

# Primary Hypertrophic Osteoarthropathy in a 20-month Girl: A Rare Cause of Clubbing

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## ABSTRACT

Clubbing is a common finding in many gastrointestinal, cardiac, and pulmonary diseases as well as some malignancies. Primary hypertrophic osteoarthropathy (PHOA) is a rare entity when clubbing occurs in conjunction with periosteal bone reaction and some other manifestations but without any secondary cause for it. Very few cases have been reported in the paediatric population. We report a case of a 20-month girl who was brought to medical attention because of bone pains and digital clubbing. Investigations revealed periosteal reaction in long bones on x-rays. The rest of the work-up including studies for possible causes of clubbing was insignificant. The girl was labelled as PHOA and managed with Zoledronate. She responded well to the medication. This case aims to emphasise the need to keep PHOA in the list of differentials of clubbing.

**Key Words:** Clubbing, Hypertrophic osteoarthropathy, Paediatric.

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## INTRODUCTION

Children with chronic disease can demonstrate clubbing of terminal phalanges and have an association with periosteal reaction and arthritis, in which case, it is called secondary hypertrophic osteoarthropathy (HOA). Primary HOA (PHOA) is a rare, multisystemic disorder in which HOA occurs without any underlying cause.<sup>1</sup> This disease entity, also known as Touraine-Solente-Gole Syndrome and pachydermoperisotosis, is characterised by three main features which include; clubbing of the digits, thickening, and coarsening of the skin of the face and scalp as well as the periosteal reaction of the bones.<sup>2</sup> The diagnosis is usually made using typical clinical and radiographic findings but genetic studies can also be carried out. PHOA generally presents at the age of adolescence and with a male predominance.<sup>3</sup> This case is unique as the patient presented at a very young age with clubbing and periosteal reaction.

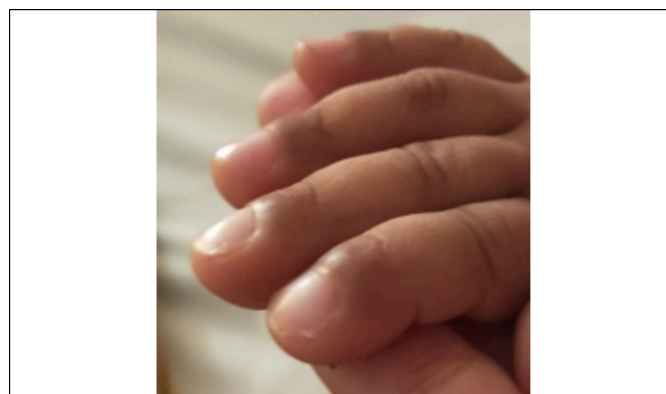
## CASE REPORT

A 20-month girl presented to the paediatric clinic for evaluation of bone pains in the lower limbs and poor weight gain. Bone pains were non-radiating, occurred throughout the day and were so severe that these made it difficult for the child to bear weight on legs. There was no preceding history of trauma, fever, rash, abdominal distension, diarrhoea, joint pain or swelling.

Parents also noticed that she was slow to gain weight and was shorter than other children of her age. The nutritional history was satisfactory with adequate caloric intake and no history of recurrent infections was found.

She was born to parents of consanguineous marriage via caesarean section. She was the fourth and youngest amongst her siblings who were all alive and healthy. Any history of similar features was not present in the family. She had normal developmental milestones and was vaccinated up-to-date.

On examination, she weighed 9 kg, and had a stature of 64 cm, both of which were below 3<sup>rd</sup> centile for age and gender. Her occipitofrontal circumference (OFC) was 47 cm falling at the 50<sup>th</sup> centile. She had coarse facies, a prominent forehead with wide open anterior fontanelle measuring 4.8 cm. There was Grade IV clubbing and bulbous tips of fingers and toes without any cyanosis (Figure 1). BCG scar was present. Rest of the systemic examination including respiratory and cardiovascular systems was unremarkable.



