The Journal of Foot & Ankle Surgery 58 (2019) 586–590

Contents lists available at ScienceDirect

The Journal of Foot & Ankle Surgery

journal homepage: www.jfas.org

Hyperhidrotic Macrodactylism Caused by Osteoid Osteoma: A Case Report and Review of the Literature

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ARTICLE INFO

Level of Clinical Evidence: 4

Keywords:
foot
hyperhidrosis
macrodactylism
macrodactyly
osteoid osteoma

ABSTRACT

Macrodactylism or macrodactyly is referred to as congenital deformity of fingers or toes, and the corresponding incidence rate is relatively low. In this article, we describe a young male with macrodactylism of the second toe of his right foot. He was suffering from persistent pain, overgrowth, and hyperhidrosis of the involved toe. Radiographic examination of the right foot showed a small translucent area surrounded by hyperplasia and sclerotic bone in the second distal phalanx, in addition to increased soft tissue density and volume. Surgical resection of the bone lesion and reduction of the soft tissue bulk were performed. Pathological findings showed osteoblast hyperplasia, which was diagnosed as osteoid osteoma, and no abnormal findings were seen in the skin. Symptoms of pain and hyperhidrosis disappeared postsurgery and did not recur over the subsequent 2-year follow-up. As far as we know, this was a rare case of osteoid osteoma occurring in the toe that resulted in macrodactylism, which was also associated with localized hyperhidrosis.

Macrodactylism or macrodactyly is a congenital and noninherited deformity of fingers or toes, or both. It refers to the abnormal growth of the phalanx (phalanges), tendons, nerves, blood vessels, subcutaneous fat, skin, and fingernail (toenail) that comprise fingers or toes (1). In appearance, the volume increases beyond normal; however, it is distinguishable from the simple macromelia and hemihypertrophy in that it localizes to the digit. The incidence of macrodactylism or macrodactyly is relatively low and is estimated to be approximately 0.9% of all congenital malformations in the extremities (2). The incidence of the condition localizing to the lower extremities is less than that of it occurring in the upper extremities (3). Case reports are the prevalent form of publication associated with macrodactyly. In this report, we describe the case of a young male patient with macrodactylism localized to the second toe of his right foot, which was considered very unusual because of its association with underlying phalangeal osteoid osteoma and localized digital hyperhidrosis.

Case Report

A 12-year-old male was admitted to our hospital owing to the pain and overgrowth of the second toe of his right foot; the patient had been complaining of the symptoms for 10 months. He was found to have "slight swelling" in the same toe approximately 3 years ago; however, no specific diagnosis was made, and no treatment had been undertaken. The asymptomatic overgrowth gradually increased, and he began to suffer from toe pain while walking. When he eventually presented to our services, he denied any history of previous trauma to the involved toe. There was obvious enlargement and deformity of the second toe of his right foot (Fig. 1*A*), accompanied with tenderness and percussion pain. Significant beads of sweat could be seen at the pulp and tip of the second toe (Fig. 1*B*), even when the ambient room temperature was considered cool. Sweat was evident on the adjacent toes of his right foot, whereas sweat was absent on the toes of his contralateral foot and the fingers of both of his hands. When the beads of sweat were toweled off of the enlarged second toe, they would reform within 1 to 2 minutes. The starch-iodine test revealed that after exposure to starch, the second toe turned blue in comparison with the other toes of his right foot (Fig. 1*C*). Despite the sudomotor abnormality, no gross evidence of abnormal sensation, myodynamia, or abnormal deep tendon reflexes was found in the patient's extremities, and his peripheral blood circulation, as determined by palpable

Financial Disclosure: None reported.
Conflict of Interest: None reported.
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https://doi.org/10.1053/j.jfas.2018.09.008

