Cardiology in the Young

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Fever without a source in children with congenital heart disease

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Brief Report

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Abstract

Two paediatric congenital heart disease patients presented with a brief history of low-grade fever without any focal symptoms. Their clinical features and laboratory tests were unremarkable; however, their blood cultures were positive that prompted further work-up. Infective endocarditis should be considered in any paediatric congenital heart disease patient who presents with fever without any other associated clinical features.

Case report

Patient 1: An 11-year-old patient of tetralogy of Fallot and pulmonary atresia, with previous cardiac surgeries, presented with 3 days of intermittent fevers ranging from 37.7 to 38.6°C who defervesced with acetaminophen and ibuprofen. There was no history of rhinorrhoea, cough, chest pain, vomiting, diarrhoea, burning micturition, myalgia, joint pain, or skin rash. His most recent cardiac intervention was dilation of the left pulmonary artery stent at 6.5 years of age and his most recent echocardiogram 3 months prior revealed moderate stenosis with maximal transvalvular flow velocity of 2.4 m/second across the valved glutaraldehyde-fixed bovine jugular vein graft (Contegra, Medtronic, Minneapolis, MN) and moderate regurgitation. His vital parameters revealed heart rate: 100/minute, blood pressure: 118/69 mmHg, temperature: 37.8°C, oxygen saturation: 100%, and his clinical examination revealed grade 2/6 systolic murmur in the left parasternal space. The clinician ordered complete blood count, urine analysis, and blood culture studies that revealed a white blood count of 7400/mcL with 85% neutrophils and normal urinalysis. He was discharged home with a presumptive diagnosis of viral fever. His blood culture study results revealed *Streptococcus gordonii* after 48 hours. He continued to have intermittent fevers responsive to antipyretics in that time period. He was admitted to the hospital and his repeat blood culture study revealed *S. gordonii*. His detailed clinical examination did not reveal a new cardiac murmur, any peripheral stigmata of infective endocarditis, or a specific focus of infection. A transthoracic echocardiogram revealed an increase in the stenosis of the Contegra conduit with a maximal transvalvular flow velocity of 3.5 m/second, severe regurgitation with diastolic flow reversal in the branch pulmonary arteries, and an 8×5 mm mobile vegetation within the conduit. He was diagnosed as a "definite" case of infective endocarditis of the Contegra conduit and initiated on a 6-week course of antibiotics with good response.

Patient 2: A 10-month-old infant with unbalanced atrioventricular canal defect and gastro-oesophageal reflux disease with previous cardiac and gastrointestinal surgeries presented with gastro-jejunal tube leakage and tactile warmth. There was no history of rhinorrhoea, cough, vomiting, diarrhoea, or irritability. She had undergone bidirectional Glenn shunt at 4.5 months of age and her most recent cardiac intervention included balloon dilation of the neo-left pulmonary artery stenosis at 7 months of age. Her most recent echocardiogram 2 months prior revealed unobstructed laminar flow in the Glenn pathway, with some narrowing in the neo-left pulmonary artery, mild right and left atrioventricular valve regurgitation with normal right ventricular systolic function. Her vital parameters revealed heart rate: 164/minute, blood pressure: 114/72 mmHg, oxygen saturation: 74%, and rectal temperature: 38 °C. Her clinical examination revealed erythema associated with formula leakage around the gastrostomy skin site. The clinician ordered complete blood count, serum chemistry, blood culture studies, and she was admitted to the hospital. Her studies revealed a white blood count of 12,200/mcL with 66% neutrophils and normal serum chemistry. Her gastro-jejunal tube leakage was corrected and enteral feeds were resumed. She developed another fever spike of 38°C in the next 24 hours. Her initial blood culture study results revealed *Enterococcus fecalis*. A repeat blood culture study undertaken after the second fever spike also revealed *E. fecalis*. Her urine culture was negative for organisms and her clinical examination did not reveal a new cardiac murmur, any peripheral stigmata of infective endocarditis, or a specific focus of infection. A transthoracic echocardiogram study revealed unobstructed laminar flow in the Glenn pathway with similar degree of neo-left pulmonary artery narrowing, mild right and left atrioventricular valve regurgitation, and a 7×4 mm mobile vegetation attached to the crux of the heart close to the left

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atrioventricular valve. She was diagnosed to have "definite" IE and initiated on a 6 -week course of antibiotics with a good response.

