Case Report

Sporadic orofaciodigital syndrome type I presenting as end-stage renal disease

E. Coll, R. Torra, J. Pascual, A. Botey, J. Ara, L. Pérez, F. Ballesta and A. Darnell

Services of Nephrology and Genetics, Hospital Clinic, University of Barcelona, Spain

Key words: orofacial syndrome type I; X-linked dominant disease; polycystic kidneys; renal replacement therapy

Introduction

Orofacial syndrome type I (OFD I) was first described by Papillon-Léage and Psaume [1] in 1954 and further defined by Gorlin and Psaume in 1962 [2]. OFD I is a hereditary condition characterized by the presence of oral frenulae and clefts, hamartomata of the tongue, alopecia, hypoplasia of the nasal alae, abnormalities of the digits such as brachydactyly with occasional preaxial polydactyly of the feet, and mental retardation in about half of affected subjects. This X-linked dominant disease is lethal in males. The coexistence of this disease with polycystic kidney disease has been reported in the literature [3–12]. The purpose of this article is to describe a patient with cystic kidneys and OFD I who presented with end-stage renal disease.

Case report

A 41-year-old female had no prior knowledge of renal dysfunction until she was noted to be azotaemic during a routine laboratory examination. She was the product of a full-term uncomplicated pregnancy and delivery. As a newborn she had multiple orofacial malformations (webbing between buccal mucous membrane and alveolar ridge, the tongue was triflobed and bound by a subglossal band, dental abnormalities, hypoplasia of alar cartilage), scarp hair was sparse and pale with dark roots, and fingers were short. No family members resemble the patient (she is the oldest of seven sisters and brothers). She underwent multiple plastic surgery procedures between the ages of 3 months and 17 years that partially repaired the orofacial malformations. She had to wear dental fixations because her teeth were poorly formed and badly placed. At 7 years of age she was unable to speak correctly because of dysarthria. She had also difficulty on moving (lack of balance, lack of accuracy). At 14 years of age she had a spinal fusion because of spondylolisthesis.

One month before admission she developed fatigue that progressively increased. On admission for evaluation for her kidney disorder her vital signs were as follows: blood pressure 160/100 mmHg, heart rate 72/min, axillary temperature 36.5°C. Her weight was 57.2 kg and the height was 1.59 m. She was noted to have abnormalities of the face, mouth and hands (Figure 1 a,b,c,d). She had microretroganitha with the chin deviated to the left, broad nasal root, down-turned eyes, and small ears correctly placed. Oral abnormalities included: down-turned corners, malocclusion with missing and supernumerary teeth, deviation of the tongue and its frenulum to the left, hamartomata of the tongue, narrow, deep arched of the hard palate, and periodontal disease. The hands were webbed with redundant skin and showed brachydactyly of the third finger. The patient was not mentally retarded. Auscultatory signs were normal. Neurological examination disclosed cerebellar ataxia on long distances and bilateral alteration on tandem walk.

Admission laboratory data revealed anaemia and renal failure: haematocrit 0.17, haemoglobin 5.7 g/dl, MVC 87.9 FL, WBC 5.3 × 109/l with WBC differential of a full-term uncomplicated pregnancy and delivery. As a newborn she had multiple orofacial malformations (webbing between buccal mucous membrane and alveolar ridge, the tongue was triflobed and bound by a subglossal band, dental abnormalities, hypoplasia of alar cartilage), scarp hair was sparse and pale with dark roots, and fingers were short. No family members resemble the patient (she is the oldest of seven sisters and brothers). She underwent multiple plastic surgery procedures between the ages of 3 months and 17 years that partially repaired the orofacial malformations. She had to wear dental fixations because her teeth were poorly formed and badly placed. At 7 years of age she was unable to speak correctly because of dysarthria. She had also difficulty on moving (lack of balance, lack of accuracy). At 14 years of age she had a spinal fusion because of spondylolisthesis.

One month before admission she developed fatigue that progressively increased. On admission for evaluation for her kidney disorder her vital signs were as follows: blood pressure 160/100 mmHg, heart rate 72/min, axillary temperature 36.5°C. Her weight was 57.2 kg and the height was 1.59 m. She was noted to have abnormalities of the face, mouth and hands (Figure 1 a,b,c,d). She had microretroganitha with the chin deviated to the left, broad nasal root, down-turned eyes, and small ears correctly placed. Oral abnormalities included: down-turned corners, malocclusion with missing and supernumerary teeth, deviation of the tongue and its frenulum to the left, hamartomata of the tongue, narrow, deep arched of the hard palate, and periodontal disease. The hands were webbed with redundant skin and showed brachydactyly of the third finger. The patient was not mentally retarded. Auscultatory signs were normal. Neurological examination disclosed cerebellar ataxia on long distances and bilateral alteration on tandem walk.

