dichotomisation, all Tp determinations were significant predictors of PS.

The ECC technique produces a systemic response consisting of adrenergic stimulation and uncontrolled activation of inflammation leading to hyperglycaemia and the release of inflammatory mediators. The relationship between hyperglycaemia and a poor prognosis is not clearly established, although in our study SHG was associated with PS (P < .05).

Elevation of Tp levels has been associated with postoperative complications, and a decreasing trend is a marker of favourable prognosis. In this study, elevated Tp was associated with long durations of mechanical ventilation and lengths of stay, and could predict PMV (Fig. 2) as well as PS. The RACHS-1 score was correlated with the duration of mechanical ventilation; and patients with a HSC were the patients that had a PS.

The conclusions of this study are that Tp is the best predictor of postoperative morbidity and that a multifactorial assessment is a useful tool to identify children at risk, as demonstrated by other authors.6

References

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Clinical and molecular diagnostics of a cartilage-hair hypoplasia: Two new cases

El diagnóstico clínico-molecular en la hipoplasia de cartílago-pelo: dos nuevos casos

Dear Editor:

The diagnosis of cartilage-hair hypoplasia, also known as McKusick type metaphyseal chondrodysplasia (OMIM 250250), is based on disproportionate short stature, bowed femurs and tibias, short and broad phalanges, loose ligaments with characteristic incomplete extension of the elbows and sparse hair, and was first described in the Amish population of the United States.1 It is caused by mutations in the RMRP gene (OMIM 157660; g913),2 a nuclear noncoding gene for an RNA chain that is a subunit of the mitochondrial RNase MRP protein complex, which is involved in ribosomal assembly and cellular cycle regulation. The disorder has a recessive pattern of inheritance, and depending on the severity of the mutation it can have a broad range of clinical manifestations (from mild to severe): metaphyseal dysplasia without hypotrichosis, cartilage-hair dysplasia and anauxetic dysplasia.3

Case 1

Boy, 7 months of age, with healthy nonconsanguineous Spanish parents. He was born at 40 weeks, with a weight of 3200 g, length of 45 cm and head circumference of 36 cm. He was admitted at 4 months of age with acute gastroenteritis. The physical examination revealed sparse, fine and brittle hair, shortened limbs, moderate varus bowing of the femurs, and short fingers. His height was 65.5 cm (−1.31 SD) and his weight 7850 g (−0.72 SD). Bone radiography showed shortening of long bones and metaphyseal widening. Immunologic testing showed moderate neutropenia and lymphocytopenia (reduced T CD4+ and B+ T cells); low levels of IgA and normal IgM and IgG levels. These findings led to a clinical diagnosis of cartilage-hair hypoplasia. An RMRP test was ordered at 3 years of age, which detected the presence of 2 heterozygous mutations [g.236A>G, paternal; g.260G>A, maternal]. This diagnosis allowed for screening the maternal

<table>
<thead>
<tr>
<th></th>
<th>Cartilage-hair hypoplasia</th>
<th>Kyphomelic dysplasia</th>
<th>Immunoosseous dysplasia, Schimke type</th>
<th>Ommen syndrome</th>
<th>Skeletal dysplasia with severe combined immunodeficiency</th>
<th>Shwachman-Diamond syndrome</th>
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<tr>
<td><strong>OMIM</strong></td>
<td>250250</td>
<td>211350</td>
<td>242900</td>
<td>603554</td>
<td>200900</td>
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<td><strong>Gene</strong></td>
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<td><em>SMARCAL1</em></td>
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<tr>
<td><strong>Location</strong></td>
<td>9p13</td>
<td>Unknown</td>
<td>2q35</td>
<td>11p12, 10q13</td>
<td>Unknown</td>
<td>7q11</td>
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<td>AR</td>
<td>AR</td>
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<tr>
<td><strong>Skeletal abn.</strong></td>
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<td>Metaphyseal</td>
<td>Spondyloepiphysial</td>
<td>Neg</td>
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<tr>
<td><strong>Bowed femur and tibia</strong></td>
<td>POS</td>
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<td>Neg</td>
<td>Neg</td>
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<td>Neg</td>
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<tr>
<td><strong>Short stature</strong></td>
<td>Disproportionate</td>
<td>Disproportionate</td>
<td>Disproportionate</td>
<td>Neg</td>
<td>Disproportionate</td>
<td>Disproportionate</td>
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<tr>
<td><strong>Haematological abn.</strong></td>
<td>Lymphocytopenia, neutropenia, risk of malignancy</td>
<td>Lymphocytopenia, neutropenia, thrombocytopenia</td>
<td>Lymphocytopenia, neutropenia, thrombocytopenia</td>
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<td>Lymphocytopenia</td>
<td>Pancytopenia, risk of malignancy</td>
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<td>POS</td>
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<td><strong>Hair</strong></td>
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<td>Fine</td>
<td>Fine</td>
<td>Neg</td>
<td>Alopecia</td>
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<tr>
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<td>POS</td>
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<td>Neg</td>
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<tr>
<td><strong>Type</strong></td>
<td>↓ T and B cells</td>
<td></td>
<td>↓ T cells</td>
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<td>Lymphadenopathy, architectural effacement of lymph nodes, ↓ B cells</td>
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<td>NEG</td>
<td>NEG</td>
<td>Neg</td>
<td>NEG</td>
<td>Pos</td>
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<tr>
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<td>Gastrointestinal malabsorption, Hirschprung disease, oesophageal atresia</td>
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<td>Exocrine pancreatic insufficiency</td>
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<td>NEG</td>
<td>POS</td>
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<tr>
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<td></td>
<td></td>
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<td>NEG</td>
<td>NEG but described</td>
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<td>Adulthood</td>
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<td></td>
<td>Infant</td>
<td>Adulthood</td>
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Abn.: abnormality; AR: autosomal recessive; NEG: negative; POS: positive.
blood for the paternal mutation in the foetal DNA (non-invasive prenatal technique) at 8 and 10 weeks in the 2 subsequent gestations of this couple. In the first of these pregnancies, the paternal mutation in the foetal DNA was detected in maternal blood and confirmed by amniocentesis (invasive technique). The pregnancy was terminated. The paternal mutation was not detected in the second pregnancy, and this finding was confirmed by an invasive prenatal test (healthy noncarrier foetus, publication in progress). At 9 years of age, the patient still has short stature (height 108 cm [−4.06 SD]; weight 20 kg [−2.25 SD]), and moderate varus bowing of the limbs with followup in the rehabilitation department. His hair is sparse. The patient has had 2 episodes of pneumonia in which no pathogen was identified. His vaccinations are up to date with the immunisation schedule of his autonomous community, and the patient had mild febrile reactions to live virus vaccines. The patient is receiving prophylaxis with trimethoprim-sulfamethoxazole 3 days a week (Fig. 1).

