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ISOLATED PROGRESSIVE CONGENITAL LEFT THUMB MACRODACTYLY: CASE REPORT AND LITERATURE REVIEW

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ABSTRACT:
Isolated progressive macrodactyly belongs to a heterogeneous group of congenital overgrowth syndromes, resulting in enlargement of all tissues localized to the terminal portions (fingers or toes) of a limb. The aim of this case report is to create further awareness among physicians on this rare clinical entity and present a short review of the literature. We present the case of a 10-year-old Nigerian girl with a history of progressive overgrowth of left thumb since birth. The patient's facies and body habitus were normal without hemihypertrophy. Anthropometric measurements of the child's hands, revealed an overgrowth of the left thumb compared with the right. The child had no café-au-lait spots or any other skin lesions. The radiograph of the hands revealed increase in size of both soft tissue and phalangeal bones (enlongated and broadened) of the left thumb. A diagnosis of isolated progressive left thumb macrodactyly was made and the patient was referred to the orthopaedic surgeon for surgical intervention. The child and her parents suffered psychological distress. Isolated progressive macrodactyly is very rare but it is cosmetically displeasing to the child, resulting in psychological distress.

Key words: Congenital, localized gigantism, macrodactyly, overgrowth syndrome, Nigeria.

INTRODUCTION:

Macrodactyly is a rare group of congenital anomaly characterized by the enlargement of one or more of the fingers or toes in the absence of other lesions. The overgrowth involves all the digital structures (nail, tendons, intrinsic tissue, joints and phalanges) in the true variety [1]. False macrodactyly presents as hypertrophy of primarily one tissue type [2]. The incidence in one active paediatric orthopaedic clinic in USA was 0.035%, with a slight male preponderance (male: female ratio 1.2:1) [3]. Macrodactyly represents 0.9% of all congenital anomalies of the upper limb [4]. There is no familial inheritance pattern and it

usually presents as an isolated, non-syndromic condition [5].

According to the classification proposed by Upton [6], there are four types of macrodactyly: Type I is macrodactyly with lipofibromatosis of nerve, either static or progressive subtype; Type II is macrodactyly associated with neurofibromatosis; Type III has associated hyperostosis; and Type IV is associated with hemihypertrophy. A true macrodactyly may also be associated with other syndromes such as Proteus, Beckwith-Wiedermann and Klippel-Trenaunay-Weber syndromes [1,7]. In the static type the enlarged digit is present at birth but its growth is proportional to the growth of the child's other fingers whereas in the progressive type, it may or may not be present at birth but the growth of the involved digit is in excess compared to the growth of the child's other fingers [3]. Isolated macrodactyly belongs to a heterogeneous group of congenital overgrowth syndromes, resulting in enlargement of all tissues localized to the terminal portions of a limb, typically within a 'nerve territory' (nerve-territory-oriented macrodactyly) [8,9]. The classic terminology for this clinical entity is lipofibromatous harmatoma of nerve or type I macrodactyly [9]. The affected peripheral nerve itself is enlarged both in circumference and length. In the hand, the reported clinical distribution of macrodactyly was as follows: thumb 9%, index finger 20%, middle finger 34%, ring finger 22% and small finger 15% with slight male preponderance 1.0:0.66 [10]. In that study, there was no laterality or gender difference and only 5 of 33 cases analyzed involved isolated digits [10].

The pathogenesis of isolated macrodactyly has not been fully elucidated. It has been associated with lipofibromatosis of peripheral nerve, most commonly the median nerve [11-14]. In Lebanon, Fares et al [11] reported a case of an 18-year-old boy with neural fibrolipoma of the median nerve causing progressive macrodactyly of the left thumb. Recently, isolated macrodactyly has been linked to activating somatic mutation in the phosphatidylinositol-3-kinase catalytic alpha (PIK3CA) gene and a new term referred to as "PIK3CA-Related" Overgrowth Spectrum (PROS) has been proposed to accommodate the broad range of clinical manifestations in these patients [15]. Using whole-exome sequencing, Rois et al [9] identified somatic mutations present in the affected nerve of a single patient. In that study, they confirmed a novel mutation in PIK3CA in the patient's affected nerve tissue. In the same study, immunocytochemistry confirmed AKT activation in cultured cells from the nerve of a patient with macrodactyly. They stated that isolated congenital macrodactyly is caused by somatic activation of the PI3K/AKT cell-signaling pathway and is genetically and biochemically related to other overgrowth syndromes [9]. In another study in USA, it was found that a developmental cytokine, pleiotropin (PTN) was significantly overexpressed across all samples

obtained from patients with macrodactyly [5]. The authors stated that the function of PTN correlated closely with the clinical characteristics of macrodactyly [5].

