CASE REPORT

Cortical hyperostosis, rare adverse effect of prostaglandin

Ng Rui Lun, MRCPCH, Koay Han Siang, MRCPCH, Mohammad Tamim Jamil, MPAEDS

Department of Paediatric Cardiology, Penang Hospital, Georgetown, Penang, Malaysia

SUMMARY

We describe here an infant girl with ductal dependent complex cyanotic heart disease, who required prostaglandin infusion for a total of five months prior to Blalock-Taussig shunt procedure. Her alkaline phosphatase activity was raised after seven weeks being on prostaglandin and only dropped to the normal range seven days after discontinuing prostaglandin infusion. During our review at five months old, her limbs were grossly swollen and radiographic examination showed dense periosteal reaction in the long bones. Based on the clinical findings and investigations, she was diagnosed to have cortical hyperostosis, which is an uncommon side effect of prostaglandin. She underwent right Blalock-Taussig Shunt procedure successfully with no major complications. Unfortunately, she succumbed to infection two months after surgery.

INTRODUCTION

Prostaglandin is the medication of choice used to maintain patency of ductus arteriosus in newborns with ductal dependent congenital heart diseases. Many clinicians are familiar with the common side effects of prostaglandin infusion such as apnoea and respiratory depression. Prostaglandin induced bony changes is a relatively uncommon adverse effect but important for clinicians to recognise the features and hence to avoid unnecessary tests and treatment.

CASE REPORT

An infant girl was cyanosed immediately after birth and required oxygen supplementation. In the Penang Hospital (PH), Malaysia, a detailed transthoracic echocardiography performed by the paediatric cardiologist confirmed the diagnosis of complex cyanotic heart disease (dextrocardia, atrial septal defect, tricuspid atresia, transposition of great arteries, right sided aortic arch, pulmonary atresia and both branches of pulmonary artery were supplied by patent ductus arteriosus). Prostaglandin infusion was commenced at the dose of 5ng/kg/min to maintain the patency of ductus arteriosus.

She was planned for the Blalock-Taussig Shunt procedure, but the surgery was delayed due to the infant having recurrent chest infections. At seven weeks old, primary physician noticed an increased serum alkaline phosphatase level of 523IU/L with normal calcium and phosphate levels. Serum Vitamin D and parathyroid hormone levels were unavailable. A probable diagnosis of Vitamin D deficiency was made and she was treated with vitamin D supplementation. Despite treatment, the alkaline phosphatase level continued to rise with values ranging between 1000 and 2000IU/L.

At five months old, she was transferred to the PH for surgical procedure. On examination, all her four limbs were grossly swollen especially both her legs. Radiological studies showed dense and solid periosteal reaction predominantly affecting the long bones (Figure 1 and 2). Both vitamin D and parathyroid hormone levels were normal.

She underwent right Blalock-Taussig Shunt procedure successfully with no major complications and the prostaglandin infusion was stopped immediately after the surgery. Serum alkaline phosphatase level fell to the normal range seven days after discontinuing prostaglandin infusion. Unfortunately, she succumbed to infection two months after surgery and radiograph was still showing similar radiological changes.

DISCUSSION

Prostaglandin is an important medication in the management of ductal dependent congenital heart disease. It acts as a temporary bridge to maintain the patency of ductus arteriosus before subsequent surgery (e.g., Blalock Taussig Shunt) or procedure (e.g., Patent Ductus Arteriosus Stenting) is carried out. Short term usage of prostaglandin predisposes patients to some of the common adverse effects such as apnoea, respiratory depression, pyrexia, skin flushing and diarrhoea.[1,2]

Prostaglandin induced bony changes is a less common side effect[1-3] and the severity is related to the dosage and duration of prostaglandin infusion[3,4] The pathogenesis of hyperostosis due to prostaglandin is not fully understood though prostaglandin can stimulate both bone formation and resorption.[4] Prostaglandin is metabolised rapidly in the lungs and liver via the first pass metabolism. However, this process is reduced in infants with cyanotic heart disease, especially those with decreased pulmonary blood flow. This will in turn result in elevated circulating prostaglandin in the systemic circulation and hence aggravating the side effects.

Most of the patients with prostaglandin induced cortical hyperostosis remain asymptomatic with few presented with painful and swollen limbs.[2,4,5] Similarly, our infant had lower limbs swelling which was only visible at 5 months of age.

