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Case Report

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GROWTH HORMONE DEFICIENCY IN ACHONDROPLASIA SAUDI GIRL. RARE CASE REPORT

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ABSTRACT

Achondroplasia is the most common form of chondrodysplasia. It caused by point mutations in the transmembrane domain of the fibroblast growth factor receptor 3 (FGFR 3) gene. Achondroplasia is not associated with growth hormone (GH) deficiency however GH therapy has some beneficial effects as per some reported cases. To our knowledge only one case of Achondroplasia with GH Deficiency was reported. Here we report 8 years old Saudi girl who is a known case of Achondroplasia diagnosed at birth who presented to pediatric endocrine clinic with sever short statue. Her investigation revealed low IGF1. Low GH level after 2 chemical GH stimulation tests and one physiological test. MRI pituitary reveled small pituitary size and bone age was delayed. She was treated with GH therapy. Growth velocity improved after 6 month with no reported side effect.

KEYWARDS: Achondroplasia FGFR3, Growth hormone treatment.

INTRODUCTION

Achondroplasia is the most common form of chondrodysplasia.[1]

The incidence rate of Achondroplasia is ~1/15-40, 000 live births.[2]

The main features in Achondroplasia Newborn and children including disproportionate short limbs (rhizomelic dwarfism), a large head with frontal bossing, flat nasal bridge and mid facial hypoplasia and narrow trunk. The hands are short and broad, with a three-pronged (trident) configuration and prominent abdomen and buttocks.[3,4]

Achondroplasia is not associated with GH deficiency however GH therapy has some beneficial effects as per some reported cases. To the best of our knowledge only one case of Achondroplasia with GH Deficiency was reported. Here we report 8 years old Saudi girl who is a known case of Achondroplasia who presented with sever short statue. Her investigation revealed low IGF1. Low GH level after 2 chemical GH stimulation test and one physiological test. MRI pituitary reveled small pituitary size and bone age was delayed. She was treated with GH therapy. Growth velocity improved after 6 month with no reported side effect.

CASE REPORT

8 years old Saudi girl who is a known case of Achondroplasia diagnosed at birth. She was presented to pediatric endocrine clinic with sever short stature. She was product of full term normal spontaneous vaginal delivery. Past history was unremarkable. There was no consanguinity between parents.

Vaccination was up to date. Developmental parameters were appropriate for age. She was on family diet with average appetite.

On examination, she had full manifestation of Achondroplasia including disproportionate short limbs (rhizomelic dwarfism), a large head with frontal bossing, flat nasal bridge and mid facial hypoplasia and narrow trunk. Her hands are short and broad, her weight is 19 Kg below 3rd percentile and height 96. 5 cm below 3rd percentile on of Saudi growth chart. Examination of chest and cardiovascular systems were normal. There was no hepatosplenomegaly, no skin changes. Child had normal intelligence with normal muscle tone and power and gait.

Investigations showed Hemoglobin 14 g dl, white blood cell (WBC) 11. 9 x10^{3}/μL, ESR was 13. karyotype reveled normal female 46XX, Serum urea and electrolytes were normal. Liver function tests were normal. Bone profile was within normal limit. serum 25 OH vitamin D 183 nmol/L (normal 50 - 250) Arterial blood gas was normal. Celiac disease profile was

negative. Urine and stool analysis were unremarkable, Thyroid function tests and the levels follicle stimulating hormone, luteinizing hormone, prolactin and progesterone estradiol, cortisol and adrenocorticotropic hormone were normal. Serum somatomedin C (IGF-1) was 38 ng/ml (normal range 30-342 ng/ml). Growth hormone provocation tests including Clonidine and glucagone stimulation test were done. Peak Growth hormone was 3. 2 mIu/L(normal more than 10). The levels of GH after 20 minute of exercise was obtained with peak Growth hormone was 5. 4 mIu/L (normal more than 10). MRI pituitary gland showed small volume of pituitary gland. No suprasellar mass lesion. Normal pituitary stalk normal sellar region. Bone age according to atlas of William walter Greulich is approximately 6 year and 10 month with short metacarpal and phalanges consistent of Achondroplasia.

A diagnosis of achondroplasia with subnormal GH secretion was made on the basis of the clinical, laboratory and radiological result. The patient was started on growth hormone treatment at dose of 0. 035 mg/kg/day. After six months of treatment, the patient's height had markedly improved (to 100. 5 cm). Growth velocity was 5 cm in 6 months. No abnormality was found on the thyroid function and no reported adverse effect of growth hormone therapy.

