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Brief Report

Staphylococcus lugdunensis endocarditis in children

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Abstract We report the case of a 2-year-old boy with severe Langerhans cell histiocytosis who had tricuspid endocarditis caused by *Staphylococcus lugdunensis* and required surgery despite appropriate antimicrobial therapy. Through this case and literature review of endocarditis caused by *S. lugdunensis* in children, we highlight pitfalls and mistakes to be avoided in the management of this rare but serious infection.

Keywords: *Staphylococcus lugdunensis*; bacteraemia; infective endocarditis; children

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Case description

A 2-year-old boy was followed-up for severe Langerhans cell histiocytosis for which he received chemotherapy through a totally implantable venous access port. During follow-up, he was evaluated in the emergency department because of a 3-day fever. His general condition was good. His blood test showed a high inflammatory syndrome (C-reactive protein at 218 mg/L), and his chest X-ray showed bilateral alveolar infiltration suggestive of acute pneumonia. Four blood cultures were collected on day 4 of illness, and ceftriaxone was prescribed. Blood cultures were all positive for *Staphylococcus lugdunensis*. The first result was considered as a contaminant. The second led to treatment with vancomycin. The third led to a vancomycin lock on the implantable venous access port, suspecting a catheter-related infection. The child was sent to our university hospital on day 10 of illness. His general condition remained good despite fever. Transthoracic echocardiogram performed on day 11 showed two vegetations on the septal leaflet of the tricuspid valve (largest: 13.1 × 14.3 mm) associated with mild tricuspid regurgitation (grade I/IV). *S. lugdunensis* antibiogram revealed resistance to penicillin G and susceptibility to oxacillin, vancomycin, and aminoglycosides. The treatment was modified as follows: vancomycin was administered for 4 days, with gentamicin; and ceftriaxone was continued for 2 days and then switched to oxacillin. The implantable venous access port was removed on day 13 and was culture positive for *S. lugdunensis*. The blood culture cleared on day 13. Apyrexia appeared on day 15. On assessment, a CT scan showed a bilateral pneumonic lower lobe infarction and a left pulmonary artery embolism. In the following echocardiographies performed twice a week, the predominant tricuspid vegetation increased (21 × 14 mm) and tricuspid insufficiency worsened (grade II/IV). Surgical resection of the vegetations and tricuspid valvuloplasty were performed on day 30 because of the size of the vegetation and the risk of recurrent embolism. Oxacillin was continued for 6 weeks. After 3 years, limited mobility of the tricuspid septal leaflet with mild tricuspid insufficiency was persistent (Fig 1: per operative view).

Materials and methods

Our literature review covered the period between 1988 and 2015 of *S. lugdunensis*-related endocarditis in children using the keywords "*Staphylococcus lugdunensis*", "endocarditis", "children" in PubMed, Medline, and Google Scholar databases. Symptoms at onset, diagnosis delay, co-morbidities, echocardiographic findings, embolic events, antibiotherapy, surgery, and outcome

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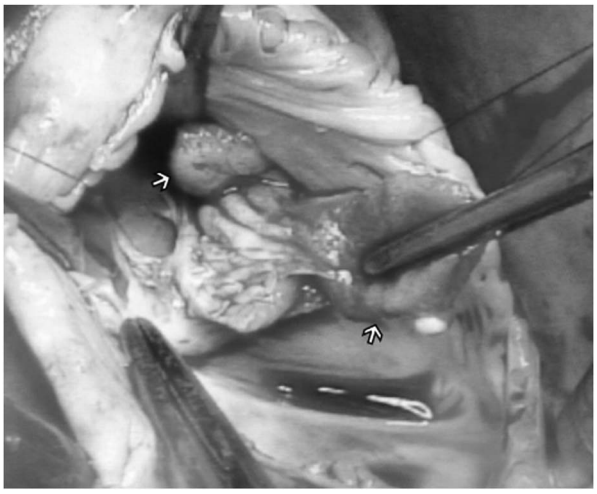

Figure 1.
Per operative view showing 2 vegetations (arrow) on the septal leaflet of the tricuspid valve

were evaluated. Synthesis of data is expressed as medians with quartiles or percentages.

A cursory review for *S. lugdunensis* endocarditis in adults was also undertaken.

