AN UNUSUAL CASE OF GROWTH HORMONE REPLACEMENT THERAPY IN A CHILD WITH HEREDITARY MULTIPLE EXOSTOSES AND GROWTH HORMONE DEFICIENCY

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OBJECTIVES

Hereditary multiple exostoses (HME) is an autosomal dominant heritable disorder characterized by exostoses located mainly in the long bones of extremities. It is caused by mutations mainly in two genes: EXT1, EXT2(1,3)
The prevalence of HME is reported to be 0,9-2/100,000 (2).
Clinical expression of HME phenotype is variable in individuals. Many exostoses are asymptomatic, alternatively some may cause pain, deformity, arthritis and impingement on adjacent tendons, nerves, vessels(1) or undergo malignant transformation to chondrosarcoma in about 2-5% (3,4). Exostoses are rarely evident at birth (1)and the age of onset is variable, from 2 to 15 years (2).
Growth hormone (GH) deficiency is very rare in children with HME and GH replacement therapy has not been well described(5,6,7)

Fig 1. Bone age with exostoses on middle phalanx on 4th finger, distal radius bone

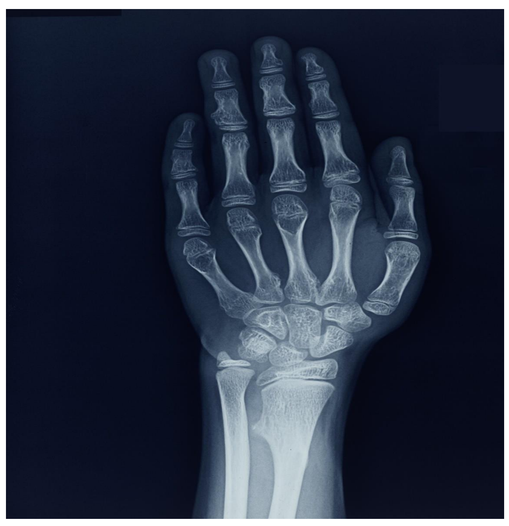


Fig 2 exostoses on thigh and both knees

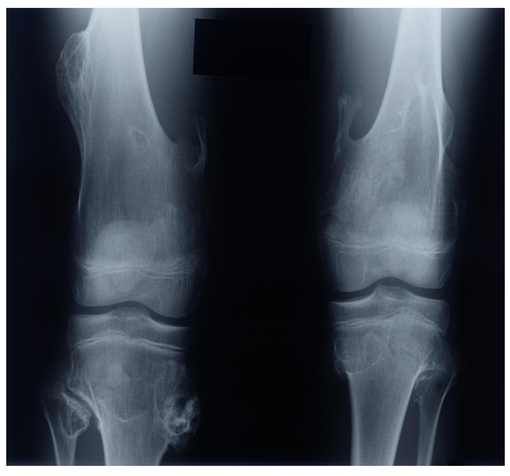
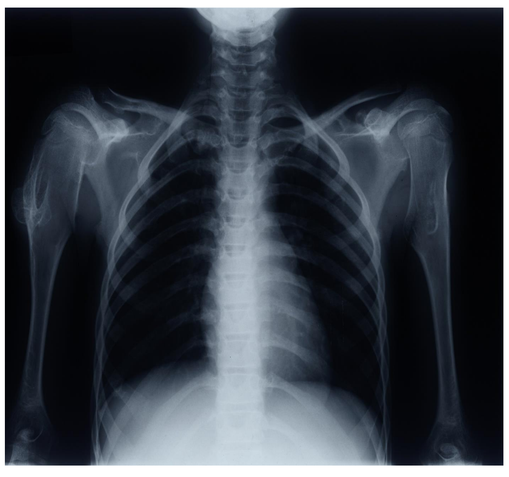


