MANAGEMENT CHALLENGES OF PEDIATRIC INFECTIVE ENDOCARDITIS AT TERTIARY LEVEL IN RWANDA

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ABSTRACT

Background: Management of Infective Endocarditis (IE) has been of great challenge for many years. Rapid diagnosis, effective treatment, and prompt recognition of complications are essential to good patient outcome as this condition is associated with a high morbidity and mortality in both adults and pediatric patients. In limited resources settings, management of IE is still a challenge due to early inappropriate antibiotherapy and therefore difficulties in its diagnosis and treatment.
Objectives: To elicit challenges in management of patients suspected of IE at tertiary level in Rwanda.
Methods: We report four patients with IE. For these patients, Duke's criteria were considered in making the diagnosis.
Results and Conclusion: IE has protean clinical symptoms and signs, and can be of challenging diagnosis. The patients reported constituted a clinical challenge in the diagnosis and management of IE but most of them had had favorable outcome. The main clinical challenge was the prolonged stay to peripheral settings with inappropriate antibiotherapy which made most of the blood cultures falsely negative. Echocardiography and serial blood cultures provide the key to diagnosis as per Dukes criteria. Being alert to this mentioned challenge is crucial. As the key investigations are not steadily available in most peripheral health facilities, we strongly recommend early referral to tertiary level for all cases of suspected IE before initiation of antibiotherapy.

Key words: infective endocarditis - salmonella typhi - staphylococcus aureus - native valve - congenital heart disease - Dukes criteria.

RESUME

Introduction: Depuis plusieurs années, la prise en charge de l'endocardite bactérienne constitue un grand défi. Cette affection étant associée à une importante morbidité et mortalité tant chez l'adulte que chez l'enfant, un diagnostic rapide, un traitement efficace, et une reconnaissance rapide de complications sont des éléments essentiels pour arriver à un bon résultat thérapeutique. Dans les pays où les ressources sont limitées, la prise en charge de l'endocardite reste difficile en raison de l'antibiothérapie inappropriée initiée préalablement au niveau des structures sanitaires de base.
Objectif: Identifier les défis dans la prise en charge des patients présentant une endocardite bactérienne au niveau des structures sanitaires tertiaires du Rwanda.
Méthodes: Nous rapportons quatre patients qui présentaient une endocardite bactérienne. Pour tous ces patients, les critères de Duke ont été utilisés pour poser le diagnostic.
Résultats et conclusion: L'endocardite infectieuse a des formes cliniques variables et peut rendre le diagnostic difficile. Bien que presque tous les patients reportés dans cette étude ont été traités avec succès, leur prise en charge n'a pas été facile d'emblée. Le plus grand défi a été un séjour prolongé sous antibiothérapie probabiliste a l'Hôpital de District, ce qui a rendu la plupart des hémocultures faussement négatives au niveau tertiaire. L'échocardiographie et une série d'au moins 3 hémocultures constituent les éléments clés des critères de Duke pour le diagnostic de l'endocardite bactérienne. Par conséquent, il est crucial pour les cliniciens de tenir compte de ces critères pour poser le diagnostic d'endocardite. Compte tenu de l'absence de moyens pour faire les hémocultures et une échocardiographie au niveau des hôpitaux de district, nous recommandons un transfert rapide au niveau de l'hôpital de référence pour tout cas suspect d'endocardite bactérienne avant d'initier l'antibiothérapie.

Mots-clés: endocardite bacterienne - salmonella typhi - staphylococcus aureus - valve native - cardiopathie congenitale - Criteres de Duke