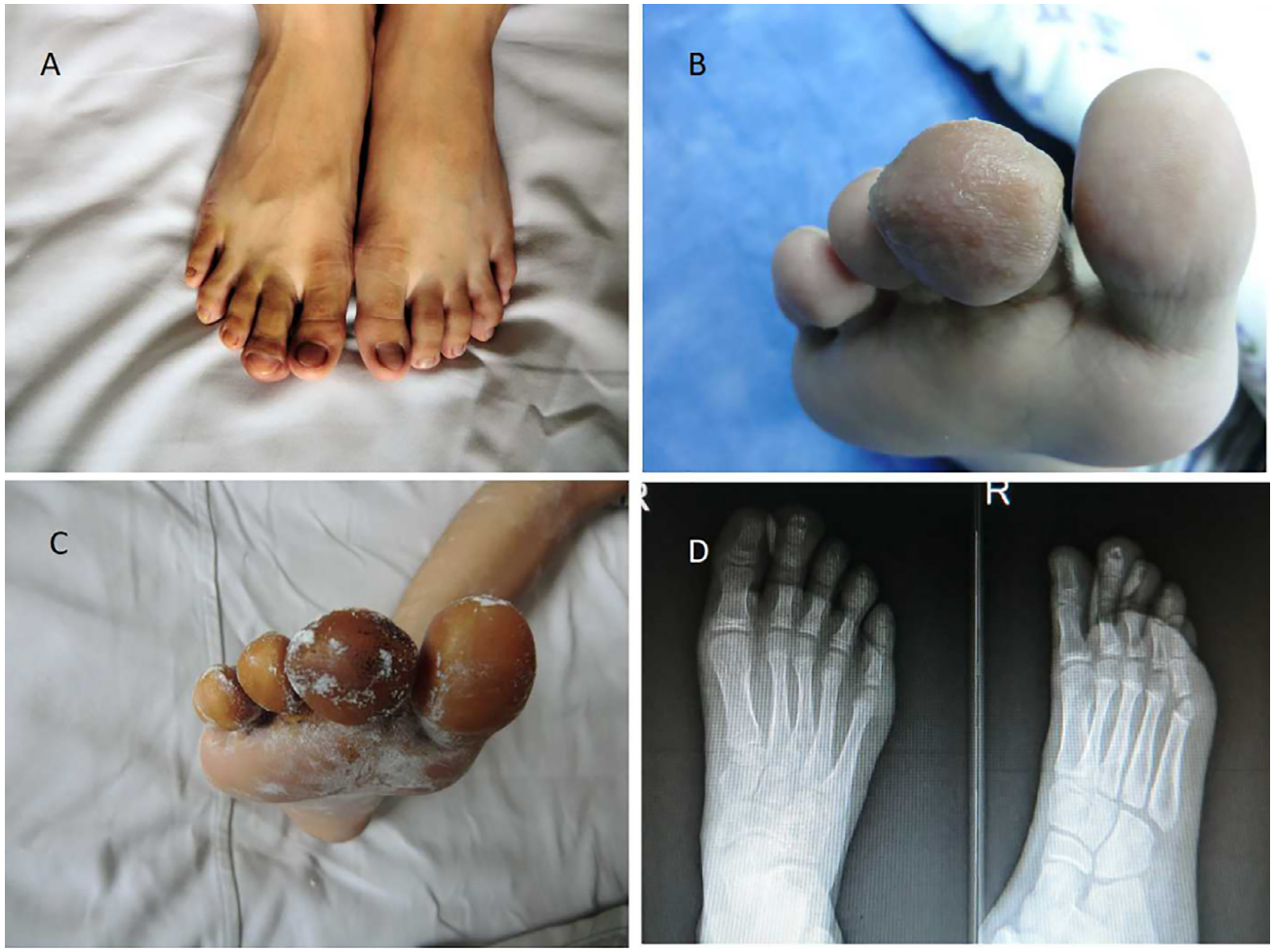

Fig. 1. Preoperative images. (*A*) The second toe of the right foot showed obvious enlargement . (*B*) Scattered sweat beads always appeared on the skin. (*C*) The starch-iodine test showed a significant change of color of the affected toe in contrast to the others. (*D*) Radiograph examination showed visible small transmission area of the distal phalanx surrounded by hyperplasia bone tissue and thickened soft tissue.

pulses, digital subpapillary venous plexus filling time (blanch and refill response), and cutaneous distal cooling gradient, was deemed to be intact and normal in both his feet and hands. In addition, the patient was afebrile, he displayed no signs of systemic disease, and his blood counts and biochemical profile were normal. Radiographs of the right foot showed a transparent area in the distal phalanx of the second toe, with surrounding sclerosis and boney hyperplasia, as well as increased density and volume of the soft tissues of the second toe (Fig. 1*D*). The patient was diagnosed with localized second digital macrodactylism of the right foot, combined with an underlying benign bone tumor, likely osteoid osteoma, and hyperhidrosis.

