INFANT WITH PHENOTYPE SUGGESTIVE OF SILVER-RUSSELL SYNDROME AND STUDY OF NORMAL METHYLATION: CONSIDER 12q14.3q15 MICRODELETION SYNDROME.

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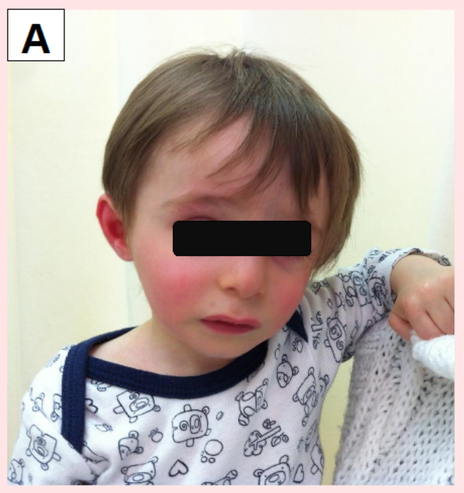
INTRODUCTION

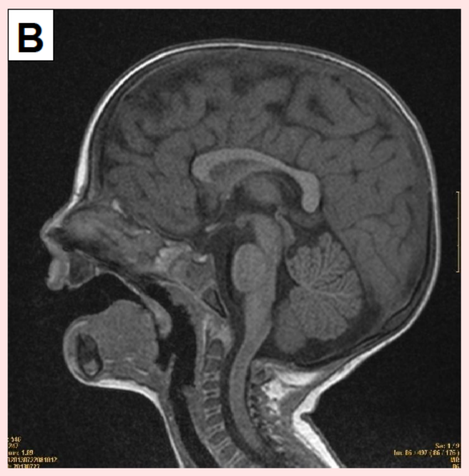
The 12q14.3q15 microdeletion syndrome is a rare entity of which only 16 new cases have been described to date. The syndrome consists of the association of severe pre- and postnatal growth retardation, proportional short stature, psychomotor retardation and osteopoikilosis. The phenotypic appearance of these patients poses a differential diagnosis with Silver-Russell syndrome, among other entities.

CLINICAL DESCRIPTION

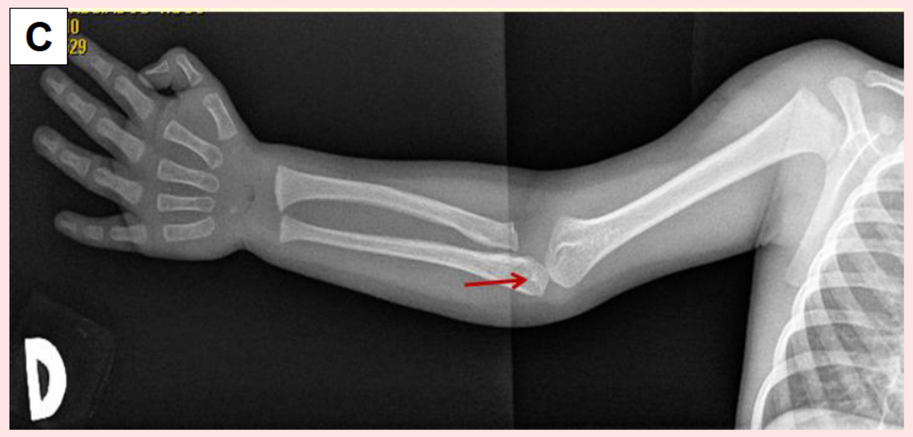
A 10-month-old boy was referred for study of growth retardation. Product of the first full-term gestation of non-consanguineous parents of normal stature.
BW: 1.800 g (–2.5 SD), length: 40 cm (–4.5 SD).

