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Concomitance of types D and E brachydactyly: a case report

T. TÜLAY KOCA[1], F. ÇILEDAĞ ÖZDEMIR[2]

[1]Malatya State Hospital, Physical Medicine and Rehabilitation Clinic, Malatya, Turkey
[2]Inonu University School of Medicine, Department of Physical Medicine and Rehabilitation, Malatya, Turkey

Abstract. – Here, we present of a 35-year old female diagnosed with an overlapping form of non-syndromic brachydactyly types D and E with phenotypic and radiological signs. There was observed to be shortening in the right hand metacarpal of 3rd and 4th fingers and left hand metacarpal of 4th finger and left foot metatarsal of 4th toe. There was also shortening of the distal phalanx of the thumbs and thoracic kyphosis. The syndromic form of brachydactyly type E is firmly associated with pseudo-hypopthyroidism as resistance to pthyroid hormone is the most prominent feature. As the patient had normal stature, normal laboratory parameters and no psychomotor developmental delay, the case was classified as isolated E type brachydactyly.

Key Words:
Brachydactyly, Skeletal disorders, Pseudo-hypoparathyroidism.

Introduction

Brachydactyly (short digits) is a general term describing extremity malformations characterised by bone dysostosis, with the meaning of disproportional shortness in the fingers and toes which develops due to smallness or absence of metacarpals, metatarsals or phalanxes. Just as brachydactyly may be an isolated malformation, it may also be a part of a complex malformation syndrome[1]. Isolated brachydactyly was first classified in 1951 by J Bell[2] according to phenotypic characteristic digit and bone involvement.

The case examined here in the light of relevant literature is of a 35-year old female patient who presented with complaints of back pain with isolated brachydactyly which was classified as a combination of D and E types.

Case Report

A 35-year old female patient presented with complaints of back pain. In the first physical examination, it was determined that the patient, who had kyphotic posture and brachydactyly in the 3rd and 4th finger of the right hand, in the 4th finger of the left hand and clinodactyly with brachdactyly in the 4th toe of the left foot (Figures 1 and 2). It was learned that these deformities had been present since birth and a younger sister had similar shortness of the fingers. There was no known systemic disease. The menstrual cycle was regular and there was no known history of osteoporosis. In the laboratory tests, the results of full blood count, sedimentation, parathormon (PTH), vitamin D, calcium, alkaline phosphatase (ALP), thyroid function tests (TFT) and urine tests were all within normal limits. In the radiological examination, shortness of the metacarpal was seen in the 3rd and 4th fingers of the right hand and in the 4th finger of the left hand (Figure 3). In addition, there was bluntness and shortness in the distal phalanx of the thumb on both hands. In the lateral thoracolumbar radiograph, wedging in the thoracic vertebrae and increased kyphosis were determined.

Discussion

Brachydactyly is a general term describing extremity malformations characterised by bone dysostosis, with the meaning of disproportional shortness in the fingers and toes which develops due to smallness or absence of metacarpals, metatarsals or phalanxes[1]. Previous studies have shown that bone morphogenic (BMP) pathways play a key role in the normal development of digits and their joints and that these pathways are associated directly or indirectly with the genes of brachydactyly disease[3].

Just as brachydactyly may be an isolated malformation, it may also be a part of a complex malformation syndrome[1]. Brachydactyly was

Corresponding Author: Tuba Tülay Koca, MD; e-mail: tuba_baglan@yahoo.com

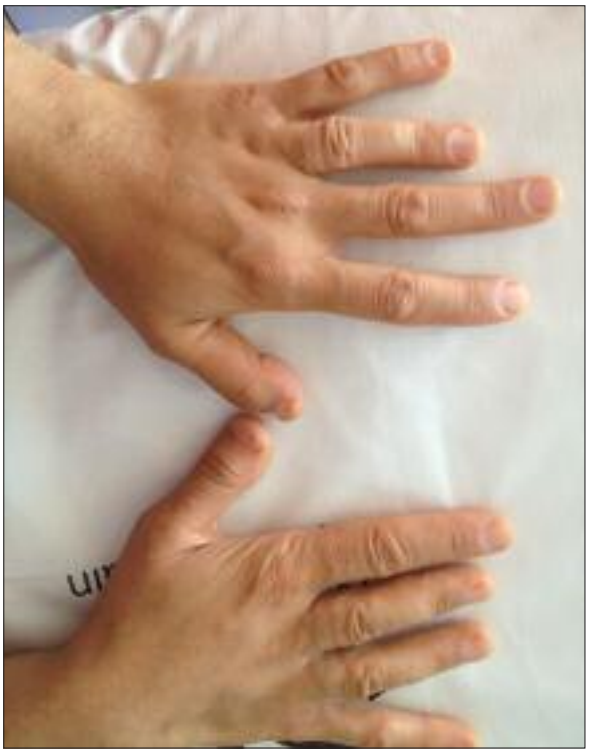

Figure 1. Shortness in the 3rd and 4th fingers of the right hand, 4th finger of the left hand and widening in the distal phalanx of both thumbs can be seen.

first classified in 1951 by Bell[2] according to phenotypic characteristics of digit and bone involvement.

