Isolated and syndromic brachydactylies:
Diagnostic value of hand X-rays

A. David a,*, M. Vincent b, M.-P. Quéré c, T. Lefrançois c, E. Frampas a, A. David c

a Department of Radiology and Medical Imaging, Hôtel Dieu, CHU de Nantes, 1, place Alexis-Ricordeau, 44093 Nantes cedex 1, France
b Department of Clinical Genetics, hôpital mère-enfant, CHU de Nantes, 7, quai Moncousu, 44000 Nantes, France
c Department of Pediatric Radiology, hôpital mère-enfant, CHU de Nantes, 7, quai Moncousu, 44000 Nantes, France

KEYWORDS
Brachydactyly; Hand abnormalities; Foot abnormalities; Hand radiography; Congenital bone malformations

Abstract  Brachydactyly, or shortening of the digits, is due to the abnormal development of phalanges, metacarpals and/or metatarsals. This congenital malformation is common, easily detectable clinically but often requires additional radiological exploration. Radiographs are essential to characterize the type of brachydactyly and to show the location of the bone shortening, as well as any associated malformation. This article reviews the radiological findings for isolated brachydactylies (according to the types classified by Bell, and Temtamy and McKusick) and for brachydactylies that are part of complex multisytem malformation syndromes. If warranted by the clinical and radiological examinations, a genetic analysis (molecular and/or cytogenetic) can confirm the etiologic diagnosis.

Brachydactyly is a congenital abnormality, which is characterized by the absence or rudimentary development of metacarpals, metatarsals, and/or phalanges. Clinically, patients present with shortened hands or feet. A postero-anterior view of the hands and feet by standard radiography is the first-line investigation to analyze the bones involved. Indeed, the analysis of the affected digit as well as the topography of the shortened bone within the digit, allows the radiologist to determine the classification of the
brachydactyly and whether the condition is to be diagnosed as syndromic. The abnormal shortness of phalanges is called brachyphalangia. Depending on the phalanx involved, there are three different types of brachyphalangia: brachybasophalangia (proximal phalanges), brachymesophalangia (middle phalanges) and brachytelephalangia (distal phalanges). Brachymetacarpia and brachymetatarsia are the abnormal shortness of the metacarpal and metatarsal bones; while the term clinodactyly refers to the lateral deviation of a phalanx, usually the distal phalanx.

A test (molecular or cytogenetic test, or both) to detect a genetic abnormality will further establish the etiological diagnosis. Brachydactyly may be an isolated condition or part of a complex malformation syndrome.

**Isolated brachydactyly**

Isolated brachydactyly is one of the ten categories of hand malformations described by Temtamy and McKusick. Bell initiated a classification in 1951 [1] and Temtamy and McKusick further completed it in 1978 (Fig. 1) [2]. This classification consists of five individualized types A to E, and four subgroups A1 to A4. These malformations are rare, except for types A3 and D, more frequent, for which the prevalence reaches 2% [2].

**Type A**

Brachydactyly type A is characterized by shortened middle phalanges. Depending on the affected digit, brachydactyly type A is subdivided into four subtypes, A1 to A4.

**Type A1**

Type A1 is shortened or undeveloped middle phalanx in all digits, as well as proximal phalanx of thumb (or big toe). Second and fifth fingers are the most frequently affected. Hand X-rays show short or absent middle phalanges, short distal phalanges, and sometimes fusion of distal and middle phalanges (Fig. 2) [3]. Metacarpals are often short with broad epiphysis [4]. Brachydactyly type A1 is inherited in an autosomal dominant pattern and is caused by mutations in gene IHH (Indian Hedgehog) located on chromosome 2 at 2q35-36 [5].

**Type A2**

Type A2 is absent or shortened middle phalanx of the index finger, or more rarely 5th digit [2]. Diagnosis is confirmed on
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Figure 2. Postero-anterior X-ray of an adult’s both hands shows brachydactyly type A1: brachymesophalangia of four digits with hypoplasia of the thumb’s proximal phalanx.

radiographs, which show an absence or shortening of middle phalanx, presenting in the latter case a distinctive triangular shape (Fig. 3) [3]. Brachydactyly type A2 is inherited in an autosomal dominant pattern and is caused by mutations in the BMPR1B gene located on chromosome 4 at 4q22-24 [6].

Type A3

Type A3 is shortened middle phalanx of the little finger (Fig. 4) [2]. This malformation is relatively common, and frequently associated to other morphological anomalies. Different definitions are found in the literature. For instance, Hertzog considers that the middle phalanx of the 5th digit must be smaller than half the middle phalanx of the 4th digit [7].