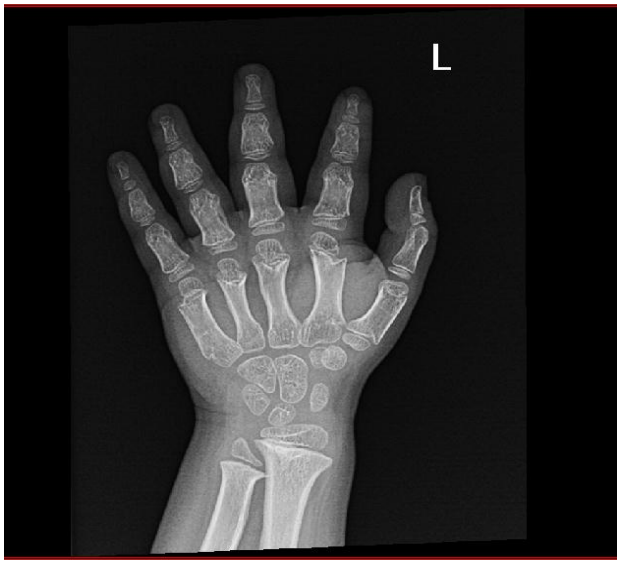

Figure 1: This is trident hand typical of achondroplasia.

All finger same length which diverge in 2 pairs plus thumb.

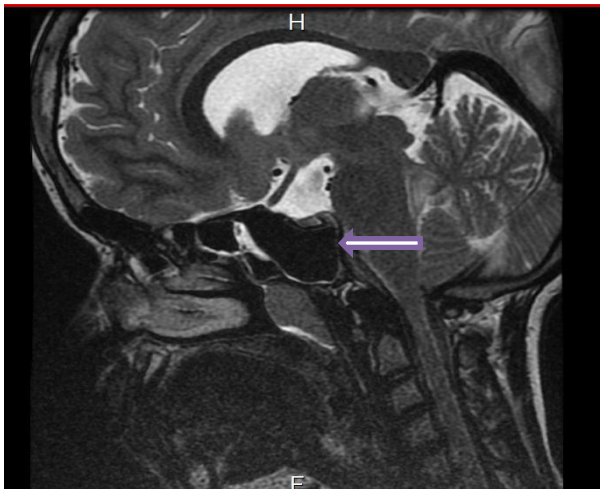

Figure 2 (A)

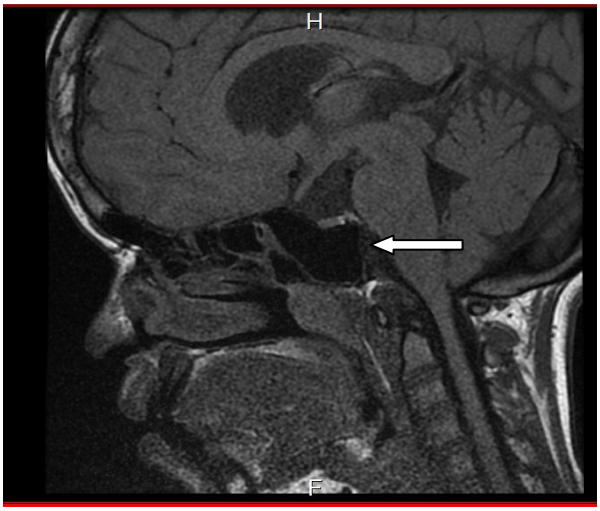

Figure 2 (B)

Small pituitary gland size is seen. Pituitary gland is slightly pushed down and posterior due to CSF herniated to pituitary fossa which can be seen due to obstruction of normal CFS flow in achondroplasia patients Ethics statement. Written informed consent was obtained from the patient's family. The study was approved by the research Ethics Committee in alyamamah hospital.

DISCUSSION

Achondroplasia is inherited as an autosomal dominant trait however most of cases are sporadic. it caused by point mutations in the transmembrane domain of the fibroblast growth factor receptor 3 (*FGFR 3*) gene.[5]

Patients with ACH do not generally have a GH deficiency.[6]

GH therapy has beneficial effects in achondroplasia as per some reported cases.[7,8] GH stimulates local cartilage cells in epiphyseal growth plate to produce insulin-like growth factors, which stimulate cartilage cell proliferation and subsequently promotes growth. This mechanism might explain effect of GH therapy in achondroplasia.[9]

In a study of Tanaka et al.[1] forty two children with achondroplasia were treated with GH for more than 2 years. The study concluded that GH treatment might be beneficial in short stature in children with achondroplasia during the first two years of treatment.[1]

Hertel et al studied 35 achondroplasia children who received GH treatment at a dosage of either 0. 1 IU/ kg/ day or 0. 2 IU /kg/day. the Mean growth velocity increased remarkably by 1. 9/ 3. 6 cm/y during the first year and by 0. 5/ 1. 5 cm/y during the second year. This study concluded that GH therapy in achondroplasia improves height during four years of therapy.[10]

In a study of Ramaswami U etal 35 children with achondroplasia were treated with recombinant hGH therapy for up to 6 y. It was noted that GH therapy increase Ht standard deviation yearly till year 4 og therapy. That was subsequently sustained with no significant further change.

There was a significant increase in the first year of therapy. The study concluded that GH therapy treatment improved the Ht position of achondroplasia children relative to their normal and achondroplasia peers without side effects. It recommended that early initiation of GH therapy prevented the characteristic height deficit from accumulating and thus decreasing the degree of disproportion.[11]

CONCLUSION

Our case report concluded that GH deficiency might be considered as cause of sever short stature among achodroplasia patients

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