Extreme Short Stature

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Background

- There are few reports of children with Down syndrome (DS) and additional genetic anomalies.
- Cognitive bias such as the anchoring effect could lead to missed or delayed additional diagnoses and thus cause postponement or sub-optimal treatment which could impact future quality of life.
- When a patient's presentation cannot be fully explained by the initial diagnosis, it is important to look for a second diagnosis as in this case of extreme short stature

Case Report

- Patient is a 17-month-old female with a diagnosis of DS who has been followed for hypothyroidism and short stature.
- She has essentially been euthyroid since starting thyroid hormone replacement at three months of age.
- Neonatal echocardiogram showed a small patent foramen ovale. She was asymptomatic at follow up with cardiology at one year of age. Cardiology did not recommend continued monitoring.
- Birth length: 16-1/4 inches
- Birth weight: 3 pounds 9 ounces.
- FAMILY HISTORY:
  Mom is 4 feet 11 inches.
  Dad is 6 feet.
  Mid-parental height is about 5 feet 3 inches
  Her sister is small for age.
  Her brother is average height.
- Parents are not overly worried about her height as there are smaller people in the family.

Physical Exam

Length: 62.5 cm, placing her 5 SDS below the mean for length.
3 SDS below the mean for length on the DS growth chart.
Weight: 7.15 kg, placing her less than the third percentile for weight.
Less than the third percentile for weight on the DS growth chart.
GENERAL: awake and alert, in no acute distress.
She was able to sit on her own.
Neck: supple, without thyroid enlargement.
Heart: regular rate and rhythm, no murmur appreciated.
Ext: warm and pink; cap refill is less than two seconds.
She appears to have proximal shortening of the extremities as well as small hands and feet.

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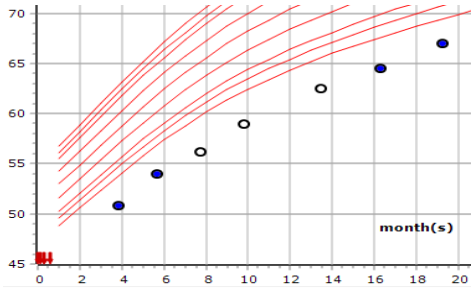
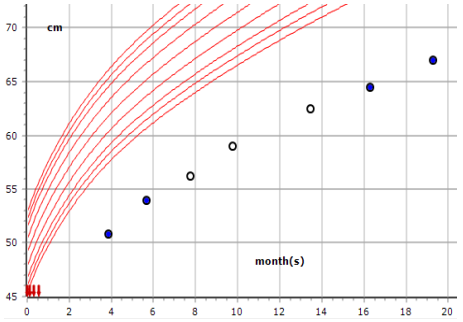
Growth Charts



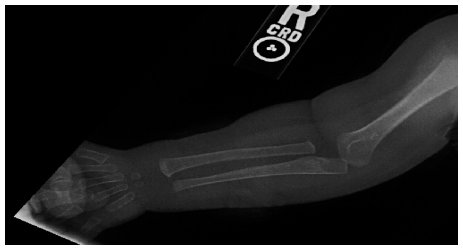
CDC Growth Chart: 67 cm ; -5 SDS



Down syndrome Growth Chart: 67 cm ; -2.8 SDS

Labs and Imaging

- Normal thyroid function tests.
- IGF-1: 33 ng/ml IGF-BP3: 3.1 mcg/ml
- Russel Silver methylation was negative.
- CMA showed a terminal XP deletion containing the pseudoautosomal SHOX gene.



Unremarkable skeletal survey

Discussion and Considerations

- The patient's extreme short stature could not entirely be explained by her diagnosis of DS.
- Medical comorbidities associated with DS that can influence growth were evaluated and if needed, treated.
- She was referred to genetics for additional testing and then diagnosed with SHOX deficiency.
- SHOX deficiency also causes short stature.
- Does having another genetic condition known to cause short stature further reduce the patient's predicted adult height and should treatment with growth hormone (GH) be considered?
- GH is an approved therapy for SHOX deficiency, but it is not approved for DS.
- Studies have shown that GH therapy improves adult height in patients with SHOX deficiency.
- Is growth hormone therapy a reasonable consideration given the ethical concerns surrounding the use of GH in patients with DS?
- Would further height reduction negatively impact quality of life such as socialization and a patient's ability to live independently?

Conclusion

- The diagnosis of SHOX deficiency would not have been discovered without the additional genetic testing.
- Further testing should be considered in patients who deviate from normal growth patterns for children with DS.
- Once potential contributing factors to short stature have been ruled out or addressed, additional genetic testing should be considered on a case-by-case basis.
- A patient with DS and SHOX deficiency is at risk for extreme short stature throughout life.
- GH is a potential therapy that could not only improve final adult height but also possibly quality of life.
- Therefore, do the potential benefits of growth hormone therapy outweigh the potential risks?
- Additional studies need to be performed to further investigate these questions?

REFERENCES

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