Brachydactyly type A3 is inherited in an autosomal dominant pattern, but no causative mutation has been identified [3].

Figure 3. Postero-anterior X-ray of a 6-month-old child’s hands shows brachymesophalangia of the 2nd and the 5th digit.

Figure 4. Postero-anterior X-ray of an adolescent’s hands shows brachydactyly type A3: brachymesophalangia of the 5th digit.

Type A4

Type A4 is shortened middle phalanx together with bifid appearance of distal phalanx of thumb as well as nail dysplasia [3]. Mutations in gene HOXD13 have been reported in a family with brachydactyly type A4 [8].

Type B

Brachydactyly type B is characterized by absence or hypoplasia of distal and middle phalanges [2]. Clinically, patients frequently present absent nails on 2nd and 5th digit, while the distal phalanges of the 1st fingers are malformed. Radiographs of hands and feet accurately determine how the bones are affected (Fig. 5). The characteristic malformation of brachydactyly type B is absent or clearly hypoplastic distal phalanges of the 2nd and 5th digit [2,3]. The thumbs’ distal phalanx is present but often looks abnormal (flattened, bifid or duplicated) [3]. Middle phalanges may show hypoplasia. Other anomalies may be associated, such as soft tissue

Figure 5. Postero-anterior X-ray of the right hand of a 2 year-old child shows brachydactyly type B: agenesis of the distal phalanges and brachymesophalangia of the 2nd, 4th and 5th digit, hypoplasia (right side) and agenesis (left side) of the distal phalanx of the third digit, bifid distal phalanx of the thumbs.
syndactyly, symphalangism, carpal or tarsal fusion, and also shortened metacarpals or metatarsals [3].

Transmission of this type of brachydactyly is autosomal dominant. It is caused by mutations in the ROR2 gene located on chromosome 9 on 9q22 [9].

**Type C**

This type of brachydactyly is more complex; it combines brachymesophalangy of the 2nd, 3rd and 5th digit with possible hyperphalangy (more than three phalanges) of the 2nd and 3rd digit, as well as shortened first metacarpal (Fig. 6). The 4th finger is not affected becoming thus the longest finger [2,3]. The proximal phalanx of the 2nd digit has an anomalous configuration with unlar deviation. Other anomalies such as short metacarpals or symphalangism may also be observed. Feet are usually normal, or show ordinary brachydactyly [2].

Brachydactyly type C is inherited in an autosomal dominant manner and caused by mutation in gene CDMP1 (also called GDF5) [10].

**Type D**

In brachydactyly type D only the distal phalanx of the thumb is shortened. The shortening occurs in varying degrees and may affect one thumb, both thumbs and even the hallux. The base of the distal phalanx is often broader than the surface of the proximal phalanx to which it articulates [2]. This brachydactyly is most common in some Arab and Japanese populations [3]. Brachydactyly type D has an autosomal dominant inheritance pattern but no causative mutation has been identified [3].

**Type E**

Brachydactyly type E is characterized by a more or less marked shortening of metacarpals, with possibly abnormal size of the phalanges. In some cases, metatarsals may also be short [2–4]. Standard radiographs show these anomalies as well as the hypoelastic appearance and partially fused metacarpal epiphyses (Fig. 7). Brachydactyly type E may be an isolated condition or part of malformation syndromes such as Turner syndrome or Albright hereditary osteodystrophy syndrome. This type of brachydactyly has an autosomal dominant inheritance pattern, but no causative mutation has been identified.

** Syndromes with brachydactyly**

Brachydactyly may also be part of multiple malformation syndromes. We describe a few examples of syndromes hereafter.

**Albright hereditary osteodystrophy syndrome**

The syndrome was identified in 1942 and is characterized by clinical and biological features of hypoparathyroidism but unresponsive to parathyroid hormone (PTH). It was given the name pseudohypoparathyroidism. Another form, but with normal calcium and phosphate levels, was identified in 1952 and was termed pseudopseudohypoparathyroidism [2]. PHP1A (pseudohypoparathyroidism type 1A) is characterized by skeletal anomalies and ectopic calcifications, short stature, obesity, rounded face, and often, moderate mental retardation. Skeletal anomalies include brachymetacarpia or brachymetatarsia, or both, mainly in the 4th and 5th digit (Fig. 8). Biological test results are those of pseudohypoparathyroidism (hypocalcemia, hyperphosphatemia, raised parathormone). The inheritance pattern is autosomal dominant, related to the inactivating mutations in the GNAS gene, located at 20q13.2-13.3 [11].

