Brachydactyly in Pseudopseudohypoparathyroidism

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A 26-year-old woman was seen for a longstanding mild elevation of parathyroid hormone (PTH), with otherwise normal serum mineral levels. Repeat testing confirmed elevated PTH 75 pg/mL (15 to 65 pg/mL) with normal calcium 9.1 mg/dL (8.6 to 10.0 mg/dL), phosphorus 3.7 mg/dL (2.5 to 4.5 mg/dL), and creatinine 0.67 mg/dL (0.59 to 1.04 mg/dL). The results of 24-hour urine calcium excretion, thyroid stimulating hormone, and free thyroxine tests were normal. Total 25-hydroxy-vitamin D level was 18 ng/mL, indicating mild deficiency. There was no history of nephrolithiasis, subcutaneous calcifications, or seizures. She was several weeks pregnant but denied meno- or metrorrhagia before conception. Family history was noncontributory.

On physical examination, the patient had brachydactyly of the fourth and fifth metacarpals bilaterally (Figure A and B), with hypoplasia of the corresponding carpometacarpal joints (Figure C). Bilateral brachymetatarsia of the fourth toes (Figure D to F) and scoliosis were also noted. The remainder of the examination was unremarkable without dysmorphic features or cognitive impairment. The patient was diagnosed with pseudopseudohypoparathyroidism, which does not typically require intervention.

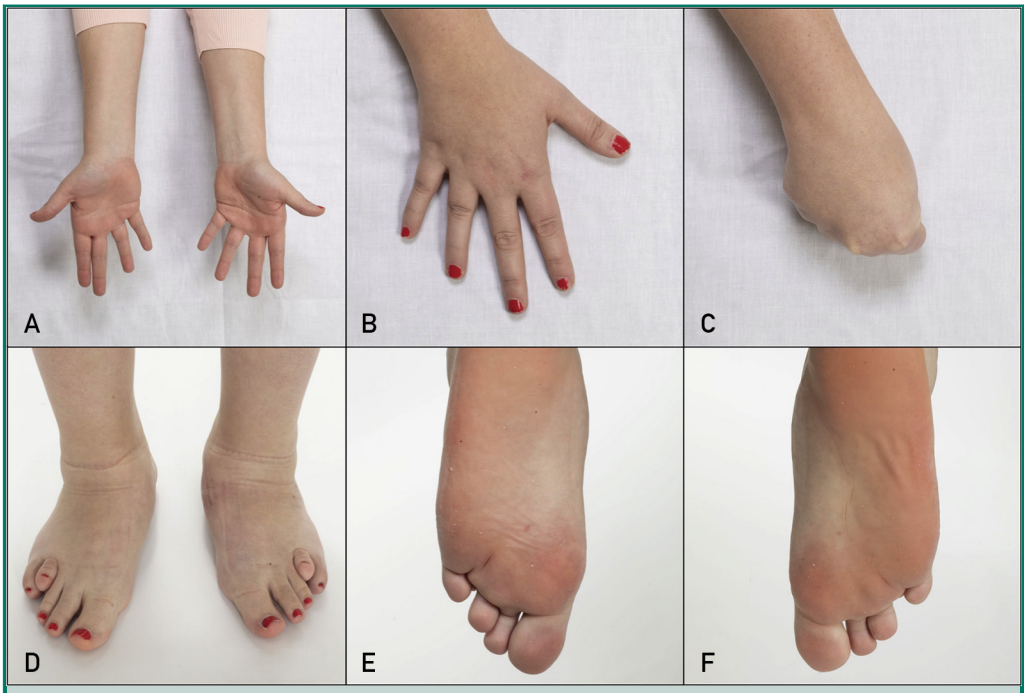

FIGURE. Physical examination findings in a case of pseudopseudohypoparathyroidism, including brachydactly of the fourth and fifth metacarpals (A-C) and the fourth metatarsal (D-F) bilaterally.

Pseudohypoparathyroidism comprises a group of disorders characterized by peripheral resistance to PTH caused by aberrancies in PTH receptor signaling, manifesting as elevated PTH with hypocalcemia and hyperphosphatemia.[1] Genetic defects in the maternal *GNAS* allele yield PTH resistance plus Albright hereditary osteodystrophy (AHO), which includes brachydactyly, ectopic ossifications, short stature, and various cognitive deficits.[2] In contrast, paternal *GNAS* alterations produce heterogeneous findings of AHO but with normal endocrine axes, hence referred to as pseudopseudohypoparathyroidism.[2] Additional mutations and methylation changes in *GNAS*, *PDE3A*, *PDE4D*, and *PRKAR1A* that produce a similar spectrum of physical and biochemical findings have since been identified.[3,4] Thus, there are efforts to reclassify these diseases using nomenclature that corresponds to the underlying molecular defects.[5]

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