INTRODUCTION

Infective Endocarditis (IE) carries a high risk of morbidity and mortality. Rapid diagnosis, effective treatment, and prompt recognition of complications are essential to good patient outcome [1]. In the pediatric wards, IE may not be as common as in the adult wards [2]. Still, this is a serious condition worldwide with different risk factors in developing and developed settings, as well as different prevalence and incidence in both settings [3, 4]. Different causes of bacteremia make the heart valves come into contact with the pathogens. Normally, blood flows smoothly through these valves. When damaged as in rheumatic heart disease [RHD], the risk of bacterial attachment is increased [5]. This also occurs with some of the congenital heart diseases [CHDs] with turbulent flow and /or high velocity [6]. Amongst the 12 CHDs, ventricular septal defect [VSD], patent ductus arteriosus [PDA], aortic coarctation [AC], tetralogy of Fallot [TOF] and Aortic Stenosis [AS] constitute the predominant predisposing conditions for IE. Conversely, defects such as secundum atrial septal defects (ASDs) are not associated with infective endocarditis [6]. Native valve IE may occur following any cause of heavy bacteremia such as urinary tract infections [UTI], indwelling venous catheters, IV drug users as well as in different cases of immune system compromise with identifiable risk factor for IE and usually involves infection of the aortic, mitral or tricuspid valve [2, 7], secondary to Staphylococcus aureus bacteremia [2, 5].

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Children with congenital or acquired immunodeficiencies but without identifiable risk factors for IE do not seem to be at increased risk for endocarditis compared with the general population [2].

While the frequency of IE among children in developed countries appears to have increased in recent years mostly due to the improvement in survival for children with complex CHD, In developing countries it is believed that the still high incidence of RHD is responsible for most cases of IE [2, 3] where antibiotic prophylaxis for potential septic procedures is not routine and the late referral is common. Over the past few years, our settings are experiencing a slight increase in survival for children with CHD due to visiting cardiac surgeons.

Many challenges are faced in the management of patients with IE in the resource restricted settings due to many causes such the late consultation, late referral, shortage of experienced health personnel to rapid diagnose and effective treatment of IE [3]. Access to new diagnostic technologies and surgical facilities remains difficult in developing countries, thus affecting prognosis of these patients [4]. Echocardiography and blood cultures required for making the diagnosis as per Duke's criteria [Table 1 – Duke's criteria] are not steadily available in most of the health facilities in Rwanda as in many developing countries. Additionally, many patients consult after inadequate antibiotherapy, making the culture falsely negative.

In the present review, we are reporting four cases of IE diagnosed and followed in both pediatric cardiology units of Kigali University Teaching Hospital (KUTH) and King Faisal Hospital (KFH).

CLINICAL CASES

Patient 1: A 9-year-old female admitted in the pediatric department/KUTH with a history of shortness of breath since birth, high grade fever, dry cough and generalized aches of one week duration. Social history was not significant. On examination she was cachectic (BMI=13.23), temperature was 38.2°C, pulse rate 104/min, blood pressure (BP) 112/70 mm Hg, respiratory rate (RR) 40/min. The cardiovascular examination revealed hyperdynamic precordium, loud S2, continuous subclavicular murmur 3/6 with axillar and back radiation, and no other murmur or added sound heard. No other abnormalities were noted on systemic examination except hepatomegaly 3cm below the right costal margin. Of note, the patient was referred from Ruhengeri District Hospital (DH) following persistent fever on Ampicillin for 5 days and Captopril for 2 days. At Ruhengeri DH, a blood culture was not done but an echocardiography was performed and revealed only a large VSD.

Investigations revealed: Urea 3.65 mmol/L, Creatinin 38µmol/L, ALT 61 iu/L, FBC: WBC 5.9x109/µL, Hemoglobin 14.2g/dl, Platelets 262,000/µL, HIV serology negative. Three cultures of blood were performed and only the second came back positive and revealed Salmonella typhi sensitive to ceftriaxone and gentamicin.

A detailed Trans-thoracic Echocardiography revealed the presence of truncus arteriosus type IV and vegetations (7.7mm) attached to the left cuspid of the truncal valve [fig. 1]. Hence, the diagnosis of IE was made on the basis

