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When growth exceeds boundaries: Tall stature, enlarged hands & feet - Is it what you think?

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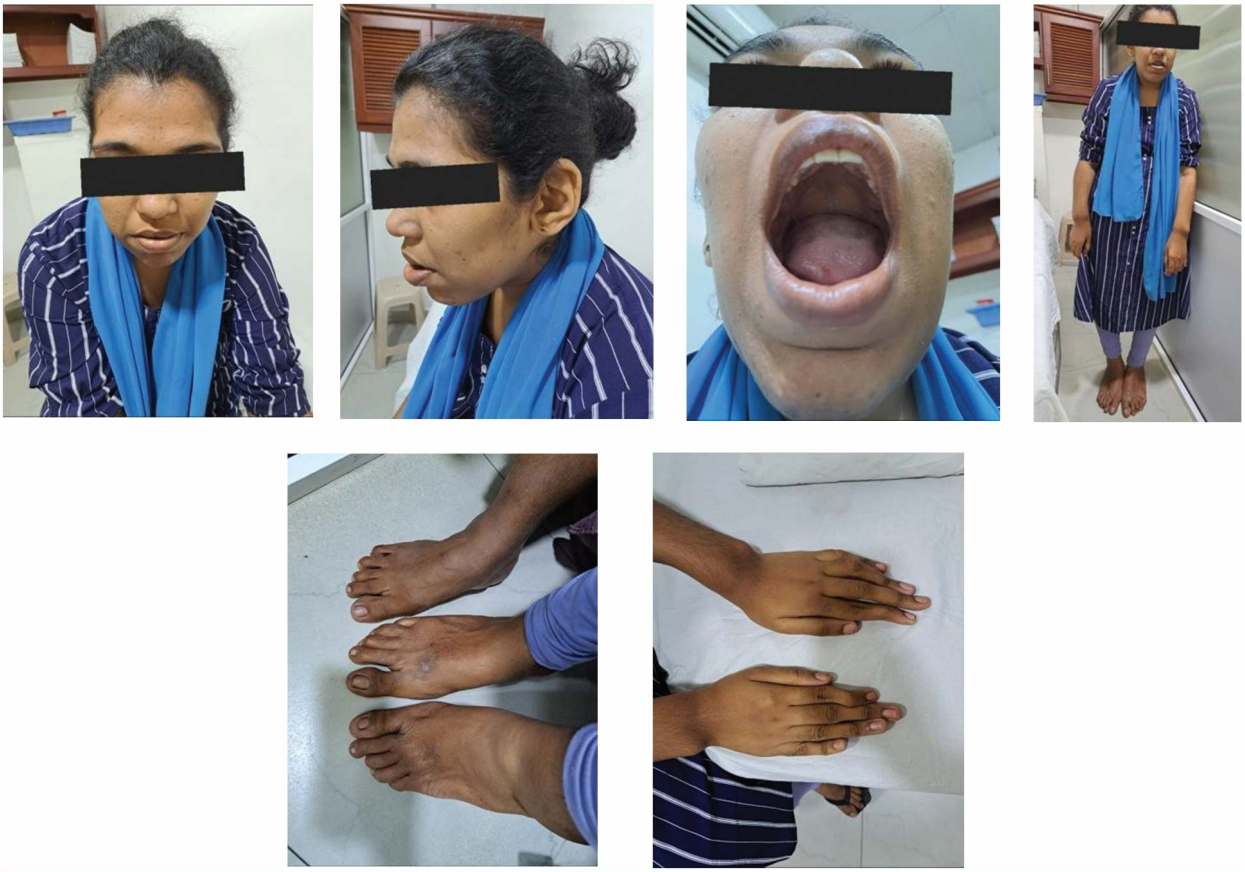

Figure 1: Clinical signs of the patient

This 17-year-old female had a BMI of 28.3 kg/m^2 with the height of 173 cm and a weight of 85 kg. Her arm span was 174 cm. She was tall in stature and was the tallest in the class among her peers during early childhood. At birth also, she was a large baby. She had mildly delayed motor and speech development and still has speech and learning disabilities. There was no history of seizures or hypoglycemic episodes.

She had a dolichocephalic head, prominent forehead and jaw, a high arched palate and a pointed chin. Her upper lip was thinner than the lower lip. She had acral enlargement with thickened subcutaneous tissues and long limbs. There were no ocular abnormalities, scoliosis or skin pigmentation. Her blood pressure was normal throughout.

