the present case also there was delay of the diagnosis of IE since two months had elapsed when the possibility of infective endocarditis was considered; and echocardiography and blood culture were drawn for the management of illness. A. actinomycetemcomitansendocarditis occurs most commonly in men (two-thirds of patients) and the mean age of patients reported was 46.8 years and prosthetic heart valve can be a risk factor in almost one third of the cases.11

The fastidious growth requirements of A. actinomycetemcomitansmay lead to delay in microbiological diagnosis.Das et al.12,reported that vegetations were seen in more than 50% of the patients, and were characteristically large which possibly reflects the delayed diagnosis of cases. TTE plays an important role in the diagnosis, assessment and management of endocarditis.11

The development of acute abdominal pain, raised liver enzymes and gallstones on ultrasound on day 25 on ceftriaxone led us to believe a drug induced liver injury (DILI) reaction due to the antibiotic8, but the HEV IgM positive reaction complicated the picture. There are reports of presumed DILI reactions subsequently proven to be cases of acute hepatitis E infection.13But on the basis of RUCAM causality assessment score14, which was calculated as 6, which suggests that drug was the "probable" cause of an adverse acute hepatotoxicity episode rather than an acute hepatitis E virus infection. His clinical and laboratory parameters improved considerably and patient was discharged after 6 weeks of hospitalization.

CONCLUSION

The acute liver injury due to antibiotic in case of prolonged course of administration should be thoroughly investigated and antibiotic change should be considered at the earliest.

CONFLICTS OF INTEREST

The author declares that he has no conflicts of interest.

REFERENCES

1. Wang CY, Wang HC, Li JM, Wang JY, Yang KC, Ho YK, et. al. Invasive infections of Aggregatibacter (Actinobacillus) actinomycetemcomitans.J MicrobiolImmunolInfec 2010;43:491–97.
2. Steckelberg JM, Wilson WR. Risk factors for infective endocarditis. Infect Dis Clin North Am1993;7:9-19.
3. Gersony WM, Hayes CJ, Driscoll DJ, Keane JF, Kidd L, O'Fallon WM, et al. Bacterial endocarditis in patients with aortic stenosis, pulmonary stenosis, or ventricular septal defect. Circulation1993;87(2 suppl):121-26.
4. Gould FK, Denning DW,Elliott TSJ, Foweraker J, Perry, JD, Prendergast BD, et al. Guidelines for the diagnosis and antibiotic treatment of endocarditis in adults: a report of the Working Party of the British Society for Antimicrobial Chemotherapy. J AntimicrobChemother2012;67(2):269-89.
5. Bell MJ, Stockwell DC, Luban NL, Shirey RS, Shaak L, Ness PM, Wong EC. Ceftriaxone-induced hemolyticanemia and hepatitis in an adolescent with hemoglobin SC disease. PediatrCrit Care Med2005;6:363–66.
6. Longo F, Hastier P, Buckley MJ, Chichmanian RM, Delmont JP. Acute hepatitis, autoimmune hemolyticanemia, and erythroblastocytopenia induced by ceftriaxone. Am J Gastroenterol1998;93:836–37.
7. Nadelman RB, Arlin Z, Wormser GP. Life-threatening complications of empiric ceftriaxone therapy for 'seronegative Lyme disease'. South Med J1991;84:1263–65.

8. Peker E, Cagan E,Dogan M.Ceftriaxone-induced toxic hepatitis. World J Gastroenterol2009;15(21):2669–71.
9. Rivera M, García-Herrera AL, Burguera V, Sosa-Barrios H, Palomares JRR,Quereda C.Ceftriaxone-Associated Gallbladder Pseudolithiasis in a PD Patient. Perit Dial Int2011; 31(1):97-9.
10. Zambon JZ.Actinobacillusactinomycetemcomitans in human periodontal disease. J ClinPeriodontol1985;12 (1):1–20.
11. Paturel L, Casalta JP, Habib G, Nezri M, Raoult D.Actinobacillusactinomycetemcomitans endocarditis.ClinMicrobiolInfec2004;10(2):98 –118.
12. Das M, Badley AD, Cockerill FR, Steckelberg JM, Wilson WR. Infective endocarditis caused by HACEK microorganisms. Annu Rev Med 1997;48:25–33.
13. Davern TJ, Chalasani N, Fontana RJ, Hayashi PH, Protiva P, Kleiner DE, et al. Acute hepatitis E infection accounts for some cases of suspected drug-induced liver injury.Gastroenterology2011;141(5):1665-72.
14. Rockey DC, Seeff LB, Rochon J, Freston J, Chalasani N, Bonacini M, et al.Causality Assessment in Drug-Induced liver Injury Using a Structured Expert Opinion Process: Comparison to the Roussel-Uclaf Causality Assessment Method. Hepatology2010;51(6):2117–26.