According to this classification, type A, shortness in the middle phalanxes of the digits; type B, absence of or shortness of the mid and distal phalanxes of the digits together with deformity in the thumbs and big toes; type C, shortness in the mid and proximal phalanxes of the 2nd and 3rd fingers, hypersegmentation in the proximal phalanxes and ulnar deviation in the 2nd finger, type D: shortness or widening in the distal phalanx of the 1st digit of the hand or foot, type E: shortness in one or more metacarpal or metatarsal[1].

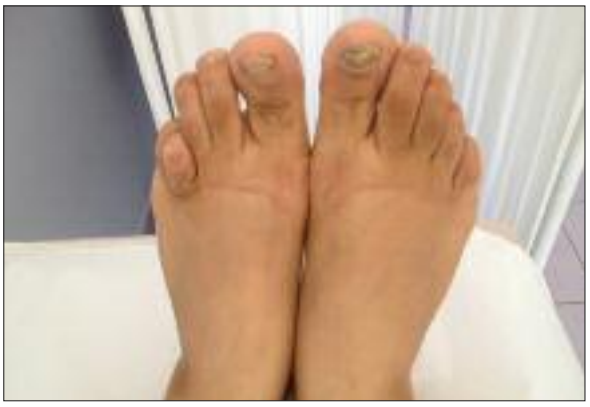

Figure 2. Clinodactyly with brachdactyly in the 4th toe of the left foot can be seen.

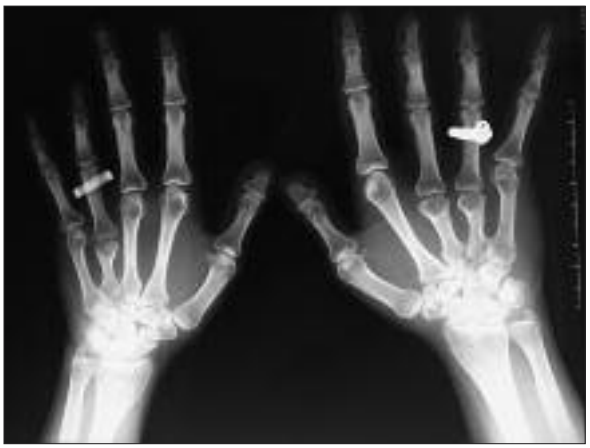

Figure 3. Shortness in the metacarpals of the 3rd and 4th fingers of the right hand and 4th finger of the left hand can be seen in conventional radiography.

The classification was modified by Temtamy and McKusick[4] in 1978. Brachydactyly, defined genetically from genetic skeletal impairments, has been included in the dysostosis group.

As the case presented here had shortness in more than one metacarpal or metatarsal, the patient was classified as type E. In addition, type D brachydactyly was seen in the bluntness of the distal phalanx of the thumb and phenotypic kyphotic posture was observed associated with wedging in the thoracic vertebrae. There are very few cases in literature of types D and E together.

Brachydactyly may also be seen together with other hand malformations such as syndactyly, polydactyly, shortness and symphalangism. Gene defects have been defined in the vast majority of isolated and syndromic forms. The transfer in isolated brachydactyly is autosomal dominant with different expressivity and penetration[1,5].

Currently, there are many forms of brachydactyly which have been defined. Subtypes of brachydactyly show high phenotypic variations. Apart from types A3 and D, isolated forms of brachydactyly are rare. Although variations are shown in all individuals, hand involvement is the dominant characteristic. However, apart from hand involvement, short stature, shoulder dysplasia, wedging in the vertebrae, radioulnar and humeroulnar joint anomalies, Madelung deformity, epiphyseal changes, toe anomalies and facial

anomalies have been reported[6,7]. In the case presented here, a wide variability of brachydactyly with hand and foot involvement and thoracic wedging was found to contribute to the clinical phenotype.

Type C brachydactyly is characterised by shortness in the mid phalanxes of the index, middle and little fingers. Shortness may be seen in the first metacarpal in most phalanxes of the index and middle fingers, which is known as hyperphalangy or hypersegmentation[8,9].

