# Neurological complications in children with infective endocarditis: report of two cases and review of literature

# Les complications neurologiques chez les enfants présentant une endocardite infectieuse : A propos de 2 cas et revue de la littérature

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## Summary

Infective endocarditis (IE) is a life-threatening condition in the pediatric community. Here we report two cases of infective endocarditis in children revealed by neurological complication to highlight the importance of the diagnosis and the challenge of management of this complication. The first case about a 10-year-old boy presented to the emergency department with a right hemi-body deficiency in a febrile context and the second one about a 7-year-old girl admitted to the pediatric emergency department for a fever that has been evolving for 15 days associated with headaches. The IE diagnosis was made according to cardiac and multimodal imaging, and laboratory exams.

IE in children is still a challenging condition. Congenital heart disease continues to be the main predisposing risk factor. Appropriate medical management and early surgical intervention have to be undertaken to prevent complications and achieve a better outcome.

## Keywords

infective endocarditis, children, echocardiography, neurological complications, congenital heart disease.

## Résumé

L'endocardite infectieuse (EI) est associée à une lourde morbi-mortalité chez les enfants.

Nous rapportons ici deux cas d'EI chez l'enfant révélés par des complications neurologiques afin de souligner l'importance du diagnostic et le défi de la prise en charge de cette entité.

Le premier cas concerne un garçon de 10 ans qui s'est présenté aux urgences pour une déficience de l'hémicorps droit dans un contexte fébrile et le second d'une fillette de 7 ans admise aux urgences pédiatriques pour une fièvre évoluant depuis 15 jours associée à des céphalées. Le diagnostic de l'EI a été posé selon les données l'imagerie cardiaque et multimodale, et les examens biologiques.

L'EI chez l'enfant reste un challenge diagnostique et de prise en charge. Les cardiopathies congénitales restent le principal facteur de risque prédisposant. Une gestion médicale appropriée et une intervention chirurgicale précoce doivent être entreprises pour prévenir les complications et améliorer le pronostic.

## Mots-clés

endocardite infectieuse, enfant, échocardiographie, complications neurologiques, cardiopathie congénitale.

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## INTRODUCTION

Infective endocarditis (IE) is a life-threatening condition in the pediatric community, that occurs less often in children than in adults with an annual incidence rate ranging from 0.05 to 0.12 cases per 1000 pediatric admissions (1).

Congenital heart disease has been described as the main predisposing factor. Rheumatic heart disease has declined in developed countries, but it remains a significant cause of IE in our country.

Complication occurrence can be the first manifestation of the IE. Neurological complications are life- threatening and not common. It may include seizures, stroke, brain abscess, hemorrhage, diffuse vasculitis, meningitis and intracranial aneurysms. Currently, the exact incidence of neurological complications in children with IE is still not well established and most reported cases focus on the adult population.

Here we report two cases of infective endocarditis in children revealed by neurological complication to highlight the importance of the diagnosis and the challenge of management of this complication.

## CASE N°1

A 10-year-old boy presented to the emergency department with a right hemi-body deficiency in a febrile context. At the age of eight, he had been diagnosed with a sub valvular aortic stenosis with a planned surgery. Physical examination on admission revealed that he had a fever at 39c; he was somnolent, eupneic, with a stable hemodynamic state. He had a 4/6 systolic murmur, without signs of heart failure.

No skin lesions were present. He had a right hemi-body deficit and his neck was rigid. A cerebral CT scan showed diffuse cerebral edema, stigmata of meningeal hemorrhage, and two intraaxial hemorrhagic edematous lesions above the tentorial area. Cerebral magnetic resonance imaging (MRI) showed a nonsurgical left frontal hematoma, subarachnoid and meningeal hemorrhage of low abundance, sub- and supratentorial microbleeds and micro addition images suggestive of mycotic aneurysms in the right superior frontal sulcus. The investigation was completed by a cardiac ultrasound which showed a7 mm mobile vegetation in left ventricular outflow tract appended to the the aortic valve. The laboratory testing revealed a hyperleukocytosis with a predominance of polynuclear cells, a biological inflammatory syndrome, and two blood cultures were positive for Staphylococcus aureus Methi S. The diagnosis of cerebral hemorrhagic vascular accident following a rupture of a mycotic aneurysm complicating an aortic IE due to Staphylococcus aureus Methi S is retained. An antibiotherapy by ampicillin, oxacillin, gentamycin was started, followed by oxacillin and ciprofloxacin according to the results of the antibiogram. The evolution was marked by the occurrence of repetitive seizures. The patient was treated by Levetiracetam and phenobarbital with a progressive improvement of the motor deficit and the absence of recurrence of convulsive seizures. A radiological assessment of extension showed on thoraco-abdomino-pelvic CT scan a focal site of splenic infarction, a small splenic effusion and a localized nephritis. Apyrexia was obtained after 10 days of the introduction of antibiotherapy. The last 2 HC were negative. The biological testing was normal, and the radiological control was marked by the disappearance of vegetation on the aortic valve on cardiac ultrasound and a slight regression of cerebral hematomas on cerebral MRI. Antibiotherapy was continued for 6 weeks. After 1 year, the child had a minimal weakness of the right lower limb and discrete handwriting disorders. MRI control showed resolution of the cerebral hematoma and the patient undergo surgical resection of the sub valvular membrane.