**Feingold syndrome (oculo-digito-esophageal-duodenal syndrome)**

The prevalence of Feingold syndrome is estimated less than one per 1 million. It is characterized by brachydactyly with microcephaly, learning disabilities, facial dysmorphism (short palpebral fissures, nose and ear anomalies, micrognathia) and digestive anomalies (esophageal or duodenal atresia, or both) [12]. Brachydactyly is characterized by
agenesis/hypoplasia of the middle phalanx of 2nd and 5th digit, making it look similar to brachydactyly type A2 (Fig. 9). Thumbs are often broad with limited mobility of interphalangeal joints. Foot anomalies frequently include toes syndactyly (toes 2/3 and 4/5) [4]. The syndrome is inherited in an autosomal dominant pattern and is caused by mutations in gene MYCN located at 2p24.1 [13]. Recently, a new form of brachydactyly with short stature and microcephaly has been identified with symptoms close to Feingold syndrome but without digestive involvement, caused by a microdeletion at 13q31.3 leading to the loss of microRNA, namely the miR-17-92 cluster [14].

Figure 8. Postero-anterior X-ray of the right hand of an 8-year-old child with Albright syndrome: brachymetacarpia of the first, the third, the fourth and the fifth digits.

Figure 9. Postero-anterior X-ray of adult with Feingold syndrome (both hands) shows brachymesophalangia of the 2nd and 5th digit.

2q37 microdeletion syndrome

This syndrome, sometimes called Albright’s hereditary osteodystrophy-like syndrome, has been reported in the literature in more than 115 patients. It is characterized by skeletal malformations associated with facial dysmorphism (round face, sparse hair and eyebrows, up-slanting palpebral fissures, midface hypoplasia, nose anomalies, ogival palate), overweight and development delay with sometimes autism spectrum disorders. The skeletal anomalies of interest here are brachydactyly type E with brachymetacarpia mainly affecting the 4th and 5th digit and sometimes the 2nd and 3rd (Fig. 10). Diagnosis is based on in situ hybridization analysis or CGH-array to detect deletion of 2q37. This region contains 197 genes, including HDAC4, which is the candidate gene for brachymetacarpia [15].

Robinow syndrome

This rare syndrome, the precise prevalence remains unknown, is characterized by digital and skeletal anomalies (mesomelic shortening of limbs, rib fusion, hemivertebra and scoliosis), distinctive facial dysmorphism (hypertelorism, midfacialrunb hypoplasia, nose anomalies), genital hypoplasia and small height [16]. Brachydactyly is characterized by shortening of the distal phalanges, nail dysplasia and clinodactyly of the 5th digit. Two forms of Robinow syndrome exist, different in transmission pattern (autosomal dominant and recessive) but with overlapping clinical symptoms [4]. The recessive form is caused by mutations in gene ROR2 [17].

Rubinstein-Taybi syndrome

Rubinstein-Taybi syndrome has a prevalence estimated at 1–9:100,000. It is characterized by mental and growth retardation, microcephaly, facial dysmorphism and anomalies of the extremities. The facial abnormalities include downward
and outward slanting palpebral fissures, ptosis, highly arched palate and characteristic broad nasal bridge and long and protruding septum. Hands are short and broad, with short thumbs where the distal phalanx is broad and often pointing outwards. The hallux is also very broad and sometimes deviated. Radiographs show a shortened and characteristic broad distal phalanx of the first digit of the foot or of the hand. This widening involves both bony and soft tissues [2, 18]. Genetically, the syndrome is associated either with a microdeletion affecting the 16p13.3 band (in about 10% of the cases), or with mutations in the CBP gene located in this region (in about 50% of the cases). Recently, mutations in EP300 gene have been identified in several patients [19].

**Turner syndrome**

Turner syndrome is estimated to have a frequency of 1—5/10,000. It is a chromosomal disorder in which an X chromosome (karyotype 45,X0) is absent. Clinical features are heterogeneous, skeletal malformations are associated with short stature, ovarian failure, deafness as well as cardiovascular, thyroid, digestive and cutaneous anomalies [20]. Skeletal malformations often consist of brachymetacarpia/brachymetatarsia, mainly affecting the 4th digit, with carpal fusion and anomalies in the knees [2].

**Disclosure of interest**

The authors declare that they have no conflicts of interest concerning this article.

**References**