Results

In all, nine patients were depicted including our case.[1–6] We excluded two cases because of incomplete data. The median age was 13 years [6.0–15.5] with five males. In all, four patients had CHD, including aortic stenosis in three and a ventricular septal defect in one; two patients had associated conditions including sickle cell anaemia and Langerhans cell histiocytosis. The median duration of symptoms before diagnosis was 3.4 weeks (with a range from 2 to 6 weeks). No infection gateway was identified in five cases. Out of seven patients, five had positive blood cultures for *S. lugdunensis*, susceptible to penicillin and/or oxacillin. All were susceptible to vancomycin and aminoglycosides. In one case, *S. lugdunensis* was primarily misdiagnosed by routine technique. Echocardiographic findings showed large vegetations in all cases, with aggressive damage of the leaflets. Embolic events were documented in three cases (42.8%). Medical treatment was not sufficient although adequate antibiotherapy was conducted. Surgery was needed in all cases but was not performed in one patient because of neurological involvement. This patient died from brain herniation (Table 1).

Discussion

S. lugdunensis is a novobiocin-susceptible, coagulase-negative *Staphylococcus*, a commensal of the skin and mucous membranes. In contrast to other coagulase-negative *Staphylococcus*, it has virulence factors similar to *Staphylococcus aureus* – toxin secretion, resistance to lysozyme, adhesion via binding protein, biofilm formation, etc. –leading to a destructive course with abscess formation and embolus.[7] *S. lugdunensis* is responsible for serious infections including endocarditis or toxic shock syndrome. Owing to these virulence factors, it is recommended to search for other locations in case of bacteraemia with *S. lugdunensis*[8] and not considering it as a contaminant when at least two blood cultures are positive.

It has been reported that *S. lugdunensis* bacteraemia is associated with endocarditis in 50% of cases,[8] is responsible for 18% of infective endocarditis due to coagulase-negative *Staphylococcus*,[7] and accounts for 1.1% of infective endocarditis.[9] These numbers are probably underestimated because *S. lugdunensis* can be missed by routine identification procedures or can produce clumping factors and then be misidentified as *S. aureus*. Some authors have recommended sequencing the 16S ribosomal DNA specific to *S. lugdunensis* in patients with endocarditis,[10] especially when blood cultures are negative to avoid missing this bacterium. At present, optimisation of identification methods is helpful to increase the rate of *S. lugdunensis* detection. In our case, ignorance of these virulence factors was deleterious because of delay in antibiotics adaptation and the search for secondary locations. In endocarditis, *S. lugdunensis* affects cardiac structures with an aggressive course and a propensity for embolisation.

Less than 100 cases of *S. lugdunensis* endocarditis have been reported in adults. A study showed that *S. lugdunensis* mainly affected the native valves,[9] and had high complication rates including heart failure, abscess formation, and embolism with a mortality rate of 42%. *S. lugdunensis* is usually susceptible to β-lactam agents, aminoglycosides, macrolides, and vancomycin, although antimicrobial resistance has been described even during treatment;[11] however, despite appropriate antimicrobial therapy, *S. lugdunensis* infection progresses, and surgery is often required to improve the prognosis. Some authors have shown that surgery is necessary in 51% of cases, and patients treated with antibiotics and surgery had a better prognosis than those with medical treatment alone.[9] Those authors have thus recommended early surgery.

Although our paediatric review reported only seven cases, the evolution was marked by a propensity for large vegetations, valve destruction, and embolic events despite appropriate antibiotherapy and the need for surgery as described in adults.

Table 1. Clinical and microbiological features, treatment, and outcome of the seven children with *Staphylococcus lugdunensis* endocarditis identified in our review of the last 28 years.