Surgical treatment was adopted for the male after consultation and consideration of the diagnostic and treatment options. The operation was conducted under general anesthesia. First, the toenail was extracted, after which a V-type incision was made in the middle of the second toe, and a full-thickness flap was excised to reduce the bulk of the toe (Fig. 2*A–D*). After exposure of the distal phalanx, the bone lesion was excised completely (Fig. 2*E*), and the toe was shortened, such that it would fit better with the adjacent digits of the right foot. Gross surgical inspection revealed no evidence of abnormal soft tissue structures, such as nerves and vessels. The soft tissue was sutured, and the volume of the toe appeared consistent with what would be considered normal (Fig. 2*F*). The resected tissues were sent for pathological examination. A sterile gauze dressing was applied, and the patient was allowed to ambulate in a protective shoe, as tolerated.

After the operation, the pathology sections were determined to represent full-thickness skin-to-bone soft tissue flaps that showed no evidence of abnormal skin, eccrine ducts, or adipose or connective tissue (Fig. 3*A–C*). The bony lesion revealed osteoblast hyperplasia, indicative of osteoid osteoma (Fig. 3*D–F*). The stitches were removed 2 weeks postoperation, and the incision was considered to heal well (Fig. 4*A,B*). Radiographs obtained when the stitches were removed showed complete elimination of the phalangeal lesion, as well as gross reduction of the soft tissue around the second phalanx in comparison with the soft tissue volume that had been present before the operation (Fig. 4*C*). The pain and hyperhidrosis disappeared, and by the 13th postoperative day, the patient's right foot healed well and was functioning properly on weightbearing. Subsequent follow-up, including long-term telephone follow-up, indicated no recurrence of pain, digital enlargement, or hyperhidrosis in the second toe of the right foot at the 3-month, 1-year, and 2-year time points.

Discussion

Macrodactylism is of unknown etiology and is considered a rare congenital malformation. Most cases are discovered and treated during the period of infancy or early childhood, and few cases are reported in

