The implications of delaying treatment in infective endocarditis

Science, Biology

Although rare, infective endocarditis (IE) can be a fatal disease and remains affiliated with a high mortality rate of around 20% even after aggressive treatment. It is defined as a microbial infection of the innermost layer lining the chambers of the heart; known as the endocardium (3) The infection occurs when bacteraemia is able to latch onto a part of the endocardium which is damaged or on abnormal heart valves. This leads to vegetations forming at the site of infection consisting of small masses of inflammatory material such as fibrin, platelets and red and white blood cells. Once the bacteria become embedded in vegetations, the body's immune system is significantly impaired to suppress the bacterial invasion. IE is most prevalent with one or more heart valves but can also occur during a septal defect or in mechanical devices such as a pacemaker.

This case study will discuss the implications of delaying IE treatment in the diagnosis and management and outlining the key investigations carried out to detect the onset of the disease. Additionally, reviewing the national guidelines for IE, the rationale behind any changes and looking at ethical care of the disease in a wider context.

A 64 year old male patient was admitted to the cardiology ward with chest pain for five days and dyspnoea for the last two to three weeks. The history of chest pain was described as a left-sided sharp stabbing pain which has now settled. There was a degree of increased shortness of breath on exertion with no orthopnoea or paroxysmal nocturnal dyspnoea. No cough, fever or night sweats were associated as was there no change to bladder or bowel habits. A previous echocardiogram revealed significant mitral

regurgitation (MR). Hence, coinciding with a past medical history of a recent admission for Streptococcus Gordonii Endocarditis that was treated with intravenous (IV) antibiotics for six weeks. Further medical history included chronic mild thrombocytopenia, chronic polyps and a non-specific gallbladder lesion. The patient reported no family cardiac history, no known allergies, has never smoked or taken recreational drugs and does not consume alcohol. On initial inspection, he was alert, comfortable at rest, exuded a positive body language and skin was intact with no obvious scars or deformities.

Upon examination, he was afebrile (36. 3°C), had a blood pressure of 116/65 mmHg, a heart rate of 84 beats per minute, a respiratory rate of 16 breaths per minute and an oxygen saturation level of 97% on air. A harsh pansystolic murmur radiating to the axilla was noted on auscultation and the jugular venous pressure was not raised. The lung fields were clear, abdomen was soft non-tender with audible bowel sounds, no pitting oedema was present and there were no focal neurology findings. Due to previous microbial infection, a working diagnosis was to rule out repeat infective endocarditis.

Key blood results on admission revealed the following; WBC (109/L): 5. 7, Urea (mmol/L): 7. 6, Creatinine (umol/L): 81, Haemoglobin (g/L): 125, Troponin I (ng/L): 128. Repeat blood cultures came back positive to confirm recurrent Streptococcus bacteraemia. The electrocardiogram (ECG) showed a sinus rhythm with wide PR intervals whilst the echocardiogram displayed vegetations on the posterior mitral valve leaflet corresponding to the pansystolic murmur on examination. The patient had a dental extraction to

remove an abscess where the bacteria colonised his teeth. In order to maintain good oral hygiene and plaque inhibition chlorhexidine (0. 2% mouthwash) was prescribed. Management of the IE followed with a PICC line (peripherally inserted central catheter) insertion to initiate four weeks of IV antibiotics (Benzylpenicillin) to treat the Streptococcus Gordonii.

As highlighted earlier, IE is considered a life-threatening condition especially when left untreated (8, 9). Moreover, the epidemiological profile and risk factors of IE continues to evolve such that associated mortality remains the same between 10% and 30%. Cardiac valvular abnormalities are well established as a risk factor. In this case, a valvular abnormality of MR was identified during examination of the patient, emphasising the need for careful management due to the high prevalence and relatively high risk (13). Similarly, dentulous cases infected with dental flora were found to be at increased risk whereas those who flossed daily were at a less risk (14). This advocates that patients who fall under the bracket of high risk IE just like in the case presented would benefit from maintaining good dental hygiene. It is therefore plausible that one of the precipitating factors leading to the dental abscess extraction could have been failure to floss regularly. Wood and Smith (4) supported this notion having acknowledged that those who floss daily could be at less risk of developing IE. Strom et al. established a connection from 97 dentulous cases where more than half of the cases with dental flora had cardiac valvular abnormalities. 75% were flossing sporadically or not even at all suggesting that those with a valvular abnormality need to also pay careful attention to their oral hygiene.