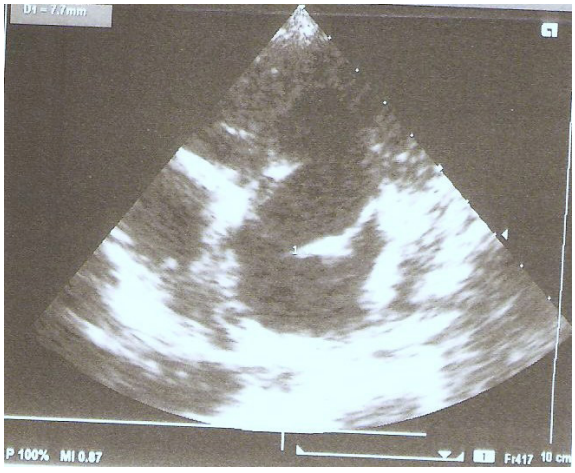

Fig. 1: Transthoracic echocardiogram (TTE): Vegetation (7.7mm) over the left cuspid of the truncal valve

The patient was treated with Intravenous ceftriaxone 1g 12-hourly for 4 weeks and gentamicin 50 mg 24-hourly for 2 weeks. She showed full clinical recovery during this period and was discharged on Furosemide 20mg. The patient was advised prophylaxis for endocarditis in special circumstances, such as dental extraction and surgical procedures. Currently, she is apparently healthy and attends clinical follow up every 6 months, and no surgery was planned because of fixed pulmonary hypertension. Counseling of parents was done regarding the next poor prognosis of the patient's heart condition.

Table 1 : Duke Criteria for Diagnosis of Infective Endocarditis (IE):

Major criteria:

A. *Positive blood culture for Infective Endocarditis*

1- Typical microorganism consistent with IE from 2 separate blood cultures, as noted below: viridans streptococci, Streptococcus bovis, or HACEK (*Haemophilus sp, Actinobacilius actinomycetemcomitans, Cardiobacterium hominis, Eikenella rodensy Kingella sp)* group, or community-acquired Staphylococcus aureus or enterococci, in the absence of a primary focus or

2- Microorganisms consistent with IE from persistently positive blood cultures defined as: 2 positive cultures of blood samples drawn >12 hours apart, or all of 3 or a majority of 4 separate cultures of blood (with first and last sample drawn 1 hour apart)

B. *Evidence of endocardial involvement*

1- Positive echocardiogram for IE defined as : oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation, or abscess, or new partial dehiscence of prosthetic valve or

2- New valvular regurgitation (worsening or changing of preexisting murmur not sufficient)

Minor criteria:

- Predisposition: predisposing heart condition or intravenous drug use
- Fever: temperature > 38.0° C
- Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway lesions
- Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth spots, and rheumatoid factor
- Microbiological evidence: positive blood culture but does not meet a major criterion as noted above or serological evidence of active infection with organism consistent with IE
- Echocardiographic findings: consistent with IE but do not meet a major criterion as noted above

Clinical criteria for infective endocarditis requires:

• Two major criteria, or

• One major and three minor criteria, or

• Five minor criteria

Patient 2: A 13-year-old female with history of post-traumatic laceration of right knee who presented to the emergency department of KFH with severe dyspnea and fever for three weeks. This was a previously well teenager girl who, 3 weeks prior to admission, fell down on her right knee and developed moderate swelling and pain. Three days after she fell, the swollen area opened and started discharging pus. This was accompanied by fever and dyspnea. She then consulted her district hospital where she underwent debridement and washout of the wound and was started on per os metronidazole and gentamicin IV. No improvement noted after 2 weeks; she continued complaining shortness of breath, persistent fever, hemoptoic cough, and lower limb swelling.

She was then transferred to KUTH in heart failure where an echocardiography was done and showed a pericardial effusion with significant fibrin deposit on visceral and parietal pericardium. An urgent transfer to KFH was requested for surgical evaluation by a cardiothoracic surgeon and possible drainage with appropriate treatment of osteomyelitis. Her past medical history includes recurrent tonsillitis, recurrent submandibular abscess, and dental caries. No history of HIV for the child, and both parents were negative for HIV. There was no previous history of heart disease or rheumatic fever. Social history was not significant.

On examination at KFH, the patient was ill-looking, weak and wasted. She was pale, in severe respiratory distress with grunting, confused and agitated; temperature was 37.6°C, regular pulse rate of 128/min, blood pressure 125/82 mm Hg, SaO2 96% on room air, Respiratory Rate (RR) 48/min.

