CASE REPORT

Thrombotic thrombocytopenic purpura-like syndrome associated with arcanobacterium pyogenes endocarditis in a post-transplant patient: A case report

Andy Sing Ong Tang, MRCP[1], Tze Shin Leong[1], Ruixin Tan[2], Hock Hin Chua[3], Lee Ping Chew[1]

[1] Haematology Unit, Department of Internal Medicine, Sarawak General Hospital, Sarawak, Malaysia, [2] Pathology Department (Microbiology), Sarawak General Hospital, Sarawak, Malaysia, [3] Infectious Disease Unit, Department of Internal Medicine, Sarawak General Hospital, Sarawak, Malaysia

SUMMARY

Systemic Arcanobacterium pyogenes is a rare bacterial infection in humans.1The diagnosis of thrombotic thrombocytopenic purpura (TTP)-like syndrome and infective endocarditis (IE) is often elusive. We report a case of TTP-like syndrome associated with A. pyogenes endocarditis in a post-allogenic transplant patient.

CASE REPORT

A female dentist was diagnosed with JAK-2 positive Essential thrombocythaemia (ET) at the age of 23 years when she presented with thrombocytosis (platelet above a million/µl). She was treated with anagrelide and hydroxyurea for almost a decade, before this transformed into myelofibrosis. She developed pancytopenia and splenomegaly. Bone marrow examination showed grade 3 myelofibrosis with no increase in blasts. She underwent a fully matched related allogenic haematopoietic stem cell transplant in 2012 and successfully engrafted two weeks later. She was put on cyclosporine post transplantation.

Two years later while on tapering doses of cyclosporine, she developed chronic graft-versus-host disease (cGvHD) of the gastrointestinal tract and eyes which was controlled with the addition of mycophenolate mofetil and prednisolone. In 2016, she developed dysphagia and scleroderma of her hands, significantly affecting her activity of daily living. She was treated with weekly rituximab for a month in addition to her existing immunosuppressants. The scleroderma improved after 6 weeks of treatment with better hand function.

A few months later, she presented with altered consciousness, disorientation and fever. She worked in a dental polyclinic and had no history of animal contact or recent travel. On examination, she appeared cachexic (27kg), pale but not jaundiced. There were multiple petechiae. Large vasculitic lesions were found on her right clavicle and arm. There was a grade III pansystolic murmur at the apex. (Figure 1). Neurological examination showed a dense right hemiparesis with fluctuating GCS.

Results of laboratory investigations showed a haemoglobin of 5.8 g/dl, white cell count of 9,380/µl, platelet of 12,000/µl, positive C-reactive protein, LDH 831 IU/L and a negative Coombs test. Full blood picture showed evidence of haemolysis with 10% red blood cell fragmentation and microspherocytes. Renal profile was normal. She was seronegative for HIV, hepatitis B and C. Blood cultures from both aerobic and anaerobic bottles were positive. Initial gram staining did not reveal any organisms. However, after 24 hours incubation in anaerobic and CO^2 enriched conditions, tiny, grey white, β- haemolytic colonies were seen growing on blood, Chocolate and Mac Conkey agar (without crystal violet). Gram stain from the colonies showed gram positive bacilli of the diphtheroidal type with some parts showing gram positive bacilli in chains or branches. The organism was catalase negative and oxidase negative. An automated ID system based on the BD Phoenix™ Automated Microbiology System was used to identify the organism as Arcanobacterium pyogenes with a confidence value of 98%. Disc diffusion susceptibility testing using the Kirby–Bauer method showed that the isolate was sensitive to gentamicin, cephalosporin, penicillin, macrolides and tetracycline. A transthoracic echocardiogram revealed oscillating vegetation on the anterior mitral valve measuring 1.58cm x 2.04cm with moderate mitral regurgitation. CT brain demonstrated multifocal intracranial septic emboli with an intraparenchymal bleed at the left temporo-parietal lobe (Figure 2). CT angiogram of brain detected unusual sites of bleeding but failed to confirm the presence of a mycotic aneurysmal rupture.

A diagnosis of TTP-like syndrome associated with IE was made. The patient was treated with ceftriaxone and gentamicin with the intention to treat for 6 weeks. Cyclosporine was withheld. The fever resolved after one week of antibiotics and 2 weeks later, the vasculitic lesions disappeared. Unfortunately, she developed a further intracerebral bleed with cerebral oedema and hydrocephalus and passed away, two months after the diagnosis was made.

