Familial Congenital Digital Clubbing - Report of Two Siblings

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Digital clubbing can be a striking physical finding. Etiology of clubbing in most of the time is secondary to some systemic illness. Familial clubbing is a rare occurrence and incidence or prevalence of such occurrence is not known. We are presenting two cases (brother and sister) with digital clubbing in all the four limbs. Systemic examination and laboratory investigation were normal. Parents were assured about the benign nature of the disease and the children were kept under regular follow up.

**Key Words:** Digital clubbing, Idiopathic, Familial

Clubbing is a bulbous enlargement of the distal portion of terminal phalanx due to proliferation of subungual connective tissue. Most of the time, it is considered as one of the signs of definite organic disease and is most commonly associated with chronic pulmonary or congenital cyanotic cardiac disorder. But clubbing may occur in the absence of demonstrable intrathoracic abnormality which is known for decades. Clubbing as a defect of congenital origin, unassociated with any definable organic cause, has been observed later. The familial tendency of this congenital abnormality has been reported in only a few instances. Mishra et al reported a family with isolated clubbing of fingers and toes in four generations [1]. As, familial digital clubbing is a rare occurrence; we are reporting two siblings who have isolated clubbing without any underlying systemic illness.

**CASE REPORT**

Two siblings; brother and sister, born out of nonconsangunious marriage, presented with swelling of tip of fingers and toes (fig 1 and 2). Brother was 8 years old and sister was 10 years old. Age of father was 36 years and that of mother was 32 years. Mother noticed these changes in the toes first and later in the fingers around 4-6 months age in both the cases. No other family members had similar complaint. Antenatal period was uneventful with routine medications in both the times. Both the children did not have any shortness of breath, exercise intolerance, recurrent loose stools, jaundice or any other respiratory symptom.

![Figure 1 - both legs showing clubbing of toes](image_url)
illness. Oxygen saturation on room air was 97% and 99% for brother and sister, respectively.

Figure 2- Both hands showing clubbing of fingers

Chest X ray and echocardiography were normal in both the cases. Hemoglobin of sister was 12.2 gm% and that of brother was 11.4 gm%. Complete blood count, renal function tests, liver function tests, calcium, phosphate and alkaline phosphatase were normal in both the cases. HIV ELISA test was also negative in both the children. As, both the children were asymptomatic, well thriving and had no systemic disease; diagnosis of familial digital clubbing was made and parents as well as patients were counseled regarding the benign nature of the illness.

DISCUSSION

Digital clubbing can be an isolated finding or may occur as a part of some systemic illness. Lovibond first described a criterion for the diagnosis of finger clubbing. Lovibond [2] defined the “profile sign” of the thumb, or Lovibond’s angle, made by the nail as it exits the proximal nail fold. The profile sign of greater than 180° could be used to differentiate true clubbing from other conditions such as simple nail curving and paronychia, which retained an angle closer to 160 degrees. Curth et al [3] described that the fingers of members of a family affected by familial clubbing were notable for a marked decrease in the angle between the back surface of the middle phalanx and that of the terminal phalanx, from 160° in control subjects to 145° in affected patients; they called this angle the “modified profile angle.” Among the various hypotheses for the pathophysiology of clubbing, the most promising is that of megakaryocyte / platelet theory of Dickinson and Martin [4]. Megakaryocytes are normally fragmented into platelets in the lungs; however, processes that disrupt normal pulmonary circulation, e.g. chronic lung inflammation, bronchial tumors, or intracardiac right-to-left shunts, allow megakaryocytes to enter the systemic circulation. There, their large size causes them to become impacted in the fingertip circulation with resultant release of platelet-derived growth factor (PDGF). This PDGF promotes growth, vascular permeability, monocyte and neutrophil chemotaxis, leading to an increased number of vascular smooth muscle cells and fibroblasts, all of which are seen in the pathology of clubbing.

Congenital digital clubbing is usually symmetrical and bilateral, but different fingers and toes may be involved to varying degrees. Some may be spared, but the thumbs are always involved [5]. Though, very rare it is found in some families. In our cases, as both the children were asymptomatic, well thriving with normal laboratory investigation, possibility of congenital and familial form was kept. Familial form of clubbing has an autosomal dominant or recessive form of inheritance. In our cases, no other family members have clubbing except both the siblings. Occurrence of two or three cases in one generation suggests autosomal recessive inheritance. However, we could not confirm it by genetic studies as these could not be done due to financial constraints.

Tariq et al have found a homozygous missense mutation in 15-hydroxyprostaglandin dehydrogenase (HPGD) in a family affected with autosomal recessive variant of isolated congenital nail clubbing. HPGD gene encodes a member of the short chain dehydrogenase family enzymes involved in regulation of prostaglandin (PG) metabolism and mutations in them results in reduced metabolic clearance of PGE2 due to diminished cellular uptake [6]. This results in major production of connective tissue in nail bed and abnormal function of nail matrix. Genetic testing for HPGD mutation and measurements of PGE2 may become an important diagnostic tool in patients with unexplained clubbing. In addition to the gene HPGD, the SLCO2A1 gene can cause digital clubbing. Mutations in the HPGD gene are responsible for autosomal recessive primary
hypertrophic osteoarthropathy and mutations in the \textit{SLCO2A1} gene are responsible for autosomal recessive primary hypertrophic osteoarthropathy [7].

In cases with bilateral clubbing, a complete history, physical examination and laboratory investigation will allow the clinician to reach at a probable diagnosis. Sometimes, despite extensive laboratory evaluation and imaging, no cause for digital clubbing is found and the patient must be reassured of the harmless nature of idiopathic clubbing [8]. There are no published reports indicating what percentage of patients presenting with clubbing will eventually prove to have idiopathic clubbing. The prognosis of clubbing is completely dependent on the underlying process. If the primary process is identified and treated, clubbing usually reverses completely. Indeed, the only recognized treatment for clubbing is the treatment of the primary lesion; however, with the recent progress in our understanding of the pathogenesis of clubbing, antiplatelet and anticytokine therapy may prove to be useful in cases of idiopathic or familial clubbing.

**CONCLUSION**

Present case report highlights the fact that despite its usual serious significance, clubbing of the fingers is not always a pathognomonic sign of severe visceral disease. Digital clubbing could be of familial nature as seen in our cases where digital clubbing was most likely had autosomal recessive pattern.

**REFERENCES**