Discussion

A high index of suspicion of infective endocarditis should be considered in congenital heart disease children who present with a non-specific febrile illness, irrespective of the duration of fever, fever pattern, or the resolution of fever with antipyretic medications. Our case series demonstrate that a fever of ≥38°C without any associated focal symptoms in paediatric congenital heart disease patients should be evaluated for infective endocarditis with the inclusion of blood culture studies.

Congenital heart disease is the leading risk factor for infective endocarditis in children.[1] The current diagnosis of infective endocarditis is based on modified Duke's criteria that amalgamate clinical features, microbiological tests, and cardiovascular imaging.[2] The two major criteria in Duke's classification require specific tests such as serial blood cultures and echocardiography to be undertaken to confirm the diagnosis of infective endocarditis.[2] Blood culture is the most important initial laboratory test in the workup of infective endocarditis. Bacteraemia is usually continuous and the majority of infective endocarditis patients have positive blood cultures.[3] Echocardiography is the second cornerstone of diagnostic testing in suspected infective endocarditis cases.[2] Transthoracic echocardiography is usually sufficient for children weighing less than 60 kg to fully understand cardiovascular findings in definite or presumptive infective endocarditis.[4] Patients with congenital heart disease may have had palliative surgeries (shunts and conduits) that are difficult to visualise on transthoracic echocardiography.[5] In these circumstances, transesophageal echocardiography may be more valuable to diagnose paravalvular leakage or dehiscence, left ventricular outflow tract complications, including root abscesses, involvement of the sinuses of Valsalva, and prosthetic valve endocarditis.[4] Vegetations in right ventricular-to-pulmonary artery conduits and prosthetic pulmonary valves, however, are difficult to visualise on both forms of echocardiography and combined studies may give a better yield than individually.[6] In the absence of a well-defined vegetation, a newly identified prosthetic valve or conduit stenosis on echocardiogram in the presence of isolated fever should raise the suspicion for infective endocarditis.[6] Additional tests including combined positron emission spectroscopy-computed axial tomography may facilitate the diagnosis of infective endocarditis affecting right ventricular-to-pulmonary artery conduits in patients with negative echocardiogram studies.[7,8] Other laboratory investigations for fever including elevated C-reactive protein or erythrocyte sedimentation rate, leucocytosis, anaemia, and microscopic haematuria lack specificity and are not included in the current diagnostic criteria of infective endocarditis.[2] Minor criteria including vascular phenomena such as Janeway lesions, splinter haemorrhages, mycotic aneurysms, major arterial emboli, and immune phenomena such as Roth spots, Osler nodes, rheumatoid factor, and glomerulonephritis are rarely seen in children.[5,9] Many children with underlying complex congenital heart disease have pre-existing murmurs that make the recognition of a new murmur difficult.[5]

The signs and symptoms of infective endocarditis in congenital heart disease children are insidious and non-specific.[5] Many children present initially with alternative diagnoses and are already receiving antibiotics.[5,10] Previous studies have failed to reveal specific initial symptoms in children that prompted the primary team to consider infective endocarditis as a possible diagnosis.[11] A discrepancy of more than 50% in the diagnosis of infective endocarditis on admission has been observed in paediatric populations.[5,10] Fever, a minor Duke's criterion, is the only consistent clinical feature reported in retrospective studies of infective endocarditis in congenital heart disease children.[5,10,11] Fever, however, is also the most common chief complaint for children younger than 15 years of age presenting to the emergency department and accounts for 15% of all visits per year.[12] Fever of short duration lasting less than 7 days in healthy children is usually due to self-limiting viral infections (common cold, gastroenteritis) or uncomplicated bacterial infections (otitis media, pharyngitis).[13] Fever without a focus in a paediatric congenital heart disease patient, however, must be approached more diligently than in healthy children as seen in our two patients.

Conclusion

Infective endocarditis should be considered in any paediatric congenital heart disease patient presenting with a fever without any focal symptoms. Addition of blood culture studies to basic investigations will facilitate further workup of infective endocarditis.

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