DISCUSSION

The diagnosis of TTP is often elusive due to variable presenting symptoms. Patients commonly present with microangiopathic haemolytic anaemia (anaemia, >4% schistocytes, raised LDH), thrombocytopenia, fever, renal and/or neurological abnormalities, although patients rarely display the pentad which characterizes the clinical signs of this disease.[2] Secondary thrombotic microangiopathy has

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Corresponding Author: Andy Sing Ong Tang
Email: atso1986@yahoo.com

Table I: Literature review of human infections with Arcanobacterium pyogenes systemic infection

Reference	Year	Number of cases	Age	Sex	Type of infection	Underlying disease	Treatment	Outcomes
Jootar *et al*	1978	1	20	F	Acute endocarditis	Not known	Penicillin, gentamicin	Died
Gahm-Hansen *et al*	1992	7	42	F	Abdominal abscess	Cervical carcinoma	Surgery, sulfonamide, chloramphenicol	Recovered
			22	M	Superficial abdominal abscess	Appendectomy 3 year earlier	Surgery, penicillin, sulfonamide	Recovered
			68	M	Sigmoiditis, cystitis	Diverticulitis	Penicillin	Recovered
			78	F	Superficial abscess	Not known	No treatment	Recovered
			15	M	Appendicitis	Not known	Surgery, penicillin	Recovered
			78	M	Cholecystitis	Cholelithiasis	Surgery, ampicillin	Recovered
			57	F	Otitis media	Cholesteatoma	Surgery, ampicillin	Recovered
Drancourt *et al*	1993	2	56	M	Infected foot ulcer, bacteremia	Diabetes	Surgery, cefotaxime, ofloxacin, metronidazole, amoxicillin/clavulanic acid	Recovered
			82	M	Subcutaneous lumbar abscess	Not known	Surgery, ampicillin	
Reddy *et al*	1997	1	64	M	Subacute endocarditis	Aortic stenosis	Cefotaxime, gentamicin, amantadine, ceftriaxone, vancomycin, ampicillin	Died
Nicholson *et al*	1998	1	46	M	Septic arthritis	Diabetes	Cloxacillin, penicillin, ampicillin, rifampicin	Recovered
Hermida Amejeiras *et al*	2004	1	81	M	Pneumonia	Not known	Cefotaxime, clarithromycin	Recovered
Ide *et al*	2006	1	56	M	Spondylodiscitis	Stroke, osteoarthritis, hypercholesterolemia	Penicillin, clarithromycin	Recovered
Plamondon *et al*	2007	1	57	M	Acute endocarditis	Diabetes, cirrhosis	Piperacillin/tazobactam, vancomycin, penicillin	Died
Levy *et al*	2009	1	27	M	Otitis media, sepsis	Not known	Cefepime, ampicillin, gentamicin	Recovered
Supavit *et al*	2014	1	64	M	Acute endocarditis	Diabetes	Ampicillin, gentamicin	Died
Present case	2017	1	42	F	Acute endocarditis, TTP	Post-allogenic transplant for ET transforming into myelofibrosis	Ceftriaxone, gentamicin	Died

F:M, female: male; TTP, thrombotic thrombocytopenic purpura; ET, essential thrombocythaemia

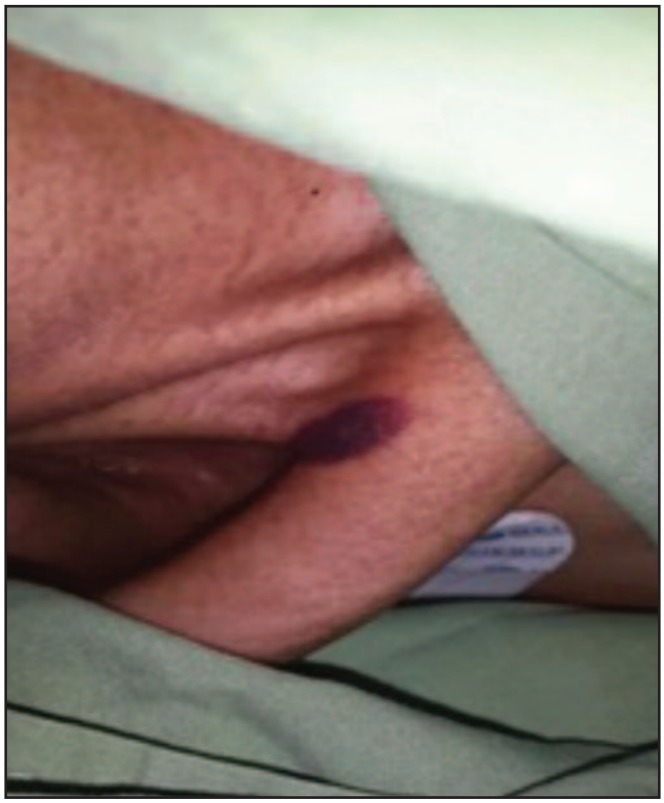

Fig. 1: Janeway lesion on right clavicle.