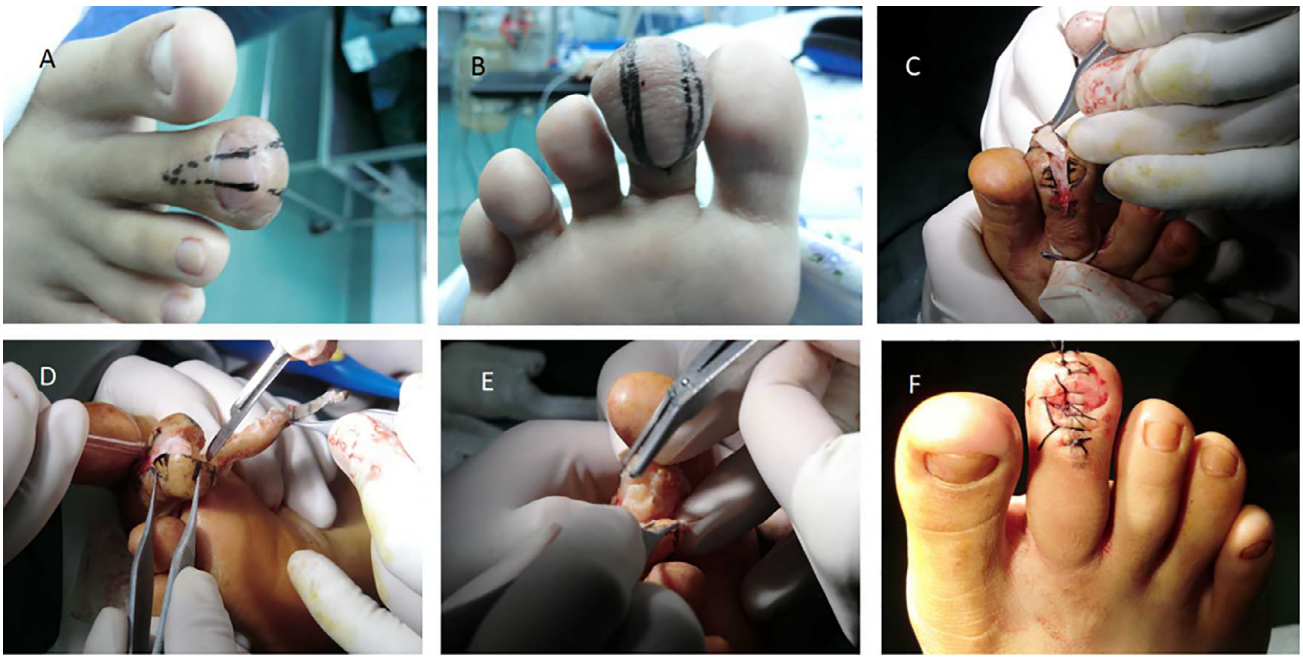

Fig. 2. Intraoperative images. (*A, B*) A V-shape incision design is shown. (*C, D*) A full-thickness flap was removed. (*E*) The bone lesion was resected completely. (*F*) The incision was sutured.

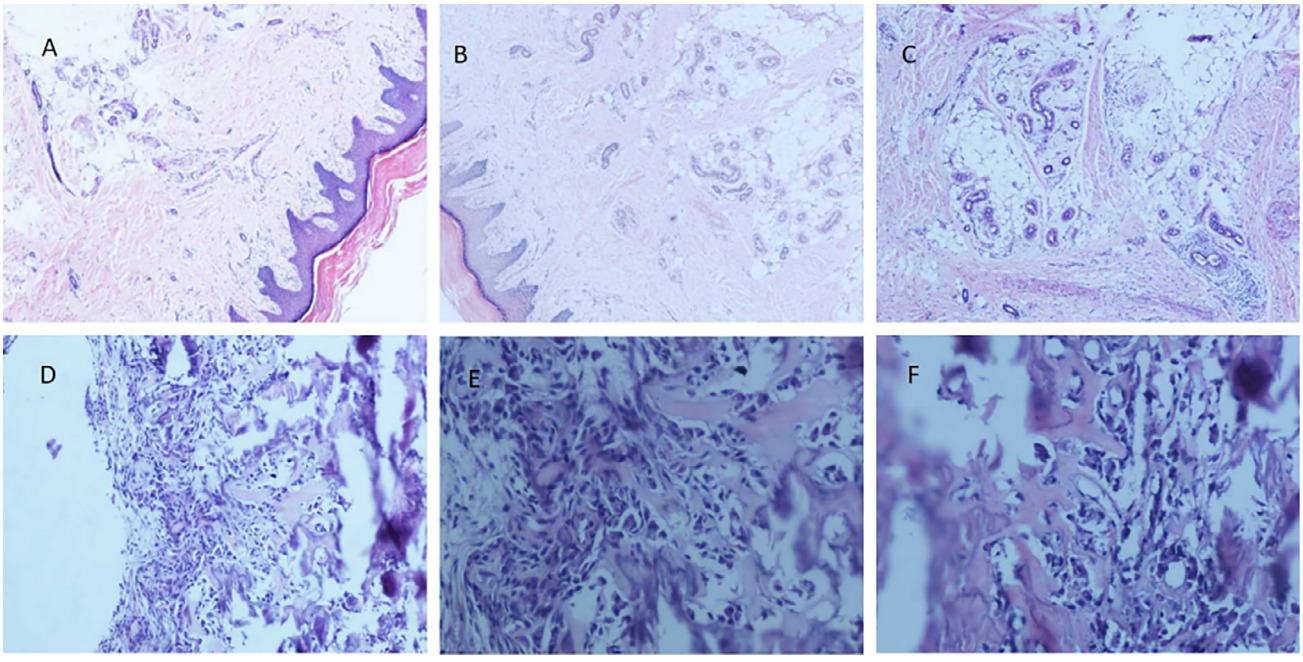

Fig. 3. Pathological findings. (*A–C*) Nothing special was found in the sections of the soft tissue; just normal structures, such as eccrine duct in plenty of adipose tissue, were observed. (*D–F*) The resected bone tissue was indicated to be osteoid osteoma with osteoblast hyperplasia (magnification *A* x 4, *B* x 4, *C* x 10, *D* x 10, *E* x 20, *F* x 20; hematoxylin-eosin stain).