## CASE N°2

A 7-year-old girl was admitted to the pediatric emergency department for a fever that has been evolving for 15 days associated with headache. She has a history of recurrent angina. On admission, she had fever at 39°c. On cardiovascular examination, a grade four harsh pansystolic murmur at the lower left sternal border was detected. Laboratory testing on admission showed an inflammatory syndrome with a CRP level of 190 mg/l with hyperleukocytosis with a predominance of polynuclear cells. An emergency Transthoracic echocardiography (TEE) showed a severe mitral regurgitation by rupture of cordage with a magma of vegetations on the two mitral leaflets (Figure 1) A cerebral and thoraco-abdomino-pelvic CT scan showed a 4 cm cerebral mycotic aneurysm with a splenic infarct. A series of blood cultures was positive for alpha hemolytic streptococcus. High dose pf penicillin G 200 000 UI/kh/d was started with diuretics (furosemide 1 mg/kg) and an angiotensin converting enzyme inhibitor (captopril 0.2 mg/kg).

After 48 hours of antibiotic, the evolution is marked by an alteration of the respiratory state with use of non-invasive ventilation and increase in diuretic doses. The patient underwent emergency surgery with a mitral valve replacement by a mechanical prosthesis n°17. The postoperative course was simple. The cerebral CT scan 10 days postoperative showed a regression of the size of the mycotic aneurysm under appropriate antibiotherapy.

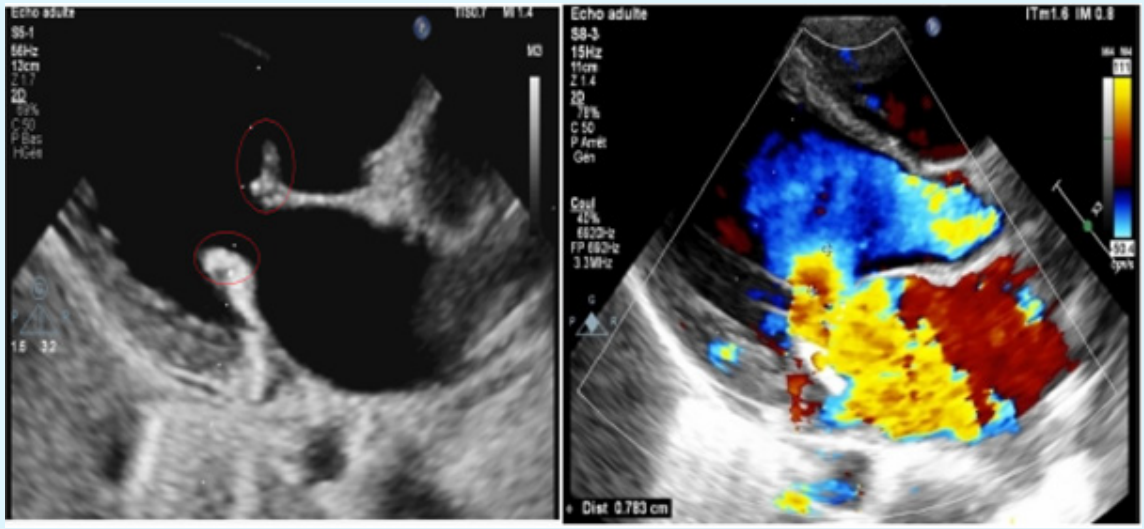


**Figure 1.** mitral valve IE with mobile vegetations on the two leaflets associated with severe regurgitation by cordage rupture.

## DISCUSSION

Despite improvement in medical management, infective endocarditis (IE) remains a serious disease that may affect children with and without preexisting cardiac conditions with significant morbidity and mortality; in recent reports, the overall frequency of endocarditis among children and a shift toward those with previous cardiac surgery appear to have increased in the last years (1).