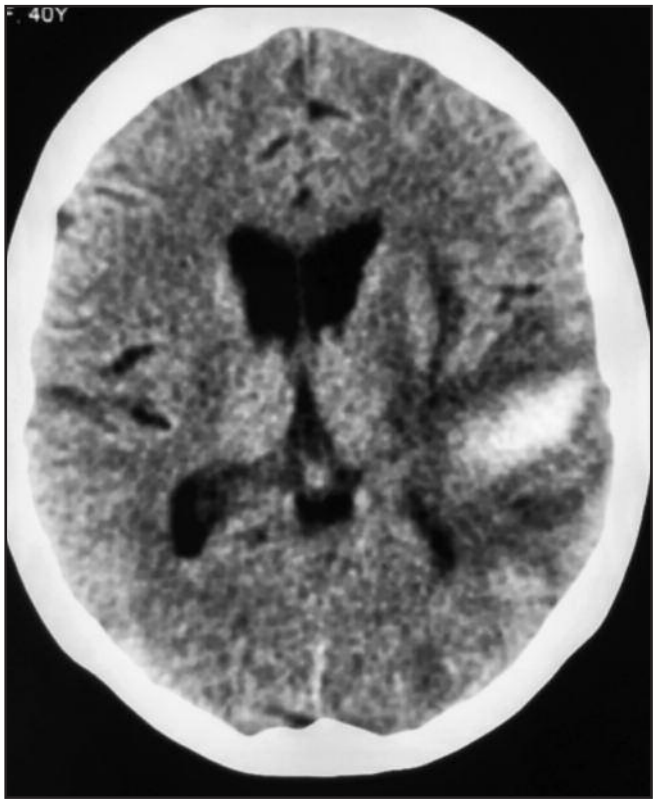

Fig. 2: CT brain showed multifocal intracranial septic emboli (due to location at periphery and grey-white matter junction) and intraparenchymal bleed at left temporo-parietal lobe.

been shown to be associated with infections, transplants, collagen vascular diseases, use of certain drugs, surgeries and malignancy.[2] TTP can occur in up to 7% in post allogenic bone marrow transplant3, usually occurring around day +60 but may present as late as 2 years later.[3] A higher incidence of TTP is often seen in patients who develop GvHD which is suspected to cause endothelial damage and calcineurin inhibitors which may have pro-coagulant effects.[4] TTP-like syndromes despite their rarity have been described as primary manifestations in two patients with infective endocarditis.[5]

A diagnosis of IE should be considered in a post bone marrow transplant patient. Endocarditis in this case fulfilled the modified Duke Infective Endocarditis criteria with demonstration of one major criteria of echocardiogram findings, which showed an oscillating intracardiac mass on mitral valve, and three minor criteria of fever, positive blood cultures not fulfilling that of major criteria and vascular phenomenon. This patient had a documented IE with A. pyogenes, an organism rarely reported in humans and associated with high mortality.[1] To the best of our knowledge, a TTP-like syndrome associated with endocarditis in a post-allogenic transplant patient with A. pyogenes has not been reported in the literature.

A. pyogenes is primarily an animal pathogen, causing pyogenic infections in cattle.1Most human cases are acquired in rural settings with exposure to farm animals. However, our patient had no typical epidemiological exposure. There have been few reported cases of A. pyogenes endocarditis in Europe and Southeast Asia (Table I). Similar to these case reports (Table I), outcome of treatment with penicillin in our case was poor with the patient succumbing to complications arising from her infection despite successful clearance of the organism. At this point in time, there has been no reports of any successful treatments of A. pyogenes endocarditis (Table I).

CONCLUSION

A correct diagnosis distinguishing between TTP and IE is of paramount therapeutic importance. Our case showed that A. pyogenes endocarditis can present as a TTP-like syndrome, albeit rare. Despite an improved ability to diagnose A. pyogenes endocarditis, patient treatment outcomes remain poor. As such, it is crucial to make a correct diagnosis promptly in order to intervene early and initiate appropriate treatment modalities before other complications arise.

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