On cardio-vascular system, there was raised Jugular Venous Pressure (JVP), and the auscultation revealed a pericardial rub, and the heart sounds were muffled. No murmur heard initially. On respiratory system, the patient had dyspnea, and showed decreased air entry in both lung bases. The abdomen was distended with mild to moderate ascitis and a hepatomegaly with 12 cm liver span was noted. No splenomegaly noted.

The musculoskeletal examination revealed a 4 x 4 cm necrotic wound at the medial aspect of the right knee, pus discharge on compression and tenderness on passive knee extension. Additionally, there was bilateral pitting edema up to the knees. The neuro-vascular status was preserved.

The investigations revealed: FBC with Hemoglobin 6.8 g/dl (normochromic, normocytic anemia), normal renal function tests, abnormal LFTs (Albumin: 16 g/dl, LDH: 256iu/L, ALT: 197iu/L), 2 consecutive negative blood cultures, normal coagulation profile and swab of the wound grew S. Aureus. The EKG tracing revealed: sinus tachycardia (at 130), and the HIV serology was negative.

The imaging tests included a chest x-ray that showed bilateral pleural effusion and a globular shaped cardiomegaly suggesting a pericardial effusion; a comparative radiography of both lower extremities showed periosteal elevation of 1/3 proximal of the right tibia suggestive of acute osteomyelitis.

Immediate resuscitation was initiated with oxygen via nasal prongs (4l/min), IV fluids and 1 unit of Packed Red Blood cells, IV digoxin Stat. The patient received IV cloxacilline, IV flagyl and IV gentamicin for a week. 24 hours later, the patient was seen by a cardiologist who performed an echocardiography which only confirmed the pericardial effusion. An urgent pericardial drainage was performed. The sample taken for bacteriology confirmed S. Aureus.

Three days after the admission, the patient had a slight improvement, but was still complaining of fever, night sweat, and dyspnea. A chest CT scan showed left pleural effusion and a right Lower lobe consolidation. Tube thoracotomy was performed.

Tuberculosis was suspected, sputum was negative but anti TB drugs were started empirically for 6 months.

A rheumatology consult aimed to exclude Systemic Lupus Erythematous (SLE) or Juvenile Rheumatoid Arthritis (JRA); and only the rheumatic factor was positive. The rheumatologist retained JRA and started the patient on

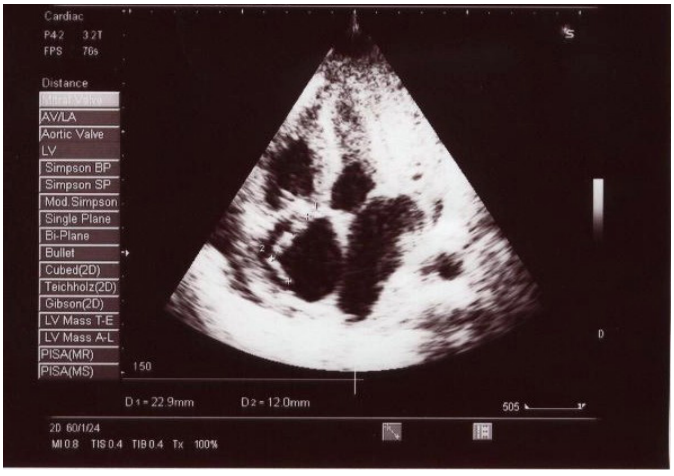

Fig.2: Transthoracic echocardiogram (TTE): Filiform vegetation (3.5cm) over the Tricuspid valve

Cloxacilline was stopped and IV Vancomycine was Started for 2 weeks combined with ceftriaxone for 1 week. At completion of the above antibiotics, the patient was still in a critical state though not febrile. The control revealed an ESR of 128 in the 1st hour, CRP was 4,8mg/L. Antibiotics were then changed to IV cloxacilline 850mg TDS for 4 weeks and IV Amikacine 250mg 24-hourly for 2 weeks.

In the following days, the patient had a remarkable improvement. There were no signs of respiratory distress,

the edema progressively resolved and she started gaining some weight too. This allowed to Surgeons to take care of the osteomyelitis. Afterwards, the patient was fully followed by the pediatricians and she was well improving on IV antibiotics.