Some clinical conditions have been associated with macrodactyly. Kalen et al [3] reviewed 167 cases and reported one case with neurofibromatosis, one with adrenal tumour and hemihypertrophy, one with epidermal naevus, one with multiple connective tissue nevi, and one with epiphysealis hemimelica. In addition, macrodactyly involving both hands and one foot associated with cutaneous haemangiomata has been reported [7]. In Brazil, a 15-year-old boy with macrodactyly co-existing with skin hypertrophy was reported by de Almeida Jr et al [16].

Let us consider the natural history of macrodactyly. With advancing age, the enlarged curved phalanges lead to osteophyte formation which causes early joint degenerative disease and pain [7]. In the affected digit, bony growth continues until epiphyseal closure but soft tissue enlargement may continue into adulthood [17]. With time, the digit enlarges and motion decreases, resulting in functional impairment [3]. According to Kalen et al [3], the basis of the functional impairment is that the soft tissue hypertrophy on the palmar surface of affected digit causes the distal interphalangeal joints to be hyperextended, preventing flexion of the digits, resulting in impairment of pincer movement where the thumb is the finger affected.

The purpose of this case report is to create further awareness among physicians on this rare clinical entity and present a short review of the literature.

CASE REPORT:

A 10-year-old Nigerian girl was referred to the Endocrinology and Metabolism Clinic of the University of Benin Teaching Hospital (UBTH) with a history of enlarged left thumb since birth. The left thumb progressively became larger (out of proportion to the right thumb) as she got older. There is no associated pain. Family history was negative. The school mates and neighbours ridiculed her and this prompted parents to seek for medical attention for their child. The patient had no other medical problem.

The patient's facies and body habitus were normal. Her anthropometry showed: weight 25.5kg (10th percentile), height 137cm (50th percentile), arm span 143cm, upper segment:lower segment ratio 0.9 and body mass index 13.6kg/m2 (3rd percentile). The left thumb was enlarged but non-pulsatile. The measurements of the fingers were as follows: The left thumb measured 9cm in length (measured from proximal crease to tip of finger) and 8.7cm in circumference. The right thumb measured 4.5cm in length and 5.5cm in circumference. Further examination of the hands revealed macrodactyly of left thumb with

hyperextension and abduction (Figure 1). The left thumb nail was enlarged compared to the right (Figure 1).

The other fingers and toes were not affected. Neither syndactyly nor polydactyly was present. The child had no café-au-lait spots or any other skin lesions. The remainder of the physical examinations was unremarkable. The radiograph of the hands revealed increase in size of both soft tissue and phalangeal bones (enlongated and broadened) of the left thumb (Figure 2).

Abdomen/pelvic ultrasound did not reveal any abnormality. A diagnosis of isolated progressive congenital left thumb macrodactyly was made (corresponding to type I macrodactyly). Subsequently, the patient was referred to the orthopaedic surgeon for surgical management.

Fig. 1: A photograph of the hands of a ten-year-old girl showing macrodactyly of left thumb

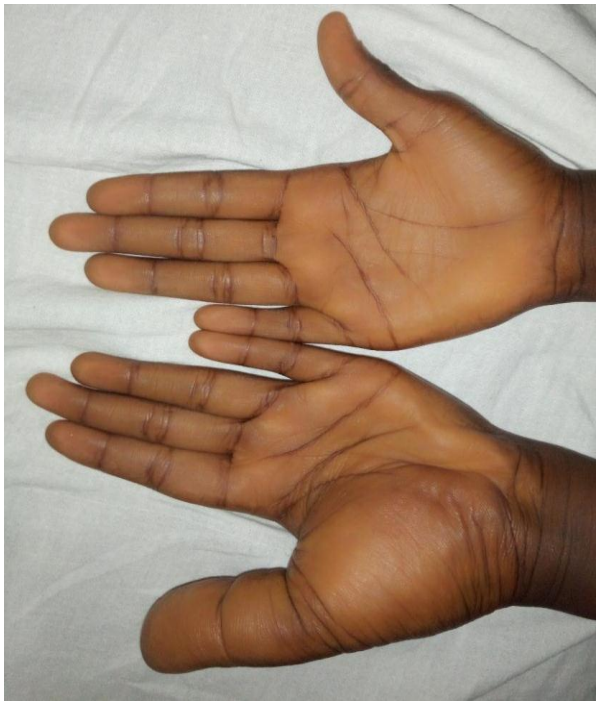
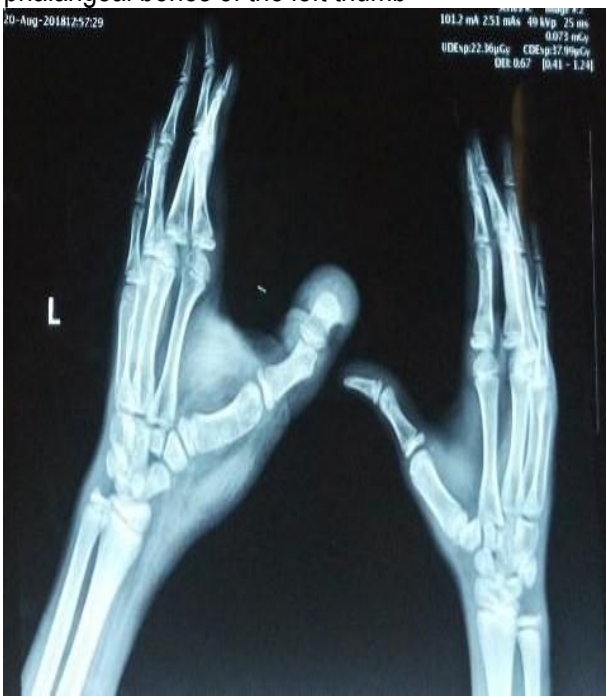