Physical exploration:
Triangular facies with prominent forehead and retrognatia. Mild clinodactyly of the little finger. No asymmetries or areas of hyperpigmentation. Mild psychomotor retardation. Weight: 5.0 kg (–3.8 SD), length: 61 cm (–4.8 SD), CP: 43.5 cm (–2.0 SD); normal genitals with testes of 1-cc.
Fig. A





Laboratorial study:
Normal biochemical profile with normal coeliac disease markers.
Hormone study: thyroid hormones normal, IGF-1 59.0 ng/ml, IGFBP3 2.40 ng/ml.
Glucagon test: : basal GH 1.8 ng/dl and peak of 4.6 ng/ml.



MRI of the sellar region: normal. *Fig. B*

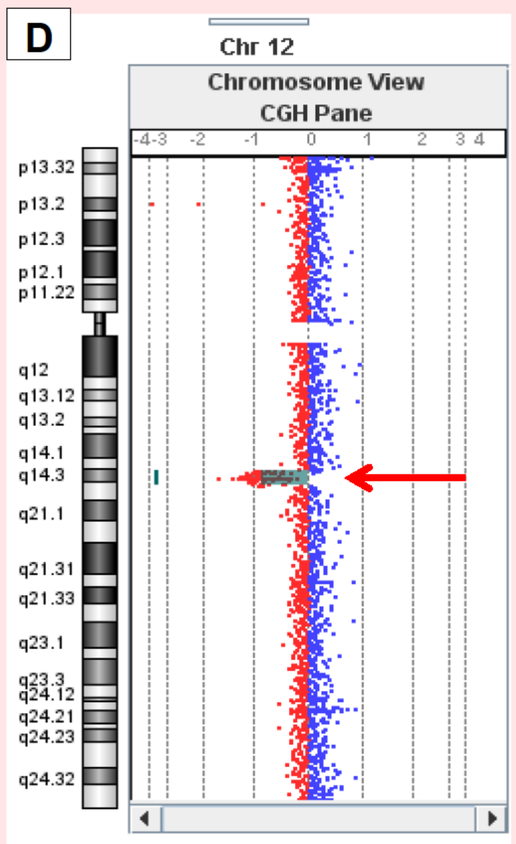
Skeletal survey: osteopoikilosis in proximal metaphysis of the right ulna. *Fig. C*

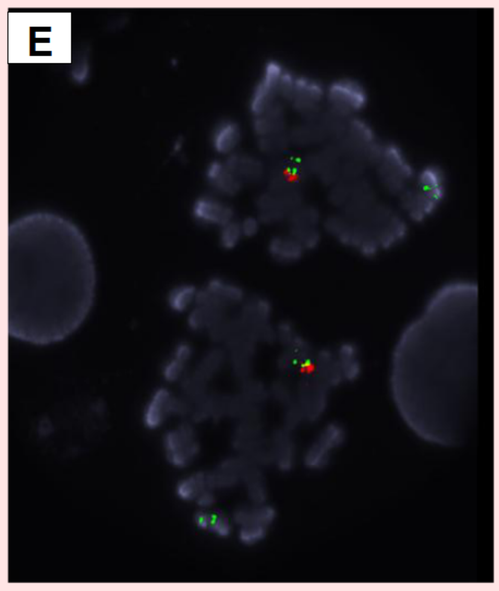
Methylation study of H19DMR and KvDMR domains, region 11p15 by sMPLA (ME030, MRC Holland): normal.

Array-CGH study (ISCA v2, 8x60K, Agilent):
Detected a deletion in the 12q14.3q15 region, involving 11 genes: HMGA2, LEMD3, GRIP1, MSRB3, RPSAP52, LLPH, TMBIM4, IRAK3, HELB, CAND1 and DYRK2. *Fig. D*

FISH study with BAC RP11-24p:
Confirmed the 12q14.3q15 deletion in the patient and was normal in the parents. *Fig. E*

Treatment: GH therapy was initiated.





CONCLUSION

Compared genetic hybridization techniques are useful to orient the diagnosis of patients with severe growth retardation and dysmorphic phenotype. Growth retardation and other clinical characteristics of the patient are considered to be related to the chromosomal abnormality detected and described as 12q14.3q15 microdeletion syndrome in other patients. Haploinsufficiency of the HMGA2 gene has been implicated as a cause of short stature in these patients.

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