dichotomisation, allTp determinations were significant pre-
dictors of PS.

The ECC technique produces a systemic response consist-
ing of adrenergic stimulation and uncontrolled activation of
inflammation leading to hyperglycemia and the release of
inflammatory mediators. The relationship between hyper-
glycemia 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 postop-
erative complications,® and a decreasing trend is a marker
of favourable prognosis. In this study, elevated Tp was asso-
ciated 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 pre-
dictor of postoperative morbidity and that a multifactorial
assessment is a useful tool to identify children at risk, as
demonstrated by other authors.®

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Clinical and molecular
diagnostic 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 lig-
aments with characteristic incomplete extension of the
elbows and sparse hair, and was first described in the Amish
population of the United States. It is caused by mutations in the
RMRP gene (OMIM 157660; 9p13), 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 anaux-
etic dysplasia.

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 shorten-
ing 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 1** Differential diagnosis of cartilage-hair hypoplasia.

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<tbody>
<tr>
<td>Cartilage-hair hypoplasia</td>
<td>Kyphomelic dysplasia</td>
<td>Immunoosseous dysplasia, Schimke type</td>
<td>Ommen syndrome</td>
<td>Skeletal dysplasia with severe combined immunodeficiency</td>
<td>Shwachman-Diamond syndrome</td>
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<tr>
<td>250250</td>
<td>RMRP</td>
<td>9p13</td>
<td>AR</td>
<td>Metaphyseal</td>
<td>Disproportionate</td>
<td>Lymphocytopenia, neutropenia, risk of malignancy</td>
<td>Frequent</td>
<td>Thin, sparse and blonde</td>
<td>POS</td>
<td>↓ T and B cells</td>
<td>POS</td>
<td>Gastrointestinal malabsorption, Hirschsprung disease, oesophageal atresia</td>
<td>NEG</td>
<td>NEG</td>
<td>Adulthood</td>
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<td>211350</td>
<td>Unknown</td>
<td>Unknown</td>
<td>AR</td>
<td>Metaphyseal</td>
<td>POS</td>
<td>Normal</td>
<td>NEG</td>
<td>POS</td>
<td>↓ T cells</td>
<td>NEG</td>
<td>Progressive nephropathy, rapid and fatal</td>
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<td>NEG</td>
<td>Adulthood</td>
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<tr>
<td>242900</td>
<td>SMARCAL1</td>
<td>2q35</td>
<td>AR</td>
<td>Metaphyseal</td>
<td>POS</td>
<td>Fine</td>
<td>POS</td>
<td>POS</td>
<td></td>
<td>NEG</td>
<td>Exocrine pancreatic insufficiency</td>
<td>NEG</td>
<td>NEG</td>
<td>Adulthood</td>
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<tr>
<td>603554</td>
<td>DCLRE1C, RAG1, RAG2</td>
<td>11p12,10’13</td>
<td>AR</td>
<td>Metaphyseal</td>
<td>POS</td>
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<td>200900</td>
<td>Unknown</td>
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<td>AR</td>
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<td>POS</td>
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<tr>
<td>260400</td>
<td>SBDS</td>
<td>7q11</td>
<td>AR</td>
<td>Metaphyseal</td>
<td>POS</td>
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<tr>
<td>Abn.: abnormality; AR: autosomal recessive; NEG: negative; POS: positive.</td>
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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 dupACTACTCTGTAAGC). 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.¹ The g.25-11 dupACTACTCTGTAAGC mutation in the Romanian patient has been described in a patient of Spanish descent.² 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 non-regenerative macrocytic anaemia should be evaluated. These patients may also develop malignancies, especially of the blood (lymphomas and leukaemia).³ 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.
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.

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

Aspectos clinico-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 osseous 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, hyperphosphataemia and elevated PTH. Thyroid function tests, insulin-like growth factor I (IGF-I), prolactin and gonadotropin levels were all normal.

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