At completion of IV Antibiotics course, the patient was doing well, no complaints and the clinical examination was of normal findings. The control with X - rays, blood cultures as well as the echocardiography was normal. The patient was discharged on continuation of Anti TB drugs (2nd phase). Currently, she is healthy and all findings are normal.

Patient 3: A 7-year-old male admitted in the Pediatric department/KUTH with a history of high grade fever for 12 days and cough for 1 week. He started a history of parietal epigastric abscess drained few days back. The patient had consulted the Gisenyi District Hospital where he was given amoxicillin and flagyl then shifted to ampicillin and gentamicin and later to cefotaxim and coartem but the fever persisted. Along the hospitalization, cough was noted. Investigations done at the district hospital revealed an anemia (hematocrit 19.6%) corrected by transfusion. The chest radiography showed nodular infiltrations in both lung fields so he was started on TB drugs before his referral to KUTH. The patient denied any drug allergies. The family history was not significant. On examination, he was asthenic, weight 18kg (-1 and -2 Z score), height 113cm, temperature 38°C, pulse rate 134/min, blood pressure (BP) 80/50 mm Hg, respiratory rate (RR) 44/min and SaO2 95% on room air. The cardiovascular examination revealed a systolic and diastolic murmur 2/6 at tricuspid area, distended jugular veins. No other abnormalities were noted on systemic examination except clean wound at the epigastrium and hepatomegaly of 10cm below the right costal margin. The chest radiography (CXR) showed nodular type of infiltration and cavities suggesting sepsis from staphylococcus. The abdominal ultrasound findings revealed a stasis hepatomegaly. The patient was initiated on lasix, half maintainance intravenous fluid, paracetamol and IV cloxacillin 600mg 8-hourly; and waited for blood culture results.

Afterward, a detailed transthoracic echocardiography was performed and revealed severe tricuspid regurgitation (TR) with rupture of tricuspid corda + septal leaflet prolapsus, vegetations (1.7x1.9cm) on the posterior leaflet of the Tricuspid valve [fig. 3], TR 4/4, Right Ventricle End Diastolic dimensions (RVEDd) 3.3cm, and Left Ventricular End Diastolic dimension (LVEDd) of 3cm. The rest of the cardiac examination was normal. The diagnosis of IE and severe tricuspid regurgitation (TR) was considered. The cardiologist recommended to continue cloxacillin 600mg 8-hourly for 4 weeks, then add gentamicin 60mg 24-hourly for 2 weeks; and hold off TB drugs. Surgery was recommended later to repair the tricuspid valve.

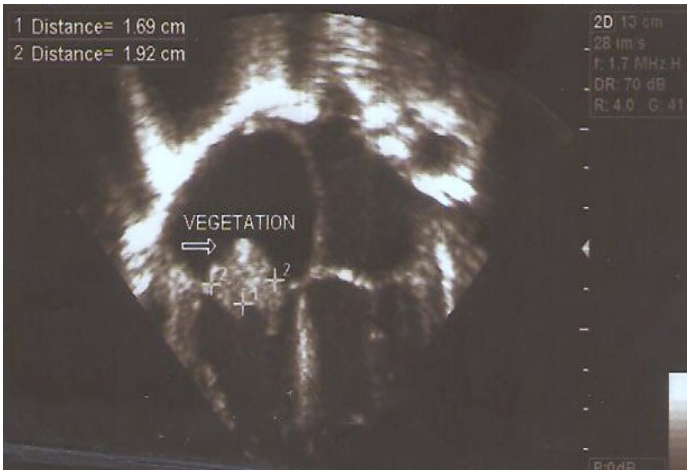

Fig.3: Transthoracic echocardiogram (TTE): Vegetation (1.7x1.9cm) over the posterior leaflet of Tricuspid valve

The investigations revealed: Creatinin 44µmol/L, FBC: WBC 3.6x103/µL, RBC 4.676x106/µL Hemoglobin 10.1g/dl, Hematocrit 35.1%, Platelets 199,000/µL, HIV serology negative and negative blood slide for malaria. Two cultures of blood were performed and both came back positive for staphylococcus aureus sensitive to cefalotine, tetracycline, erythromycin and resistant to vancomycine. Sputum revealed staphylococcus aureus and klebsiella pneumonia sensitive to meropenem and ciprofloxacin.