adults (3). The etiology of macrodactylism is still debatable. In 1976, it was reported for the first time that several deformities of the fingers and toes, which were considered hamartoma deformities, mainly manifested as benign hyperplasia of soft tissue, especially adipose hyperplasia (4). Later, in 1983, the concept of Proteus syndrome was proposed (5). Important features of Proteus syndrome are macrodactyly and deformities of other systemic structures (6). Proteus syndrome with macrodactyly as the single sign is rare. In 2011, the case of a 4-month-old infant with macrodactyly accompanied by ankylodactylia was described in the literature (7). After 1 year of conservative treatment, it was found that the child's finger joint mobility decreased, and he had to finally undergo surgical treatment. Soft tissue of the macrodactyly was pathologically examined. The results suggested lymphangioma, and a diagnosis of Proteus syndrome with the single sign of macrodactyly was made. Many scholars believe that macrodactylism or macrodactyly is a kind of neural fibrolipoma, the distinct pathological feature of which is the abnormal proliferation of the fibrous adipose cell (8). Other investigators (9) insist that true macrodactylism or macrodactyly is characterized by abnormal hyperplasia of mesenchymal cells and is distinguished from macrodactyly caused by hemangioma,

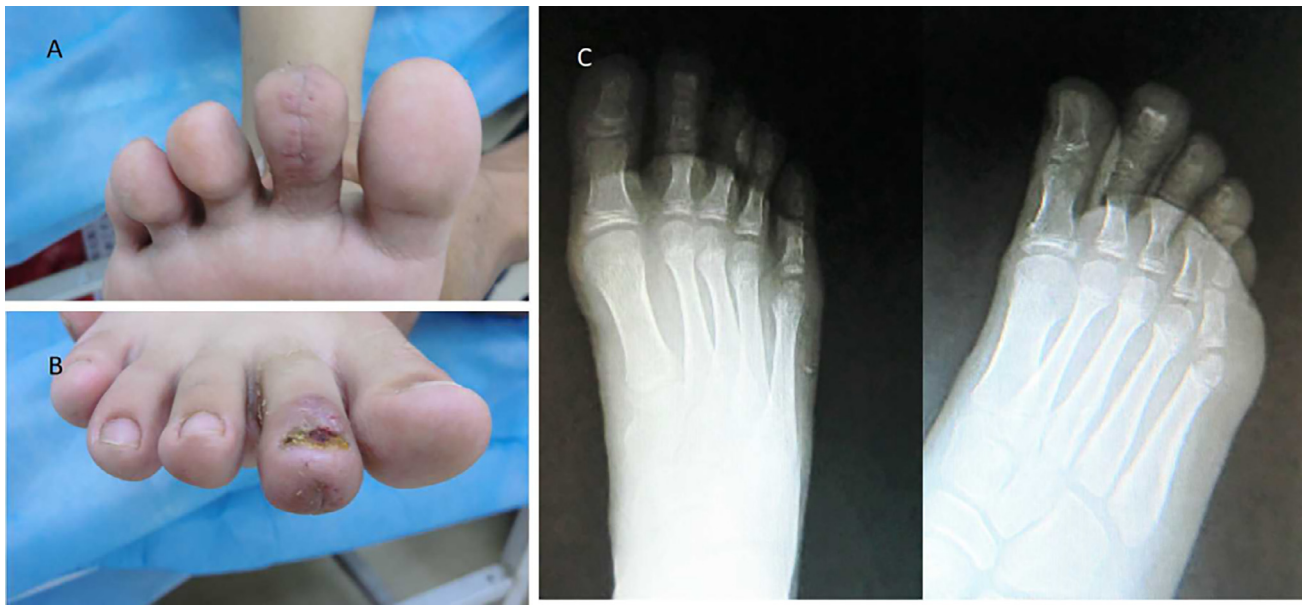

Fig. 4. Postoperative images when the stiches were removed. (*A, B*) The toe returned to an ideal size, and the sweat beads disappeared. (*C*) Postoperative radiograph examination showed that the bone lesion was completely removed, and the length of the distal phalanx and the shape of the soft tissue seem perfect.