Case 2

Boy aged 2.3 years of Romanian descent diagnosed with achondroplasia at one week of life. The parents were non-consanguineous, the pregnancy was monitored in Romania, and the patient was born to term; the birth anthropometric measurements are not known. Physical examination showed a height of 62 cm (−9.6 SD), weight of 8620 g (−3.34 SD), shortening of upper and lower extremities, thick hands and short fingers. There were no skull abnormalities, and the hair was sparse, very fine and blonde. Bone radiography showed short hand bones with cone-shaped epiphyses, knees with broad and irregular metaphyses and poorly ossified epiphyses, femoral bowing with delayed ossification of the proximal femoral epiphyses, and hip bones with normal acetabula (Fig. 1). Laboratory tests were performed (complete blood count, biochemistry panel, and immunoglobulins) the results of which were normal. At 7.4 years of age he was 90.6 cm tall (−6.25 SD), had a growth rate of 4–7 cm a year (−2.15 SD and −1.45 SD), he had not developed any severe infections or any type of gastrointestinal malabsorption. We ordered a direct RMRP gene test that revealed 2 heterozygous mutations (g.96,97dupTG, maternal; g.−25-11 dupACTACTCTGTAAG). The father did not cooperate (Fig. 1).

The mutations found in these 2 cases have been described previously in patients of European descent with a cartilage-hair hypoplasia phenotype. 5 The g.−25-11 dupACTACTCTGTAAG mutation in the Romanian patient has been described in a patient of Spanish descent. 5 Table 1 shows the differential diagnosis. A full diagnosis based on clinical and molecular findings can help predict the prognosis of the disease and inform its management. Immune function, both humoral (IgG deficiency) and cellular (lymphocytopenia), and the presence of nonregenerative macrocytic anaemia should be evaluated. These patients may also develop malignancies, especially of the blood (lymphomas and leukaemia). 6 Possible treatments include osteotomies to correct deformities, surgical bone lengthening, infection prophylaxis in the presence of an immunodeficiency, and prophylactic treatment for anaemia, should it develop. Molecular diagnosis makes it possible to provide adequate genetic counselling for family planning and reproductive health.

Figure 1  Top: case 1 patient at 9 and 18 months, and at 5 and 7 years, respectively. Mutations found in the RMRP gene. Bottom: case 2 patient at 4.5 years of age and radiographs at 2 years of age.
Acknowledgments

We want to thank the laboratory technicians, Jesús Gallego Merlo and Camilo Vélez Monsalve, for their invaluable daily work and their contribution to the diagnosis of these 2 cases. We thank the patients and their families for consenting to the publications of images and clinical data for scientific purposes.

References


Clinical and radiological findings in a case of pseudohypoparathyroidism type 1a: Albright hereditary osteodystrophy

Aspectos clínico-radiológicos en un caso de pseudohipoparatiroidismo tipo 1a: Osteodistrofia hereditaria de Albright

Dear Editor,

Pseudohypoparathyroidism (PHP) comprises a heterogeneous group of diseases characterised by insensitivity of target organs to the activity of parathyroid hormone (PTH) resulting from abnormalities in the PTH receptor, either in the alpha subunit of the stimulatory G protein or in the second messenger system. The 2 main subtypes of PHP (1a and 1b) are due to inactivating mutations in the GNAS gene (20q13.2) that encodes the alpha subunit of stimulatory G protein (Gαs).

The patient was a 13-year-old female with subcutaneous nodules in arms and abdomen, lifelong short stature and intellectual disability.

Both parents (Ecuadorean in origin) were healthy. The height of the mother was 151.5 cm and the father’s height was 160 cm. There was no perinatal or pathological history of interest. The patient experienced menarche at 11 years of age.

Physical examination: height, 143.7 cm (−2.2 SDS); weight, 55.2 kg; and BMI, 26.7 kg/m² (+2.5 SDS). The patient had a singular phenotype (Fig. 1) with a rounded face, short neck, and shortening of the first toe in both feet as well as of the fourth metacarpal and metatarsal bones in both hands and feet, respectively. Hard subcutaneous nodules 15 mm in diameter were found in the radial side of the forearm, another measuring 5 mm in the hypogastric region, and another measuring 15 mm in the palm of the hand. Palpation revealed an osseus plaque 10 mm in diameter (osteoma cutis) in the right parietal region. The patient had mild intellectual disability and had completed pubertal development.

Laboratory findings included hypocalcaemia, hyperphosphoraeemia and elevated PTH. Thyroid function tests, insulin-like growth factor I (IGF-I), prolactin and gonadotropin levels were all normal.


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