Either cefalotine or meropenem were available in the hospital.

After six weeks without clinical improvement and after discussion with Infectiologist, the patient was commenced on IV vancomycin during 4 weeks and showed clinical recovery during this period and was discharged on lasix + aldactone and scheduled for surgery to repair the tricuspid valve by visiting cardiac surgeons. He was advised prophylaxis for endocarditis in special circumstances.

Patient 4: A 9-year-old female who came to the KUTH with a history of exertional dyspnea since she was a toddler; with headache, high grade fever, lightheadedness and chest pain for three months. The family history was not significant. On examination, she was asthenic, temperature 38.2°C, pulse rate 136/min, blood pressure (BP) 90/50 mm Hg, respiratory rate (RR) 40/min and SaO2 77% on room air. The cardiovascular examination revealed a hyperdynamic precordium and a holosystolic murmur 2/6 at left lower sternal border. There were also noted digital clubbing and left hemiplegia. Note the patient was referred after consulting the Byumba District Hospital (Rwanda) where she was administered dexamethasone, paracetamol, diazepam, ampicillin and gentamicin without clinical improvement.

Arrived in the Pediatric emergency unit/KUTH, she was started on oxygen 6L/min, half maintainace IV fluids,

Aspirin 100mg 24-hourly, and blood samples drawn for relevant investigations, that revealed: Urea 3.9 mmol/L, Creatinin 39µmol/L, Na+ 131.6 mmol/L, K+ 3.64 mmol/L, FBC: WBC 8.8x109/L, Hemoglobin 18.4g/dl, Hematocrit 57%, Platelets 349,000/µL, HIV serology negative and negative blood slide for malaria. Two cultures of blood were performed and both came back negative.

On day 2 post admission, the patient stated worsening headache, fever and vomiting. On day 3, a pediatric cardiologist performed a detailed transthoracic echocardiography that revealed a 6mm muscular Ventricular Septal Defect (VSD) with right to left shunt [fig. 4.B] (irreversible pulmonary hypertension) and vegetations (6x6mm) at the level of the VSD [fig. 4.A]. The diagnosis of infective endocarditis on VSD complicated by the Eisenmenger syndrome was made and high suspicion of cerebral abscess or embolism was started.

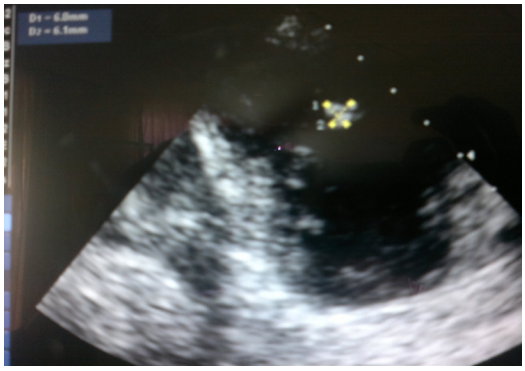

Fig. 4A: Transthoracic echocardiogram (TTE): Vegetation (6x6mm) at the level of VSD

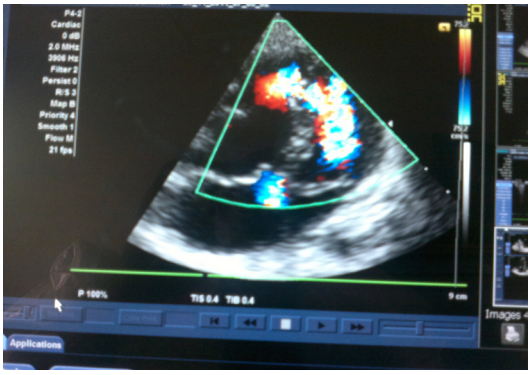

Fig. 4B: Transthoracic echocardiogram (TTE) color Doppler: Right to Left shunt through the VSD

DISCUSSION

Challenges in management of IE do exist in both developed as well as developing settings, although patients with IE in developing countries differ substantially from those in developed countries in some characteristics, including the younger age at presentation, the higher incidence of predisposing cardiac conditions such as rheumatic heart disease or uncorrected congenital heart disease,