During the biochemical evaluation, her hormone profile was normal including normal IGF 1 level and normal growth hormone level which has been done 2 hours following OGTT. Echocardiogram showed mitral valve prolapse, without aortic root dilatation or cardiomegaly. Ultrasonically there were no organomegaly or renal anomalies.

MRI brain with pituitary cuts showed a normal pituitary gland, but had mildly dilated ventricles. Otherwise, it was normal.

Question

What can be the most likely clinical diagnosis for the above patient in the context of given history.

1. Marfan syndrome
2. Acromegaly
3. Pituitary Gigantism
4. Sotos syndrome
5. Beckwith-Wiedemann syndrome

Answer

Sotos syndrome or Cerebral gigantism. (A cause of Pseudoacromegaly)

Pseudoacromegaly or acromegaloidism refers to the conditions with features of acromegaly or gigantism, but with normal IGF-1 level and suppressed GH with OGTT. This patient's clinical history was very suggestive of a childhood overgrowth syndrome in the context of normal GH and IGF-1.

Clinical diagnosis of Marfan syndrome was unlikely according to the 2010 revised Ghent criteria. She had no cardinal features such as ocular abnormalities or aortic root dilatation.

Acromegaly and pituitary gigantism were excluded with normal IGF-1 and GH and normal pituitary in MRI.

Beckwith-Wiedemann syndrome is another childhood overgrowth syndrome with overlapping features of Sotos syndrome, but the diagnosis is in the period of neonate or in more early childhood. Other than that, in comparison to Sotos syndrome, they characteristically are associated with organomegaly including cardiomegaly, abdominal wall defects and sometimes hypoglycemic episodes.

Therefore, the most likely clinical diagnosis for the above patient is Sotos syndrome (also known as cerebral gigantism). Sotos syndrome is characterized by typical facial features such as dolichocephaly, prominent forehead, ears, jaw and pointed chin and high arched palate. Though the patients with Sotos syndrome have phenotypically acromegaloid features, their GH secretion and IGF-1 level are normal. Usually MRI brain is normal except in some, there can be ventriculomegaly. But intracranial pressure is normal. Sotos syndrome is due to loss of function mutation in the NSD1 gene.

As in this case, we have to evaluate further for a cause of acromegaloidism or pseudoacromegaly, when a patient is having acromegaloid features with normal GH and IGF-1 level.

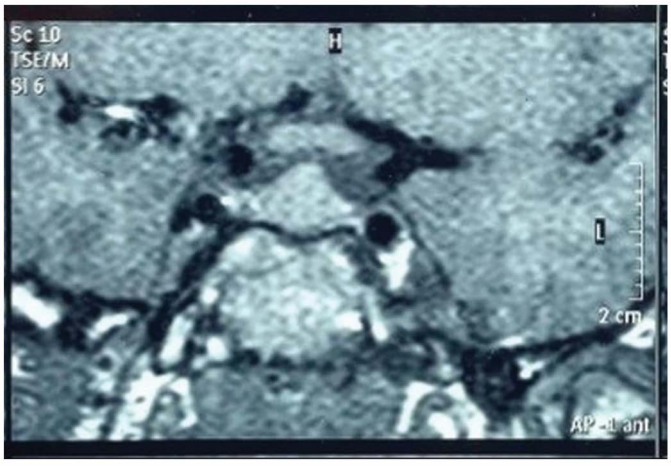

Figure 2: MRI showed normal pituitary

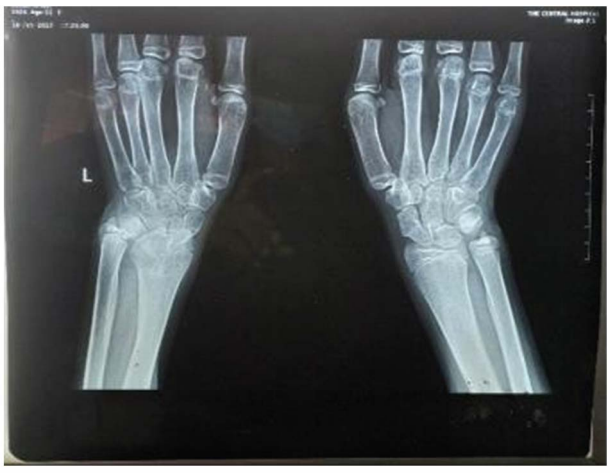

Figure 3: An x-ray taken at the age of 11 years showed advanced bone age.

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