**Figure 1: Clubbing and bulbous tips of fingers.**

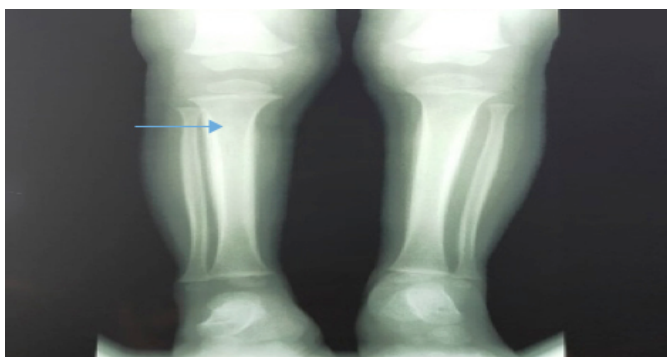
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Investigations revealed haemoglobin of 7.7 g/dl, white cell count was  $13 \times 10^9/l$ , and platelet count was  $713 \times 10^9/l$ . Peripheral film showed microcytic hypochromic picture but no atypical cells. Inflammatory markers including CRP and ESR were normal. Serum urea, creatinine, and electrolytes were also within normal limits. Values of alanine aminotransferase (ALT) and alkaline phosphatase (ALP) were 12 U/L and 489 U/L, respectively (reference ranges for age: ALT <33-41 U/L and ALP <390 U/L). She had normal bone biochemistry with serum calcium of 9.6 mg/dL, serum magnesium, 2.2 mg/dL, and serum phosphorous, 4.8 mg/dL. Vitamin D level was 43.01 ng/ml. Thyroid function tests revealed TSH of 1.65 uIU/ml and FT4 of 1.41 ng/dL. Serum ferritin was very low with a value of 7.85 ng/mL. Her celiac serology was negative. Radiographs of hands and wrists showed narrowed tapering of distal phalanges of fingers with soft tissue swelling but no evidence of rickets. Chest x-ray was normal. X-rays of long bones revealed periosteal bone reaction (Figure 2).



**Figure 2: Typical periosteal bone reaction, most evident in the tibia (arrow).**

Her clinical evaluation and investigations were all negative for possible causes of clubbing, i.e. there were no symptoms to suggest a respiratory or cardiac cause such as chronic cough, breathlessness or cyanosis. Also, she had no contact with a tuberculosis patient. BCG scar was present. There was no heart murmurs and chest x-ray was normal. Echo was not done since it was not clinically warranted. The absence of history of chronic diarrhoea or blood in stools ruled out gastrointestinal (GI) causes of clubbing. Celiac disease can present without obvious GI signs, so it was ruled out by negative celiac serology. Moreover, a normal thyroid function helped us exclude thyroid acropachy as a reason for her clinical presentation.

The child was treated for iron deficiency anaemia with iron supplements and was initially given a trial of NSAIDs for symptoms of HOA, but she did not improve. However, she responded well to Zoledronate from Bisphosphonates class of drugs. It was given as first dose at 0.012 mg/kg by slow intravenous injection, followed by 3 monthly injections at 0.025 mg/kg.

On 3-month follow-up, there was improvement in bone pain and height gain of 2 cm.

## DISCUSSION

The exact mechanism of PHOA is not well understood. An impaired metabolism of prostaglandin E2 is thought to be the cause of this disease process.<sup>4</sup> In the clinical presentation of

PHOA, not all features are necessarily present in all cases. The finding of clubbing is universally present. In 20-40% of cases, arthritis is present commonly involving knees, ankles, and wrist joints. Other features may variably occur including coarse facial features due to thickening of facial and scalp skin, seborrhoea, increased sweating, and long bone periostosis.<sup>5</sup>

In this case, the child presented with bone pains, coarse facies and clubbing. Upon evaluation, no underlying pathology for these symptoms was found. It was labelled as PHOA based on digital clubbing with thick finger pads, coarse facies and periosteal reaction seen on long bone X-rays. The periosteal reaction of long bones as a diagnostic feature was similarly reported in 2009 by Zanon *et al.*<sup>6</sup> However, presentation at an early age and lack of joint involvement are unique features in this case, which is contrary to the study described by Kamruzaman *et al.*<sup>7</sup> X-rays of the extremities are usually the initial modality of investigation in HOA, since periostosis, the cardinal feature of the disease can be easily detected on these as it was picked up in this case.<sup>8</sup> Genetic and molecular diagnosis of peripheral blood leukocytes is specific and diagnostic. The genes involved include *HPGD* and *SLCO2A1*.<sup>9</sup> However, genetic testing could not be done in this case due to the resource limitation.

It is postulated that *HPGD* genetic mutations lead to increased levels of prostaglandin E2 due to changes in its metabolism. Hence, drugs that reduce prostaglandin production can be used as a treatment options. However, conventional NSAIDs such as ibuprofen do not cause substantial improvement in symptoms in patients of PHOA. Selected COX-2 inhibitors such as etoricoxib have been reported to be helpful in relieving pain. Bisphosphonates, such as pamidronate, given intravenously is also one of the treatment options. Other options include corticosteroids and immunomodulators.<sup>10</sup> Surgical management of clubbing and bone deformities may also be a consideration.<sup>10</sup> The present patient did not show good response to NSAIDs but responded well to Zoledronate.

In conclusion, PHOA is a rare and overlooked cause of clubbing in children. The patient in this case presented very early with disease manifestations with negative family history, highlighting the significance of suspecting PHOA as an important cause of clubbing.

### PATIENT'S CONSENT:

Informed consent was obtained from the patient's parents to publish this case.

### COMPETING INTEREST:

The authors declared no competing interest.

### AUTHORS' CONTRIBUTION:

MA: Conception, drafting, approval, and agreement.

SW: Interpretation of data for the work, revision, approval, and agreement.

AZ: Conception, revision, approval, and agreement.

MAQ: Analysis, drafting, approval, and agreement.

All authors approved the final work for publication.

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