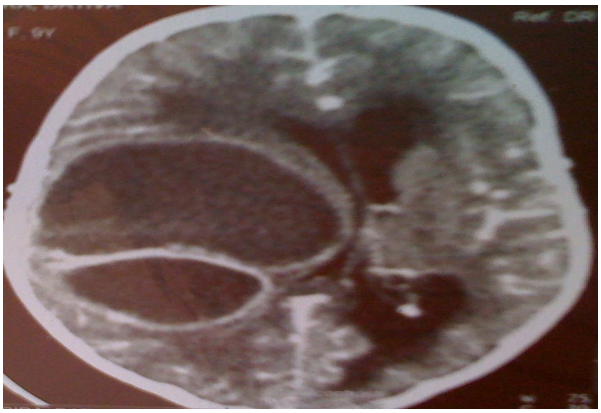

Fig. 4C: CT-Scan of the brain: Abscesses in the right hemisphere

and higher incidence of culture-negative endocarditis. Moreover, the access to new diagnostic technologies and surgical facilities remains difficult in developing countries, thus affecting the prognosis of these patients [4].

Patients 2 and 3 were at relatively lower risk for IE as this condition usually occurs in the setting of either an existing RHD [5] or a predisposing congenital heart disease [6].
Salmonella typhi as cause of endocarditis is very rare, accounting for 1.3-4.8% of cases [8]. Elderly patients are most likely to have endocarditis occurring during salmonella bacteremia. Salmonella have a predilection for heart valves, while atrial thrombus formation, myocarditis, and pericarditis are the usual complications in cases of salmonella endocarditis. However, such complications, which are associated with bad prognosis, were not seen in patient 1.
Salmonella serotypes commonly known to cause endocarditis include S choleraesuis, S typhimurium, S enteritidis, and infrequently the S thompson and S derby serotypes [8]. S typhi has been reported previously as a cause of endocarditis [9, 10, 11, 12]. Infection of the endocardium with multidrug resistant salmonella is associated with poor prognosis [10]; however, the patient 1 made an uneventful recovery after treatment with ceftriaxone and gentamicin. To the best of our knowledge, this is the first case of salmonella typhi endocarditis seen in a pediatric patient with Truncus Arteriosus [TA].

Infection of the right heart valves appears in 5-10% of all cases and is almost always associated with injection drug use (IDU), with more than 80% of tricuspid valve endocarditis (TVE) cases occurring in drug addicts [13]. However, this condition has continued to be a frequent clinical problem even in communities like ours where IDU is relatively uncommon. Both patients 2 and 3 are good examples of IE from spread of a primarily localized infection. TVE in a patient with no predisposing conditions and a structurally normal heart, as occurred in patients 2 and 3 of the present review, is a clinical rarity in which the diagnosis can be quite challenging. The patient 2 was treated with intravenous cloxacillin, and also received

Table 2: Summary of patients reported

Patient	Echocardiography	Blood cultures	Antibiotics	Outcome	Comments
Patient 1	T. A. type IV and vegetations (7.7mm) attached to the left cuspid of the truncal valve	Salmonella Typhi	IV ceftiaxone 1g 12-hourly for 4 weeks + Gentamycine 50mg 24-hourly for 2 weeks	Good	Clinical rarity
Patient 2	Tricuspid Valve with a long filiform vegetation (approx 3.5cm). Normal Heart anatomy elsewhere	Negative (2 consecutive)	IV cloxacilline 850mg TDS for 4 weeks and IV Gentamycin for 2 weeks	Good	S. aureus associated generalized mediastinal infection (pleural, pericardial and endocardial)
Patient 3	Rupture of tricuspid corda + septal leaflet prolapsus, vegetations (1.7x1.9cm) on the posterior leaflet of the Tricuspid valve [*fig. 3*]. TR 4/4.	*staphylococcus aureus*	IV vancomycin	Good	An example of Oxacilline Resistant S. Aureus.
Patient 4	VSD 6mm with right to left shunt, vegetations (6x6mm) at the level of the VSD	Negative (2 consecutive)	Ceftriaxone 1g 12-hourly for 4 weeks, gentamicin 80 mg 24-hourly for 2 weeks, Flagyl 250mg TDS	Poor	Complication with Eisenmenger and Brain abscess.

