Solitary kidney in a patient with Pallister-Hall syndrome

Ines Vanderheyden[1], Saskia Bulk[2] and François Jouret[1]

[1]Division of Nephrology, ULiège Academic Hospital, Liège, Belgium; and [2]Center of Human Genetics, ULiège Academic Hospital, Liège, Belgium

Correspondence: Francois Jouret, Division of Nephrology, ULiège Academic Hospital, Avenue Hippocrate, 11, B-4000 Liège, Belgium. E-mail: francois.jouret@chuliege.be

Kidney International (2024) **106,** 155; https://doi.org/10.1016/j.kint.2024.01.026

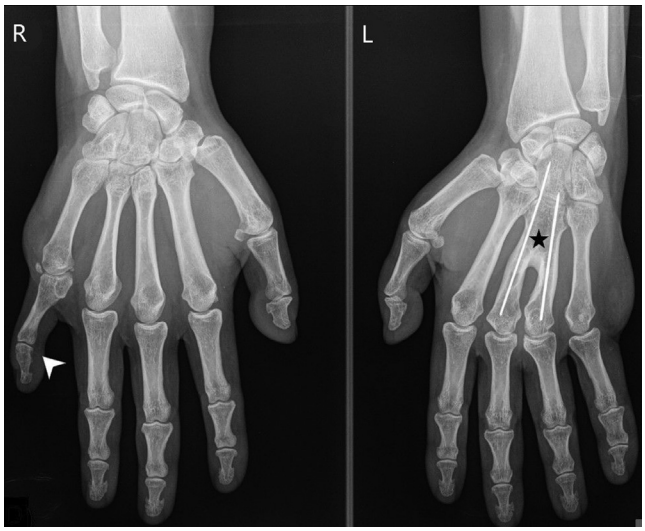

Figure 1 | X-ray of both hands. The right (R) hand is characterized by a short fifth ray and the absence of the middle phalanx (arrowhead). The left (L) hand shows a carpo-metacarpal arthrodesis of the third and fourth radii, with synostosis of the proximal half of the third and fourth metacarpals (star).

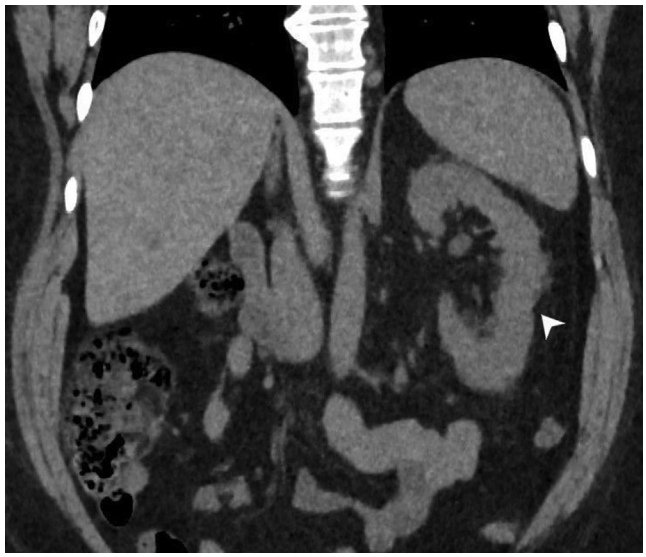

Figure 2 | Spontaneous contrast-computed tomography of the abdomen. Single left kidney with irregular cortical contours (arrowhead), consistent with sequelae of pyelonephritis.

A 58-year-old female patient was referred for solitary kidney management. She was born following a full-term pregnancy, with a weight of 2.2 kg. Her medical history included the following: (i) "Y-shaped metacarpals" and postaxial polydactyly (15 fingers *in toto*) bilaterally operated (Figure 1); (ii) foot deformities; and (iii) congenital absence of the right kidney (Figure 2). The patient had no hearing deficits or visual deficits. Retinitis pigmentosa was ruled out. Her psychomotor development was unremarkable. Her body mass index was excessive: 39.1 kg/m^2. She was 1.56 meters tall. She had been hypertensive since age 40 years. The patient had no children. The pituitary hormone workup revealed no hormonal deficiency, except for low gonadotropin levels in the context of menopause. Still, a 19-mm hypothalamic hamartoma was revealed by magnetic resonance imaging. Her serum creatinine level was 1.51 mg/dl (European Kidney Function Consortium (EKFC)-based estimated glomerular filtration rate: 37 ml/min per 1.73 m^2, confirmed by iohexol plasma clearance), with no ionic disturbances. The urine sediment was bland, with no glomerular or tubular proteinuria. Exome sequencing was performed, and variant filtering focused on genes associated with skeletal dysplasia: a heterogeneous pathogenic c.1995delT p.(Gly666Alafs*27) variant in the *GLI3* gene was detected. The *GLI3* gene belongs to the GLI family of transcription factors involved in the Hedgehog pathway. This signaling cascade is essential for organogenesis and tissue differentiation in the nervous system and the limbs. Mutations in the *GLI3* gene have been associated with various ciliopathy-related conditions. Among these, Pallister-Hall syndrome is a pleiotropic autosomal dominant malformation constellation characterized by the following: (i) postaxial polydactyly; (ii) hypothalamic hamartoma; (iii) bifid epiglottis; and (iv) genitourinary malformations, including renal agenesis or dysplasia. The diagnostic workup of congenital single kidney associated with extrarenal manifestations, such as hand and foot abnormalities at birth, facial dysmorphia, hypopituitarism, or epilepsy, should include analysis of the *GLI3* gene. The management of patients with Pallister-Hall syndrome requires multidisciplinary care.