lymphangioma, or enchondroma. Macrodactylism or macrodactyly can exist either alone or in conjunction with other syndromes.

According to previous reports, no obvious genetic factors are associated with macrodactylism or macrodactyly, and no positive findings have been found in chromosome studies. In recent years, significant progress has been made in genetic studies of macrodactylism or macrodactyly. In 2012, it was confirmed in a study of the R115P mutational site of the phosphatidylinositol-3-kinase catalytic α polypeptide (PIK3CA) gene in the nerve cells in diseased tissue of a patient with isolated macrodactyly; however, the genetic alteration was not found in the blood samples of the patient (10). The authors of that study concluded that isolated congenital macrodactylism or macrodactyly and other dysplastic syndromes were caused by the activation of the PIK3CA/AKT signaling pathway in the nerve cells. In 2016, the p.Glu542Lys mutational site of the PIK3CA gene was found in the cells of diseased tissue of a 4-year-old girl with macrodactyly combined with ankylodactylia (11). The authors of that report believed that p.Glu542Lys mutations in somatic cells at different stages of embryonic development might be responsible for a high diversity of malformations, including macrodactyly. They further suggested that rapamycin, a small molecule inhibitor of the PIK3CA-AKT-mTOR signaling pathway, might be a useful drug for the treatment of macrodactylism or macrodactyly. Clinical trials with rapamycin for this condition have yet to be published.

In the present case report, we postulate that macrodactylism was caused by an underlying osteoid osteoma. As far as we know, it is the first report in the literature to describe this association. Although it may not be considered true macrodactylism (9), our clinical and pathological observations suggest that it was true macrodactylism. In 1935, osteoid osteoma was described (12), and it is known to occur mostly in the diaphysis of the femur or tibia and less often in the phalanx (13). Although we observed no neural or vascular tissue abnormality during the surgery or in the pathological sections, we think that local soft tissue hypertrophy could be caused by stimulation related to the bone tumor, which in our patient's case is an osteoid osteoma. Osteoid osteoma is sometimes difficult to distinguish from osteoblastoma in pathological morphology, and the diagnosis has to be made by combining clinical and imaging studies, as well as the microscopic inspection of the pathology sections. Benign osteoblastoma is a lesion with greater progression, and it is usually accompanied by a small amount of reactive bone formation, and the corresponding diameter of the tumor is often >1 cm, whereas osteoid osteoma is a small quiescent lesion with pain and more reactive bone formation; most of these lesions are <1 cm in diameter (14). Some scholars believe that osteoid osteoma, osteoblastoma, and osteosarcoma are gradual processes and that the corresponding degree of malignancy increases gradually (15).

In conclusion, the young male that we described in this report also displayed nearly constant sweating in the affected toe in the resting state, despite normal body temperature, even when the ambient room temperature was cool (air conditioned). To our knowledge, such overlying hyperhidrosis has not been described in association with osteoid osteoma or even macrodactyly. Hyperhidrosis refers to the phenomenon of increased sweat secretion from the sweat glands of a part of the body, which can be generalized sweating and localized sweating, and has been divided into primary and secondary hyperhidrosis (16). Primary hyperhidrosis is an idiopathic sympathetic nervous system lesion (17,18), characterized by bilateral or symmetrical sweating in individuals <25 years of age, a family history of the condition, and cessation of sweating during sleep and is easily affected by nervousness and anxiety. Secondary hyperhidrosis is often localized and unilateral, and it can be caused by drugs or diseases, such as spinal cord injury, cerebrovascular disease, thoracic tumor, Harlequin syndrome, Frey syndrome, and sympathetic abnormality (16). The digital hyperhidrosis observed in our patient with macrodactyly cannot be explained by the known reasons described previously. Moreover, microscopic inspection of the excised tissues did not reveal hyperplasia of the local sweat glands, a finding previously associated with hyperhidrosis (19). We hypothesized that hyperhidrosis may have been due to the stimulation of a heretofore unidentified substance secreted by the bone tumor, because the persistent focal sweating ceased after excision of the boney lesion, and the toe no longer swelled or displayed hyperplasia of any sort.