Type E brachydactyly is separated into isolated and syndromic forms. The syndromic form type E brachydactyly occurs in 70-78% of pseudohypoparathyroid patients, and with type E brachydactyly pseudohypoparathyroidism may be seen to be part of a complex syndrome such as short stature, mental retardation and hypertension. Resistance to parathyroid hormones more at the thyroid and renal tubule level and associated with that, the pseudohypoparathyroidism which develops, is the most evident clinical characteristic. While shortness is seen in all the bones of the hand in some patients, in the majority, involvement is more in the metacarpals and distal phalanxes. As there was shortness in more than one metacarpal and metatarsal, the current patient was seen to be consistent with the type E classification and the TFT and PTH levels were normal. Moreover, short stature and mental retardation were not considered[9,10]. Hypocalcemia and hyperphosphatemia may develop in these cases. As a result of the laboratory and clinical evaluation of the current patient, syndromic form brachydactyly was not considered.

In isolated type E brachydactyly, four heterozygote mutation has been determined in the homebox C13 gene (HOXD 13, 2q31.1). Phenotypically, syndactyly in the 3rd and 4th fingers, synopolydactyly in the 5th finger and long distal phalanxes may be seen. The reason for HOXD13 mutation in affected individuals is the many phenotypic variations. In most patients, there may be accompanying shortness in the 3rd metacarpal and less frequently in the 4th and 5th metacarpals. In the foot, shortness primarily in the 4th metatarsal and sometimes in the 1st, 3rd and 5th metatarsals and widening in the hallux may be seen. In the majority of patients, there is normal stature and retarded psychomotor development is not seen[8].

There are very few cases in literature where types D and E brachydactyly are seen in the same patient. As there is phenotypic overlap in types D and E brachydactyly, a common etiology is suggested. In a genetic study by KD Williams et al[10], a strong relationship was determined beween chromosome 7p21-7p14 and types D and E brachydactyly.

The current case constitutes an example of typical extremity involvement for type E isolated form. In addition, widening in the distal phalanx of the first finger in both hands demonstrated the characteristic of type D brachydactyly. Therefore, it was seen to be appropriate to evaluate the patient as a combination of non-syndromic types D and E.

The diagnosis of brachydactyly is made clinically, anthropometrically and radiologically. For isolated forms a prenatal diagnosis is not necessary, whereas there may be a need in syndromic forms. If there is familial genetic mutation, antenatal diagnosis can be made in the 11th week from chorionic villus samples and in the 14th week from amniocentesis. There is no specific approach or treatment choice for all forms of brachydactyly. If brachydactyly affects the hand functions or leads to cosmetic problems, plastic surgery may be required. Physiotherapy and ergotherapy are useful in the improvement of hand functions. Prognosis varies between different forms with prognosis in syndromic forms associated with the related anomalies[1,4,5,9].

Conclusions

Brachydactyly is a bone dysostosis which shows high phenotypic variability with isolated and syndromic forms. Type E brachydactyly in particular may show syndromic properties characterised by pseudohypothyroidism which develops associated with resistance to PTH and thyroid hormones. In addition, it may be seen in combination with type D brachydactyly.

It is hoped that the presentation of this case with the rarely seen combination of non-syndromic form of type D and E brachydactyly, will contribute to literature.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

References

1) Temtamy SA, Aglan MS. Brachydactyly. Orphanet J Rare Dis. 2008; 3: 15.

2) Bell J. On brachydactyly and symphalangism. In: Penrose LS, ed. Treasury of human inheritance. vol 5. London. Cambridge University Pres, 1951; 5: 1-31.

3) Guo Y, Liang H, Deng H. Advanges in the molecular genetics of brachydactyly. Yi Chuan 2012; 34: 1522-1528.

4) Temtamy SA, McKusick VA. The Genetics of Hand Malformations. New York: Alan R Liss Inc., 1978.

5) Nural MS, Yalin CT, Yildirim MÖ, Diren HB. Brakidaktili Tip C: Olgu Sunumu. [Brachydactyly type C: a case report]. J Firat Med J 2009; 14: 219-221.

6) Fitch N, Jequier S, Costom B. Brachydactyly C, short stature, and hip dysplasia. Am J Med Genet 1979; 4: 157-166.

7) Rennel C, Stenbach HL. Epipyhseal dysostosis without dwarfism. Am J Roentgenol Radium Ther Nucl Med. 1970; 108: 481-487.

8) Seo SH, Park MJ, Kim SH, Kim OH, Park S, Cho SI, Park SS, Seong MW. Identification of a GDF5 mutation in a Korean patient with brachydactyly type C without foot involvement. Ann Lab Med 2013; 32: 150-152.

9) Pereda A, Garin I, Garcia-Barcina M, Gener B, Beristain E, Ibañez AM, Perez de Nanclares G. Brachydactyly E: isolated or as a feature of a syndrome. Orphanet J Rare Dis 2013; 8: 141.

10) Williams KD, Blangero J, Subedi J, Jha B, Dyer T, Vandeberg JL, Towne B, Williams-Blangero S. Non-syndromic brachydactly type D and type E mapped to 7p15 in healthy children and adults from the Jirel ethnic group in eastern Nepal. Am J Hum Biol 2013; 25: 743-750.