Admission laboratory data revealed anaemia and renal failure: haematocrit 0.17, haemoglobin 5.7 g/dl, MVC 87.9 FL, WBC 5.3 × 109/l with WBC differential normal, blood urea nitrogen 64 mg/dl, creatinine 6.6 mg/dl, uric acid 4.5 mg/dl, serum sodium 143 mEq/l, potassium 4 mEq/l, calcium 8.8 mg/dl, phosphate 5.4 mg/dl, albumin 26 g/l, and total protein 64 g/l. Urine sediment showed glucose negative, protein 1.06 g/day. Acid–base balance revealed: pH 7.24, plasma bicarbonate 17 mEq/l, pCO2 39.4 mmHg. Chest X-ray was normal. Abdominal ultrasonography disclosed small cysts throughout both kidneys (Figure 2). The right kidney measured 12 × 6 × 6.8 cm and the left 13 × 7 × 7.4 cm. Only one cyst was observed in the liver. A computerized tomography confirmed the presence of multiple renal bilateral cysts. A funduscropy eye study was normal. A cerebral magnetic resonance scan showed displaced normal hypophysis,
Discussion

OFD I is a rare disorder that affects many parts of the body and is usually diagnosed in paediatric patients. The external features concerning face and limbs are well described in the literature but controversy existed as to whether polycystic kidneys are a relatively common internal feature of the disease [3]. Nowadays, with 15 cases of this association reported in the literature, we think that there is enough evidence to consider polycystic kidneys as a frequent feature of this syndrome [3–12]. The onset of end-stage renal failure at 42 years of age in our patient makes us think that the cystic renal lesion needs considerable time to become manifest. The course of the renal disease seems to be more severe than in autosomal dominant polycystic disease (ADPKD) [13]. The age of onset of end-stage renal disease in OFD I ranges from 11 to 64 years [7,8]. Based on sonographic findings the cysts seem to be smaller and more uniform in size in OFD I than in ADPKD. The kidneys are also less enlarged and deformed in OFD I than in ADPKD [7]. The case presented here is the fourth in which hepatic cysts are reported in OFD I [3,10,11]. Thus, although hepatic cysts are to be a common feature for both diseases they seem to be more frequent in ADPKD [14]. A microscopic study of renal cysts in OFD I disclosed that as in ADPKD they were located all along the nephron, but glomerular cysts were more frequent in OFD I than in ADPKD [7].

The case we describe hereby is an apparently sporadic case of OFD I. The patient had at birth some facial malformations that were surgically repaired but had never been told that she had OFD I. The first notice she had about her cystic kidneys were at the age of 42. The long period elapsed between the diagnosis of the syndrome and the onset of end-stage renal disease made it difficult to link both entities. But eventually an accurate physical examination pointed to the diagnosis of OFD I.

OFD has a highly variable clinical expression that may range from severely mentally retarded and malformed children to slight facial and digital abnormalities with no mental retardation. The association of this entity with CNS abnormalities such as agenesis of the corpus callosum, hydrocephaly, cystic brain lesions, berry aneurysm, and seizures. This is the third case were cerebellum atrophy with its consequent ataxia is reported [9,10]. It is also the second case were periodontal disease is present.

We suggest that OFD I should be looked for in families were only females have cystic kidneys and also but with less possibilities in sporadic cases. It is important to establish the correct diagnosis and to differentiate it from ADPKD. Genetic counselling differs between both entities, while in ADPKD the risk for the offspring is 50%, in the OFD I syndrome normal males and phenotypically normal females are not at risk for kidney disease. Only females with external features of OFD I are at risk for polycystic kidney disease.

Fig. 1. a, b Frontal and lateral view of the face showing facial asymmetry, microretroglnathia, malocclusion, broad nasal root, and down-turned eyes; c brachydactyly and slight soft-tissue syndactyly; d, irregular tongue margin.

Fig. 2. Sonographic scan of the kidneys, showing multiple cysts.

cortical atrophy and cerebellum atrophy. An electroencephalogram was normal. Bone X-ray showed microcephalia with enlargement of Turkish chair and small phalanges. Karyotype revealed a normal 46xx female. The patient’s family history was uninformative for the presence of either kidney disease or facial and hand abnormalities. The parents were not consanguineous. The mother had no history of miscarriages. Abdominal ultrasonography of her parents, brothers, and sisters was normal.
disease. Since most patients with OFD I come to medical attention in early childhood for repair of external malformations, their kidney involvement may not be apparent at the time of the initial diagnosis, thus a follow-up of the kidney function is warranted.

References


Received for publication: 30.12.96
Accepted: 3.1.97