In terms of the delay in IE treatment, the patient mentioned that he had a previous CT scan which showed the dental infection but according to him this was not followed up during the previous admission. This subsequently raises concerns in the medical management especially considering the fatality risk of IE. Sadaka et al. (15) found that incidence rates of IE in males (58%) was greater than in females (42%). Beynon et al. (16) supported this finding with men twice as likely to be affected than in women. As the patient in question is a male, it outlines that male sex is significantly associated with an increased risk of IE. Sadaka et al. (15) established that delayed diagnosis of the disease is common with a study showing a mean duration of delay from the onset of symptoms till diagnosis of 54 days. Habib (17) discussed that IE requires a collaborative approach involving physicians, cardiologists, surgeons, microbiologists and infectious disease specialists. For this reason, there can be some form of delay in diagnosis and treatment as IE presents in a variety of different forms. Chu (5) presented the clinical features of IE which can include fever, heart murmurs, splinter hemorrhages, Osler’s nodes and Roth’s spots. These can be subtle and at times can present for several weeks and thus requires a high index of suspicion to avoid missing the diagnosis. Clinicians can use the modified Duke criteria when facing diagnostic uncertainty for IE. Essentially, it is a set of clinical criteria for possible IE. To meet the criteria, there must be 1 major criterion (positive blood culture) and 1 minor criterion (fever > 38°C) or 3 minor criteria (predisposing heart condition, Janeway’s lesions and intracranial hemorrhage).

With a high morbidity rate, failure of early IE diagnosis has its implications. Fukuchi et al. investigated IE diagnosis in Japan which revealed significant delay in the diagnosis due to frequently prescribing inappropriate antibiotics and the misinterpretation of blood cultures (BCs). Unquestionably alarming but does imply a poor prognosis of the disease and educating the medical team including the students on IE would hopefully see an improvement. This case highlights the importance of prescribing correctly and knowing when or not to proceed by following trust and national guidelines. In accordance with NICE clinical guideline No. 64, a complete cessation of antibiotic prophylaxis before invasive dental procedures was implemented for patients at risk of IE. Thornhill et al. discussed the impact of the NICE guideline recommendation. Their finding was that despite a significant reduction (76%) in the prescribing of antibiotic prophylaxis and with the use of hospital episode statistics there had been no remarkable increase in the incidence of IE. In line with this case, NICE guidelines states that chlorhexidine mouthwash should not be given as prophylaxis against IE for patients undergoing dental procedures (22). Bearing that in mind, the patient was prescribed chlorhexidine (0. 2% mouthwash) after his dental extraction and therefore clearly follows the national guidelines.

Referring back to Fukuchi et al. where BCs were misinterpreted in diagnosing IE, it has been acknowledged according to Tabriz et al., that BCs can be a key diagnostic and prognostic indicator of suspected infection in patients. For this patient repeat BCs were ordered with possible factors being a new septic episode, persistent fever and leukocytosis. Once initial cultures are

obtained, requesting additional cultures can be brought into question however, as studies have shown repeat BCs to be superfluous as they are costly for national health services. Although, when there are confirmed cases of bacteraemia, repeat cultures are advocated for the presence of Staphylococcus aureus bacteraemia and infective endocarditis. This is turn concurs with the management of repeating the BCs as the patient was diagnosed with IE. Makrides et al. reported that Staphylococcus aureus bacteraemia is the second leading cause of IE. Moreover, their research revealed there can be difficulty diagnosing because of limited clinical presentations of the disease. Conversely, there are studies that have shown a number of clinical features that present in IE. Makrides et al. revealed that their case, like others did not consider an initial diagnosis of IE, thus leading to delays in diagnostic investigations.

Both transthoracic and transesophageal echocardiography (TOE) are considered vastly important as they aid in the detection of vegetations, abscesses, valve leaflet perforations and valve leaks TOE is a more sensitive and specific diagnostic tool than a transthoracic echocardiogram (TTE) and thereby should be considered in the initial stages of diagnosis especially if there is any clinical suspicion whatsoever. Ellison (7) conferred when deliberating the role of echocardiography to diagnose IE. His research revealed that despite a TTE having a rapid and non-invasive approach with very good specificity for vegetations, it may be inadequate in up to 20% of adult patients. This is due to a lack of sensitivity and also because of obesity, chest-wall deformities and chronic obstructive pulmonary disease. On the

contrary, TOE is a more costly and invasive approach but as Mügge et al. confirmed it increases the sensitivity and specificity for detecting vegetations (7). For this purpose, TOE is a more reliable diagnostic tool and hence was used during the investigation to detect the recurrent Streptococcus Gordonii. However, Chu (5) pointed out pitfalls in the echocardiogram assessment of vegetations. With IE commonly occurring on an abnormal heart valve and any pre-existing abnormality such as myxomatous mitral valve disease can actually become mistaken for vegetations. In light of this, recognising an existing vegetation can be more challenging than meets the eye. Now as the patient discussed in this case had a recurrence of IE, the vegetations which appeared on his posterior mitral valve leaflet could have been mistaken for any remnants of the old vegetation treated previously. Thus, any slight hesitations from the surgeon on inspection, then a second medical opinion should be sought to increase the likelihood of diagnosing correctly. Furthermore, when it comes to treating children with IE, TTE is the actual investigation of choice with a reported level of 81% in the paediatric population (28). Echocardiography is also used to monitor the progress of certain patients hence the need for repeat echocardiograms as was the case for this study. Specifically, clinicians would be looking out for cardiac size, worsening of valve incompetence, increase in size of vegetation or any development of myocardial abscess.