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Corresponding Author: Ng Rui Lun
Email: rolandnrl@yahoo.com

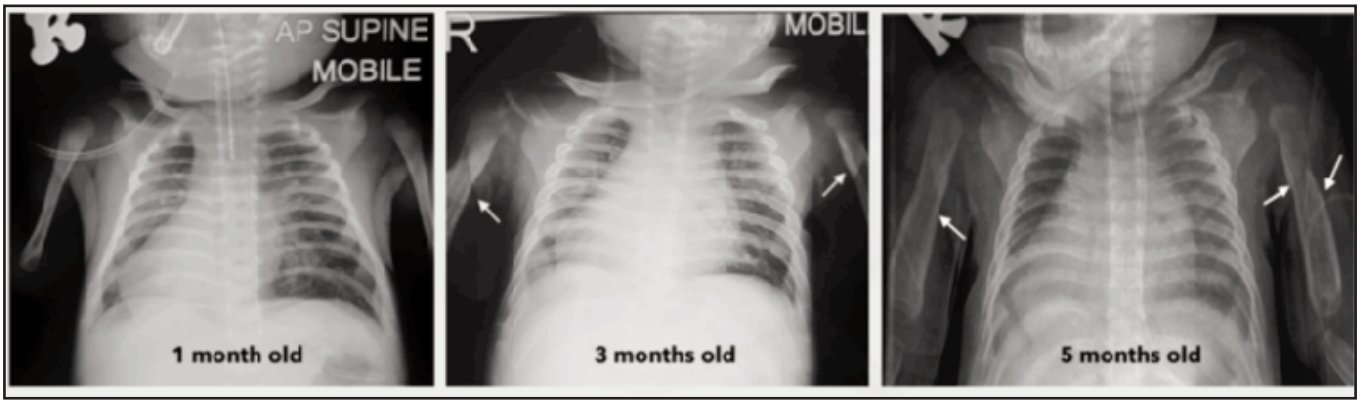

Fig. 1: Radiological changes of cortical hyperostosis (dense and solid periosteal reaction) were not present during the early month (at 1 month old) but became more prominent in the subsequent months (at 3 and 5 months old). These were marked with arrows.

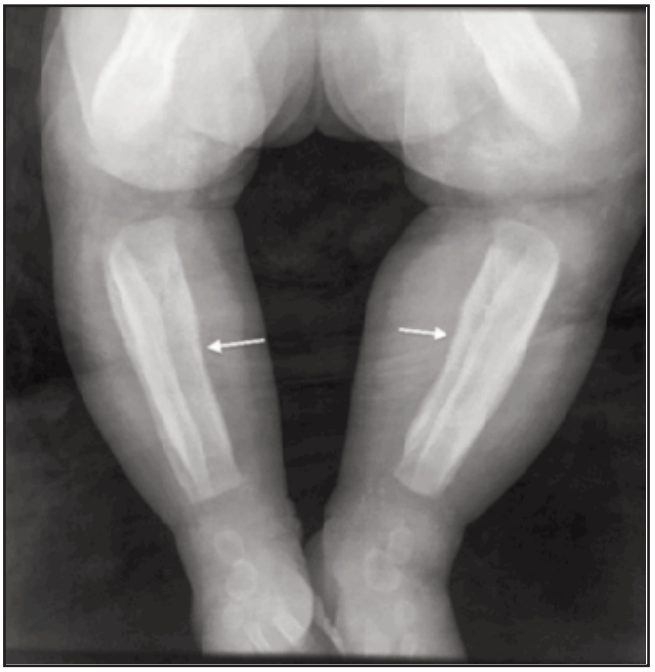

Fig. 2: Radiograph of the lower limbs showed evidence of cortical hyperostosis as marked with arrows.

Diagnosis of cortical hyperostosis secondary to infusion of prostaglandin is based on clinical findings and exclusion of other serious differentials by radiological and laboratory investigations. Radiological appearance can be visible as early as within nine days on prostaglandin infusion[2] and it is crucial to differentiate it from other conditions that shared similar radiographic findings, i.e., Caffey's disease, congenital syphilis, scurvy and hypervitaminosis A.[3,4] From earlier studies it is noted that resolution of radiological changes can be delayed to as long as six weeks to three months after cessation of prostaglandin infusion.[2,5] We retrospectively reviewed the serial radiographs and found that the radiological changes, that were suggestive of cortical hyperostosis, were already present in the patient from three months of age. Regrettably, we were unable to see the resolution of radiographic changes since the patient expired two months post-surgery.

Serum alkaline phosphatase is a useful marker to detect periostitis as radiological presentation is often delayed.[1,3,4] In fact, normalisation of alkaline phosphatase levels often precede radiological resolution which was observed in our patient. Fortunately, this condition is benign and reversible once prostaglandin is discontinued.

CONCLUSION

Cortical hyperostosis due to prolonged prostaglandin infusion is a reversible condition and serum alkaline phosphatase is an effective marker for monitoring this condition. Clinical awareness of this entity will potentially avoid unnecessary investigations and treatment.

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