Fig 3. exostoses on right scapulae

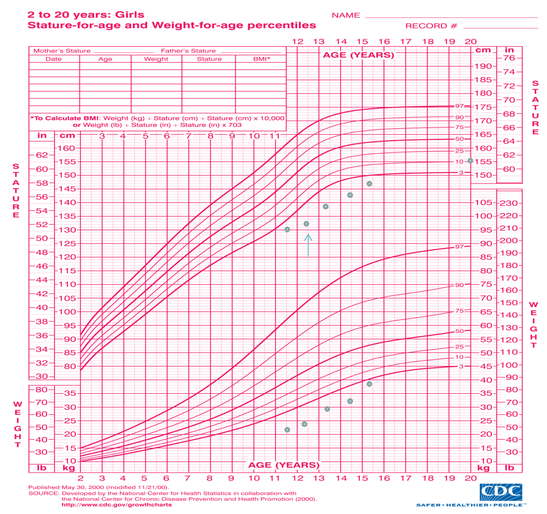


CLINICAL PRESENTATION

A 12.5 years old girl was referred to our Department because of short stature. She showed a stature of 132cm (-2,8SDS), weight of 24kg ((BMI-13,8, -2,59z-score), reduced growth rate (2,3cm/year) and she was on pre-pubertal maturation stage. Genetic target was 155+/-4.5cm. On physical examination she had multiple exostoses on right scapulae, right thigh, right arm, right knee joint and very short fingers. The mobility of the joints adjacent to the exostoses remained free and muscle strength was normal.
Her father had also multiple exostoses on scapulae and long bones and was under orthopedic follow up.
Hypothyroidism, chronic diseases, malabsorption and skeletal dwarfism were excluded. GH deficiency was diagnosed by two stimulation tests: insulin (GH peak: 5.36 ng/ml) and L-dopa administration (GH peak: 7.35 ng/ml) and confirmed by low IGF-I values (214 ng/ml). Bone age was delayed (10.5years) with exostoses on distal radius bone and middle phalanx of fourth finger..(fig1)
X-rays showed exostoses on right scapulae, right distal femurs, both knees (fig 2,3), right arm, right clavicles and pelvic bones. .
She was referred to orthopedics who confirmed the diagnosis of HME.

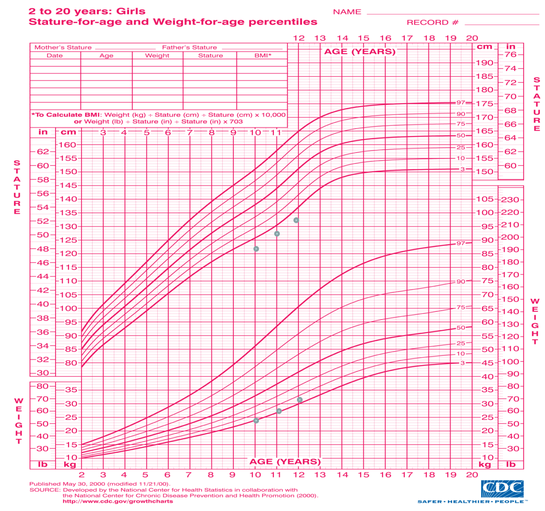
GH replacement therapy (0.025 mg/Kg/day) showed good response on linear growth: 6.1 cm (1.4 SDS) during the first year and
4.2 cm (3.0 SDS) the second year of therapy (fig 5).
Her mother was negative for exostoses .

Fig 5. Growth chart after GH replacement therapy



Her sister (10years old) showed short stature (121.8cm, -2,5SDS), reduced growth rate 2.8cm/year and exostoses (right scapulae and knees) at x-ray examination. GH deficiency was diagnosed by insulin (GHpeak2.11 ng/ml), L-dopa stimulation tests (GHpeak2.35 ng/ml) and low IGF-1 207ng/ml. GH replacement treatment (0.025mg/kg/d) showed moderate response: 5.5cm/year (-0.8SDS) the first year and 3.8cm/year (-0.8SDS) the second. (fig 6)

Fig 6. Growth chart after GH replacement therapy



CONCLUSIONS

- GH deficiency has rarely been found in HME patients.
- It is necessary to investigate GH secretion in patients with HME and short stature, because when GH deficiency is confirmed by clinical features and classic pharmacological tests, GH replacement therapy could be started to improve their stature.
- Moreover, a close follow-up of exostoses and HME before and during a long-term GH treatment is mandatory, as exostoses could transform into chondrosarcoma.
- However, studies with a longer follow-up are needed in order to define long-term effects of GH treatment on HME patients.

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55ESPE 851--P2
Syndromes : Mechanisms and Management
MARIA CHATZIPSALTI
DOI: 10.3252/pso.eu.55ESPE.2016
Poster presented at: ESPE 2016 PARIS
PosterSessionOnline.com