gentamicin for the first two weeks for its synergistic effect; then cloxacillin was continued for the remaining 4 weeks with favorable outcome. However, patient 3 did not respond to IV cloxacilline but instead showed full recovery on IV vancomycin. The benefit of gentamicin in native valve endocarditis lies in earlier defervescence of fever and the sterilization of blood cultures; otherwise there is no proven survival advantage [14]. Before discharge, temperature, blood counts, coagulation profile, renal, and hepatic functions had normalized without additional interventions. Several studies have reported the benefits of combined intravenous β-lactam + short-course aminoglycoside (2 weeks) therapy in patients with complicated Staphylococcus aureus endocarditis [15, 16]. This confirms our experience with patient 2.

By contrast, glycopeptide (teicoplanin or vancomycin) plus gentamicin-based short-course regimens appeared to be less effective for right-sided S. aureus IE caused by oxacillin-susceptible S. aureus (OSSA) [17]. However, vancomycin was effective for our patient 3. Glycopeptides are intrinsically less active against staphylococci than are antistaphylococcal β-lactams [18, 19]. This might not be the case in our settings but no studies are yet done to guide our discussion.

One of the biggest challenging cases of IE as far as the management is concerned is the so-called Blood-culture-negative-endocarditis (BCNE). Studies have shown that blood cultures are negative in 25% to 31% of all IE cases [20, 21]. Although cases of culture-negative endocarditis are often related to a previous antibiotic therapy (which is inadequate in most cases), a substantial number result from infection with obligates intracellular bacteria, fungi, and fastidious pathogens. To isolate these organisms, they need to be cultured on specialized media, and their growth is slow on artificial culture media [4]. In the present review, blood cultures were request for all the cases, and came positive for the 2 of the 4 patients [Table 2].

The prognosis of tricuspid valve endocarditis is favorable, and most cases respond to antibiotic therapy [22]. However, surgical treatment should be considered for those with severe congestive heart failure, persistent sepsis, development of abscesses, and mycotic endocarditis [23]. Other major indications for surgery will include the presence of large tricuspid valve vegetations (>1 cm) with persistent fever, tricuspid valve insufficiency or pulmonary embolization [23, 24]. The patient 2 did well on medical therapy alone despite the large tricuspid vegetation (3.5 cm) whilst patient 3 required surgery to repair the tricuspid valve.

Moreover, the positive rheumatoid factor for the patient 2 doesn't necessarily rule in JRA, it is an immunologic phenomenon in case of IE [Table1].

Patient 4 is a good example of the risk of both lateness in seeking medical care and late referral to tertiary level. VSD is one of the leading predisposing congenital heart lesions for IE [4]. Delaying to make the diagnosis of a VSD bears lethal consequences as this condition not only predisposes to IE, but also to pulmonary hypertension which, with time, becomes irreversible and causes the relatively benign Left to right shunt to reverse and becomes right to left. This constitutes the Eisenmenger Syndrome – a condition which made the patient 4 hypoxic (O2 saturation of 77% upon admission) and predisposed her to cerebral abscesses.

CONCLUSION

The protean character of the IE, the latency of the cardiac symptoms and close simulation of other disorders combine to render the detection of IE peculiarly difficult. Clinicians should be aware of variety of clinical presentations in patients with IE. We recommend a high index of suspicion of IE in all cases of prolonged fever for patients with any risk factor for IE. As the key investigations (Echocardiography and Serial blood cultures) are not steadily available in most peripheral health facilities (District Hospital level), we strongly recommend early referral to tertiary level for all cases of suspected IE.

Additionally, high suspicion index should be kept in all cases of bacteremia even if at low or no risk. Effort should be put on getting the adequate blood cultures before initiation of antibiotherapy to avoid the high rate of false negative culture. Always refer to Duke's criteria for making the diagnosis of IE and avoid unnecessary antibiotics whenever possible.

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