Congenital heart disease (CHD) has been described as the main predisposing factor of IE in children (2,3). Ahmadi and al reported that 76.5% of patients < 18 years with IE had a history of CHD or cardiac surgery (3). Gupsta and al showed in a Nationwide Inpatient Sample (NIS) database, during 11 years, that 81.4% of children aged 19 years old hospitalized for IE had congenital heart disease (2). Another large study conducted in Norway at the Clinical Teaching Hospital for Congenital Heart Malformations between 1994 and 2016 showed a much higher incidence among patients with congenital heart disease, i.e., 2.2/10,000/year. Most of these patients (75%) had severe congenital heart diseases (CHDs) and had undergone open heart surgery during the last year prior to IE diagnosis setting (4) The type of congenital heart disease influences IE risk. In a large population-based cohort of children with CHD, the most common CHD group among children with IE were cyanotic CHD lesions, present in 34% of case, followed by Endocardial cushion defects (ASD (16%) and VSD (15%)) and left sided lesions. Our first patient had left ventricular outflow obstruction by sub valvular membrane (5).

Improved survival of patients with CHD and development of surgical options has implications on the prevalence of IE among this population. In fact, surgical repair with no residual shunt is supposed to reduce or even eliminate the risk for endocarditis in children with ventricular and atrial septal defects or patent ductus arteriosus 6 months after surgery. However, surgery itself, including valve and prosthetic material implantation, grafts patches, central vascular catheters, intravenous alimentation, and days the patient resides in the intensive care unit, may be important risk factors for the development of IE.

Approximately 50% of children with IE complicating CHD have had previous cardiac surgery, particularly palliative shunt procedures or complex intracardiac repairs (6).

Because the prevalence of rheumatic heart disease has declined in developed countries, it has now

become relatively unusual for children with IE from the developed world to have underlying rheumatic heart disease. But It continue to be a public health problem in developing countries. Our second patient had a rheumatic mitral valve insufficiency.

Viridans-type streptococci and Staphylococcus aureus remain the leading causative agents for endocarditis in pediatric patients: In a large study by Day et al. Staphylococci or Streptococci were the predominant IE pathogens identified in more than 90% of their culture-positive cases (7)

The diagnosis of IE is complex in children. The Duke criteria were primarily tested in adult patients and few studies have evaluated the diagnostic performance of the current criteria for the diagnosis of pediatric IE (8,9).

The modified Duke classification is more sensitive in diagnosing IE in children (10).

Neurological complications of IE represent a serious damage. A recent study published by AlBassri and al, analyzing neurological complications specifically in children with IE found that they could occur in up to a quarter of cases. The authors identify Possible risk factors including lower body weight, left-sided valvular lesion, and higher levels of inflammatory markers (CRP). Stroke was the most common neurological complication encountered in this study (11).

The incidence of stroke has been reported to be 6% in pediatric populations145 and 11% in those of all ages with CHD (12). Intracranial hemorrhage is one of the severe dramatic neurological complications and can complicate rupture of mycotic cerebral aneurysms (13).Adults' studies have shown increased risk for embolization with large vegetations >10 mm. Recently, this finding was supported in a pediatric study(14). Other nonspecific complications include meningitis or brain abscess.

The underlying CHD may significantly increase the risk of neurological complications: a study conducted by Walker et al. in which they reviewed 18 patients with stroke due to confirmed IE, found that 15 of them (83%) had left-sided heart lesions (15). The role of inflammatory biomarkers in the prediction of the prognosis of IE has been investigated in many studies.A large cohort study published by Mohanan emphasized the role of CRP levels in the prediction of adverse outcomes of IE, including neurological complications (16). Both of our two patients had a high CRP level and showed severe neurological complications.

The principles of treatment of pediatric endocarditis are similar to those for treatment of adult endocarditis (1). Regarding surgical indications, recommendations are mostly an extension of recommendations of experts for management of adult IE. Several studies have shown that early surgery can be performed in pediatric population with low morbidity and mortality and improves the overall outcome (17). In a recent review of children treated for IE at the Texas Heart Institute in Houston, early surgery was performed in 61% of patients, with most of these surgeries occurring within 7 days and half within 3 days of diagnosis (18). For ou r first patient , considering the presence of intracerebral hemorrhage, the surgical management was postponed until the hematoma was fully resolved .For our second patient, an urgent surgery was performed on day 3 of the admission.

## CONCLUSION

IE in children is still a challenging condition. Congenital heart disease continues to be the main predisposing risk factor but rheumatic fever continue to be a public health problem in our countries and lead to a consistent number or pediatric IE. Despite advances, a high suspicion is needed for diagnosis because the onset of the IE might be insidious, and complications such as ischaemic stroke can be the first sign of the disease. Appropriate medical management and early surgical intervention have to be undertaken to prevent complications and achieve a better outcome.

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