Fig. 2: A radiograph of the hands of a ten-year-old girl showing increase in size of both soft tissue and phalangeal bones of the left thumb



DISCUSSION:

As in our patient, localized gigantism is often recognized at birth but begins to cause problem as the child grows. In the index case, the diagnosis of isolated progressive congenital left thumb macrodactyly was made based on history, physical examination and radiologic findings. This is in consonance with method of

diagnosis employed in other studies [18,19]. Increase in size of the phalanges has been noted as a primary feature of the anomaly with or without the involvement of the metacarpals [20]. Our patient had evidence of overgrowth in the left thumb when compared to the right thumb. The increase in size of the affected digit involved both the soft tissues and the phalangeal bones as demonstrated in our patient's left hand radiograph. Although macrodactyly is a rare clinical entity, its diagnosis is straightforward. The rare nature of the condition is evident from the report of a retrospective review involving an active paediatric orthopaedic clinic in USA where only 21 cases were seen over a period of 15 years [21]. In United Kingdom, 41 cases were seen over a period of 17 years [10]. The report of a study conducted at one of Nigeria's National Orthopaedic Hospitals revealed that of the 43 patients with anomalies of the hand only one had macrodactyly of the middle finger [22], further supporting its rarity. Indeed, it has been reported that macrodactyly is rarer in Blacks than Caucasians but the author did not provide any explanation for this racial difference [23].

Some of the clinical features in our patient are in keeping with those reported in literature in patients with macrodactyly. The index case had soft tissue hypertrophy on the palmar surface of affected digit as well as over the thenar eminence, hyperextension and abduction of the affected left thumb. The thumb nail is also enlarged. The patient did not have difficulty with performing pincer movement (able to pick up a pen from the table, using thumb and index finger), suggesting that functional impairment of the affected thumb is yet to set in. The apparent preservation of function may be explained by the report of Yang et al [24]. In that study, the authors concluded that although the morphology and function of the median nerve was impaired, the unaffected ulnar nerve partially compensated for the lost function of the affected median nerve under certain conditions. The results of some studies indicate that in macrodactyly, the index finger is the most frequently affected of all the fingers [3,23] but it was the thumb that was affected in our patient, supporting the recognized heterogeneity of clinical phenotypes [9]. Our patient presented at the age 10 years but in one Nigerian study, the reported peak age at presentation was 0-11 months [22].

The negative family history in our patient is in keeping with the sporadic nature of isolated macrodactyly. Both the patient and her parents suffered psychological distress because of ridicule by school mates and neighbours. This prompted parents to seek for medical attention for their child. This scenario is not surprising because concealing macrodactyly of the finger is difficult.

The anatomic extent of involvement varies from one or more digits to entire hand or foot. In addition, the rate of growth differs from patient to patient [5,9]. According to the report of Rois et al [9], the observed phenotypic

variability of PI3K-AKT-associated overgrowth syndromes might be due to the timing of the mutational event during development as well as tissue specificity, leading to distinctly different disease syndromes.

Although isolated progressive congenital macrodactyly is a benign condition, it is deforming and cosmetically displeasing to the child, siblings and parents. The reports of other studies have cited displeasing cosmetic appearance as the main reason for seeking medical attention [19]. Given that macrodactyly exhibits varying clinical phenotypes, there is no defined treatment algorithm. Therefore, treatment is usually decided on individualized basis. According to Carty et al [25], the treatment principles in the index case are those of provision of an esthetically acceptable hand with pincer capacity for gripping objects. In the same report, the authors stated that because of the uncertainties surrounding the outcome of surgical intervention, the International Federation of Societies for Surgery of the Hand described macrodactyly as an 'unsolved condition'. In a retrospective study involving 32 patients in Birmingham Children's Hospital, Hardwicke et al [10], concluded that in vast majority of cases the functional and cosmetic outcomes were good, with good patient acceptance. The paediatric patient with macrodactyly may require additional surgical procedures because the deformity will continue to grow. However, early treatment will provide for the affected child the benefit of functional and cosmetically appealing hand.

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