Acknowledgments

We thank Professor Hongtao Xu from the pathology department of China Medical University for interpreting the pathological sections.

References

1. Kotwal PP, Farooque M. Macrodactyly. J Bone Joint Surg Br 1998;80:651–653.
2. Klein W, Germann G, Bosse A, Müller KM, Steinau HU. Clinical aspects, morphology and therapy of an unusual case of bilateral macrodactyly. Handchir Mikrochir Plast Chir 1993;25:12–19.
3. Fengdong Z, Rongrong Z, Peihua S, Shunwu F. Macrodactyly of the great toe for thirty-five years. J Plast Reconstr Aesthet Surg 2009;62:e520–e522.
4. Barsky AJ. Macrodactyly. J Bone Joint Surg Am 1967;49:1255–1266.
5. Wiedemann HR, Burgio GR, Aldenhoff P, Kunze J, Kaufmann HJ, Schirg E. The Proteus syndrome. Partial gigantism of the hands and/or feet, nevi, hemihypertrophy, subcutaneous tumors, macrocephaly or other skull anomalies and possible accelerated growth and visceral affections. Eur J Pediatr 1983;140:5–12.
6. Almeida Jr HL, RC Fiss, Happle R. Macrodactyly with skin hypertrophy: a minimal form of the Proteus syndrome. An Bras Dermatol 2011;86:557–559.
7. Türk CY, Güney A, Oner M, Halıcı M. An unusual initial presentation of Proteus syndrome: macrosyndactyly. Eklem Hastalik Cerrahisi 2011;22:56–59.
8. Ben-Bassat M, Casper J, Kaplan I, Laron Z. Congenital macrodactyly. J Bone Joint Surg Br 1966;48:359–364.
9. Yüksel A, Yagmur H, Kural BS. Prenatal diagnosis of isolated macrodactyly. Ultrasound Obstet Gynecol 2009;33:360–362.
10. Rios JJ, Paria N, Burns DK, Israel BA, Cornelia R, Wise CA, Ezaki M. Somatic gain-of-function mutations in PIK3CA in patients with macrodactyly. Hum Mol Genet 2013;22:444–451.
11. Tripolszki K, Knox R, Parker V, Semple R, Farkas K, Sulák A, Horváth E, Széll M, Nagy N. Somatic mosaicism of the PIK3CA gene identified in a Hungarian girl with macrodactyly and syndactyly. Eur J Med Genet 2016;59:223–226.
12. Jaffe HL. Osteoid-osteoma. Proc R Soc Med 1953;46:1007–1012.
13. Basar H, Topkar OM, Erol B. Osteoid osteoma of distal phalanx of toe: a rare cause of foot pain. Case Rep Orthop 2013;2014:560892.
14. Yip WK, Lee HT. Benign osteoblastoma of the maxilla. Oral Surg Oral Med Oral Pathol 1974;38:259–263.
15. Tan XJ, Liu YS. Analysis of four cases of osteoblastoma. J Guangdong Med Coll 1996;24:76–78.
16. Eren Y, Yavasoglu NG, Comoglu SS. Post-traumatic unilateral plantar hyperhidrosis. Clinical Clin Auton Res 2016;26:75–77.
17. Walling HW. Clinical differentiation of primary from secondary hyperhidrosis. J Am Acad Dermatol 2011;64:690–695.
18. Vlahovic TC. Plantar hyperhidrosis: an overview. Clin Podiatr Med Surg 2016;33:441–451.
19. Thomas I, Brown J, Vafaie J, Schwartz RA. Palmoplantar hyperhidrosis: a therapeutic challenge. Am Fam Physician 2004;69:1117–1120.