Delayed diagnosis can be critical dependent on the presenting complaint. Mohamed and Mayala (29) presented a case of delayed diagnosis of IE

complicated with stroke. Their research established that patients with IE can develop neurological complications mainly due to a vegetation embolism. The main point highlighted was the importance of diagnosing early for IE in order to prevent the occurrence of neurological sequelae. As mentioned earlier Dukes criteria can aid in the diagnosis of IE and hence as IE can complicate with ischaemic stroke a rapid diagnosis using Dukes criteria is critically vital in the prevention or reduction of neurological sequelae. Mohamed and Mayala reported patient findings of splenomegaly and clubbing which suggests endocarditis that had existed for some considerable time meaning it could have potentially been identified much earlier.

Martí-Carvajal et al. acknowledged that antibiotics are the cornerstone of IE treatment. Al-Omari et al. (6) explained in further detail that antibiotics delivered intravenously result in rapid therapeutic concentrations in blood and are more potent and reliable than compared to oral antibiotic therapy. Antibiotic regimen use for IE are not standardised because of the differences in clinical presentation and wide array of bacteraemia that could be responsible. In relation to the patient, it was mentioned earlier that they were put on a course of IV Benzylpenicillin for four weeks to treat the Streptococcus Gordonii. It is recommended that a minimum of four weeks of antibiotic therapy is prescribed to treat IE (31). This confirms that guidelines were followed, and the correct course of treatment was administered. Also, Elliott et al. discussed IE patients would benefit from six weeks of penicillin with symptoms of more than three months. Such individuals have larger vegetations and mitral valve disease and would require more aggressive

treatment for a longer duration. In addition, endocarditis falls into two categories acute and subacute. Durack differentiated the treatment strategies in both forms of endocarditis. For acute endocarditis, treatment must be initiated rapidly cannot due to the sudden onset of bacteraemia. Comparatively, in subacute endocarditis time pressure is less critical and in fact delaying antibiotic treatment can be beneficial as there is a gradual onset of bacteraemia growth. This is turn can guide the clinician as to which should be the initial antibiotic therapy once the species of bacteraemia has been identified. If a patient fails to respond to antibiotic treatment, then it may indicate the need for surgical intervention.

As a whole, the case raises some key questions. Firstly, why was his dental infection not followed up in the previous admission for IE or could it have been actually a case of the patient being misinformed. Certainly, delaying IE treatment can have serious implications as discussed thus far. However, there may have been a reason not to treat the dental infection immediately due to complexities of the IE or multidisciplinary team meetings to establish the best way to move forward with the case. Communication in the medical setting is very important and specially to form not only a good rapport with the patient but also to maintain smooth running of a General practice, medical ward or accident and emergency department. Another point to raise was there seemed a considerable delay for the patient just to have the PICC line inserted to initiate antibiotic treatment for the Streptococcus Gordonii. Delaying treatment is associated with high risk and also considers the comorbidities of a patient. From discussions with the patient there was

detection of slight frustration because he honestly just wanted to be back home due to work commitments and to spend time with his wife. Looking at the patient journey from admission, it seems the management could have been improved to effectively treat the IE, but this could have been down to limited resources, staffing and increasing demand on the National Health Service (NHS).

Physician Associates (PA) form an integral part of the medical team. Regarding the role of a PA in this clinical setting would be firstly to perform a thorough history and examination of the patient. This is essential for an initial diagnosis, but also gives a clear impression to the consultant what path of management needs to be implemented to treat the IE. With the consultant having very limited time, a PA has the added flexibility and will have more contact with the patient. Therefore, its essential to show empathy when necessary, informing them of their progress and educating them as to why this line of treatment is being arranged. Moreover, communicating in a clear, concise and personal manner will avoid confusing the patient and enhance the patient experience. It’s also vital for a PA to continue learning and developing their clinical acumen. Discussing any concerns with a senior clinician will perhaps even alter the management or at least make them known. In addition, doing further background reading on the condition is a crucial element to understanding the case overall. Knowing the patient story is vital to board rounds as well, so keeping up to date with any blood results or treatment timelines will ensure continuity of care.