References	Age	Sex	Past medical history	Symptoms	Duration of symptoms before diagnosis	Portal of entry	Number of positive blood cultures	Antibiogram	Initial antibiotic treatment	Adapted antibiotic treatment	Echocardiographic findings	Embolic events	Surgery	Outcome
1	16y	M	Congenital aortic stenosis	Fever and headache	2 weeks	Skin abrasions by a gardening tool	6	Penicillin, oxacillin, cefazolin, erythromycin, rifamycin, and gentamicin sensitive	Oxacillin, gentamicin	–	Vegetations (16.6 × 6.7 mm) in RA and LV septum, and on the MV	None	On day 28: debridement and repair of the MV and TV leaflets, closure of VSD, and reconstruction of the aortic outflow tract	Alive
2	7y	M	Aortic bicuspid valve stenosis	Fever, tiredness, sweating episodes, lethargy	4 weeks	Unknown	4	First one: penicillin sensitive Second one: penicillin and oxacillin resistant	Penicillin, gentamicin	Vancomycin, gentamicin	Thickening of bicuspid AV, no vegetation. Aortic insufficiency during follow-up, and then vegetation, worsening of aortic regurgitation, and more thickening of AV	None	On day 20: Ross procedure	Alive
3	13y	M	None	Fever, rigors, night sweats, fatigue, nausea, vomiting, weight loss	6 weeks	Unknown	3	Penicillin, aminoglycosides, and vancomycin sensitive	Ceftriaxone, gentamicin, and vancomycin	Flucloxacillin, gentamicin, vancomycin	Thickened MV leaflets, severe MR; 2 vegetations (7 × 8 mm and 3 × 6 mm) on mitral valve leaflets. Mild TR, mild left atrial and ventricular dilatation	Embolic infarction in the left middle cerebral artery territory	After 6 weeks: MV replaced by a tissue Perimount valve	Alive
4	5y	F	Sickle cell anaemia, congenital VSD	Fever, abdominal pain, diarrhoea, vomiting	2 weeks	Unknown, but did have dental decays	3	Penicillin and oxacillin resistant; aminoglycosides, vancomycin, and rifamycin sensitive	Vancomycin, ceftriaxone	Rifamycin, gentamicin, vancomycin	Small perimembranous VSD. Large oscillating vegetation (16.6 × 6.7 mm) on the TV. Flailed chord and severe TR. Vegetation (14 × 6 mm) on the right ventricular side of the VSD rim	None	On day 32: patch closure of the VSD, repair of the TV, and closure of a patent foramen ovale	Alive
5	17y	F	None	Fever, headache	3 weeks	Unknown	3	Penicillin and aminoglycoside sensitive	Gentamicin, oxacillin	Vancomycin, gentamicin	Vegetation (17 × 5 mm), several other vegetations on mitral valve. Severe MR with MV perforation. Left atrium and left ventricular dilatation	Thrombosis of a mycotic cerebral aneurysm, complicated by ischaemic and haemorrhagic infarction. Bilateral tibial and pedal mycotic aneurysm	Not performed because of severe neurological involvement	Death
6	15y	M	None, undiagnosed bicuspid AV	Fever, flu-like illness, chest pain, shortness of breath	2 weeks	Unknown	3	Sensitive to oxacillin	Vancomycin	Vancomycin, gentamicin, switched to nafcillin and gentamicin	Bicuspid AV with a vegetation (6 × 8 mm) on its left cusp, perivalvular abscess posterior to the AV with extension to the mitral annulus and into the left ventricular outflow tract	None	On day 10: debridement of the aortic annular disruption, replacement of aortic root and AV, reconstruction of the left outflow tract	Alive
This study	2y	M	Langerhans cell histiocytosis	Fever	2 weeks	TIVAP	4	Penicillin resistant; aminoglycosides, macrolides, and vancomycin sensitive	Ceftriaxone	Ceftriaxone, vancomycin, gentamicin	2 vegetations on the septal leaflet of the TV (the largest 13.1 × 14.3 mm), progressing (21 × 14 mm) associated with TR (grade II/IV)	Bilateral pneumonic lower lobe infarction and a left pulmonary artery embolus	On day 30: resection of vegetations and tricuspid valvuloplasty	Alive

AV = aortic valve; F = female; LV = left ventricle; M = male; MR = mitral regurgitation; MV = mitral valve; RA = right atrium; TIVAP = totally implantable venous access port; TR = tricuspid regurgitation; TV = tricuspid valve; VSD = ventricular septal defect; y = years of age

Conclusion

Blood cultures should be repeated even if one is positive for *S. lugdunensis* to confirm true infection, which should lead to search for secondary locations, particularly endocarditis. In endocarditis, early surgery associated with antimicrobial therapy is highly recommended. Delaying surgery could worsen the outcome because of the progression of cardiac damage and high risk for embolic events.

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Conflicts of Interest

None.

Ethical Standards

The authors assert that all procedures reported comply with the ethical standards of the Helsinki convention, and consent for publication was obtained from the patient's family.

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