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CASE REPORT

Idiopathic digital clubbing

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Introduction

Digital clubbing is defined as the focal enlargement of the terminal phalanx, resulting in an increased curvature of the nail plate. First described by Hippocrates in 5 BC, clubbing has different degrees of severity. This ranges from grade 1, which shows an increased fluctuation of the nail bed, to grade 5, which shows an evident increase in the extremity with thickening of the terminal phalanx associated with longitudinal striations on the fingernail. Although the grading system has been proposed, it bears no relationship to the severity of the underlying cause (Sarkar et al, 2012).

Case report

An Asian man first presented with atypical chest pain at 14 years of age. On examination he was found to have significant clubbing of his hands and feet. Ten years later he was referred for further investigations and underwent chest radiography, echocardiography and an exercise tolerance test, all of which were normal. Subsequent lung function tests and testing for tuberculosis showed no abnormality. Further rheumatological and routine blood tests were normal and no cause was identified for his clubbing. He was diagnosed with likely idiopathic congenital clubbing (Figure 1). He remains well at 28 years of age, with no new symptoms to explain his initial presentation.

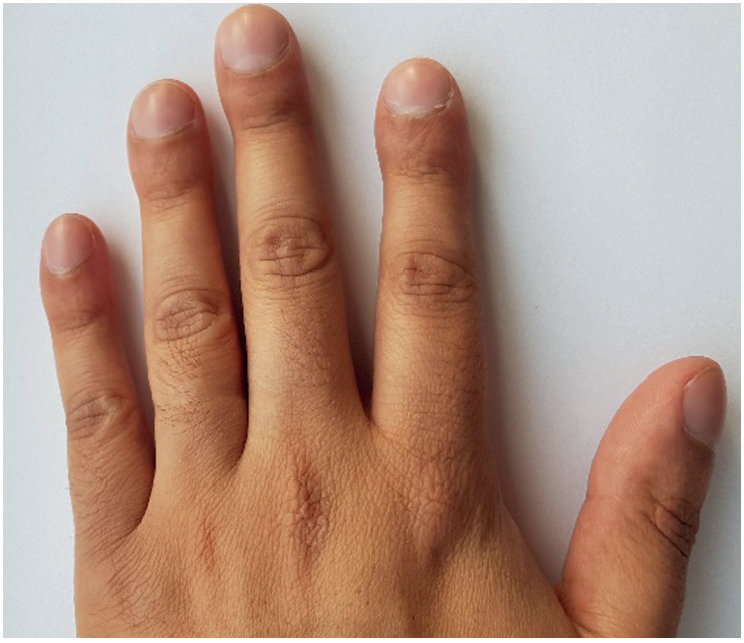

Figure 1. Clubbing of the fingers – patient is 28 years old.

Discussion

The mechanism of clubbing has been hypothesised to arise from an increase in capillary density at the nail bed, arising from an upregulation of platelet-derived growth factor (PDGF) and vascular endothelial growth factor (VEGF), both produced by peripheral megakarocytes. This increased vascularity and permeability ultimately causes connective tissue changes (Marrie and Brown, 2007). The underlying physiological condition is frequently driven by hypoxia, although this does not explain idiopathic presentations or those not associated with hypoxia. While multiple associated conditions ranging from cardiovascular, gastrointestinal and respiratory systems are recognised (Table 1), a unifying mechanism has always proved elusive (Dubrey et al, 2016).

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Table 1. Common causes of digital clubbing	
Cardiac	Subacute endocarditis
	Atrial myxoma
	Cyanotic congenital heart disease
Respiratory	Lung cancer
	Bronchiectasis
	Idiopathic pulmonary fibrosis
	Cystic fibrosis
	Empyema
Gastrointestinal	Cirrhosis of the liver
	Inflammatory bowel disease
	Coeliac disease
	Primary biliary cirrhosis
Other	Hypertrophic osteoarthropathy
	Thyroid acropachy

Learning points

- Digital clubbing may be congenital.
- Digital clubbing is associated with several different organ systems and disease types, including infections, cancers, chronic inflammation and endocrine.
- A unifying mechanism for the clinical phenomena of digital clubbing remains elusive.

More recently, the gene 15-hydroxyprostaglandin dehydrogenase (HPGD), which normally encodes for a member of the short-chain non-metalloenzyme alcohol dehydrogenase protein family, was found to also be responsible for the production and regulation of prostaglandins, specifically prostaglandin E_2 (PGE_2) (Tariq et al, 2009). Mutations in this gene result in primary autosomal recessive hypertrophic osteoarthropathy (clubbing) (Diggle et al, 2010). PGE_2 is involved in bone reabsorption and formation (Tariq et al, 2009). It is hypothesised that chronically elevated levels of PGE_2 contribute to the pathogenesis of congenital clubbing.

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