A Case of Growth Delay

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PATIENT HISTORY

CHIEF COMPLAINT:

An 8-year-old female presents to the pediatric office for follow-up after seeing pediatric endocrinology for

- Mildly abnormal glucose tolerance test (GTT)
- Short stature since birth
- Poor weight gain

PAST MEDICAL HISTORY:

- Growth charts show a downward trend falling below the 5th percentile
- Eating habits and nutritional causes were ruled out
- Gastroenterology workup negative
- No history of polyuria, polydipsia, polyphagia
- Review of systems was negative

FAMILY HISTORY

Mother has a history of:

- Gestational diabetes
- Occasional elevated morning blood sugars
- Maternal grandfather: diagnosed with diabetes at age 20, not requiring meds until later in life.
- Both maternal grandparents of short stature

PHYSICAL EXAMINATION

Physical exam was negative except for

- Short stature
- Growth chart demonstrated slowed weight gain in the last few years

GROWTH CHART

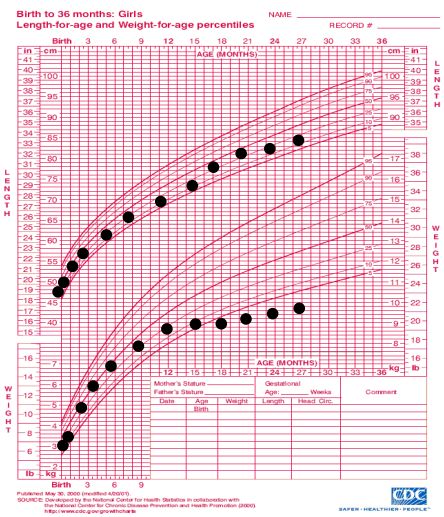

Figure 1. Growth chart demonstrating decelerated weight gain

DIAGNOSTIC TESTING

Laboratory tests ordered:

- Comprehensive metabolic panel
- Urinalysis
- Thyroid function tests
- Vitamin D
- CBC and ESR.

Because of the mildly abnormal GTT, the endocrinologist ordered re

- Repeat GTT, Hemoglobin A1c
- Insulin-like growth factor binding protein-3
- insulin-like growth factor and blood karyotype

With the exception of a Hgb A1c of 7.0, all results were within normal limits

DISCUSSION

DIAGNOSIS: Familial short stature and a suspicion of monogenic diabetes of youth (MODY). No specific cause was identified for the poor weight gain.

- A positive family history of diabetes and one mildly elevated Hemoglobin A1c is insufficient to diagnose monogenic diabetes, however, the concern for developing this condition remains.
- Monogenic diabetes, or "MODY" - "maturity onset diabetes of youth" is a group of rare genetic mutations that causes diabetes.
- MODY-2 makes up 32% of patients with genetic diabetes.
- Common presenting complaints include weight loss (44%), polyuria, nocturia, or polydipsia (82%) and gastrointestinal symptoms (59%).[1] Onset is earlier than in typical non-insulin-dependent diabetes.
- The age at diagnosis of MODY is younger than in type-2 diabetes mellitus (T2DM) patients (mean 13.6 (11.5-15.3); $P < 0.01$), but older than in T1DM patients (mean 8.2 (4.6-11.4); $P < 0.01$).[2]
- What usually initiates the workup for MODY is an incidental finding since patients do not present with typical signs and symptoms of insulin resistance or uncontrolled hyperglycemia.
- This patient's delayed growth can be considered the incidental finding that resulted in a workup revealing a mildly elevated A1c.
- The patient's parents were reassured and regular follow-up visits were scheduled to detect early development of MODY.

CONCLUSION

The most common cause for short stature is familial so providers should always inquire about the height of others in the family. Although metabolic causes for short stature are rare, MODY-2 should be considered in the differential if a patient has an unusual presentation, "mild" diabetes and positive family history of diabetes.

REFERENCES

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2. Schober E, Rami B, Grabert M, et al. Phenotypical aspects of maturity-onset diabetes of the young (MODY diabetes) in comparison with Type 2 diabetes mellitus (T2DM) in children and adolescents: experience from a large multicentre database. *Diabet Med*. 2009;26(5):466-73.

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ABSTRACT

An 8-year-old Caucasian female presents to the pediatric office for follow-up after seeing pediatric endocrinology for a mildly abnormal glucose tolerance test (GTT), short stature since birth and delayed weight gain.

HISTORY

The patient's weight and height remained below the 10th percentile until 7 years of age at which time she demonstrated only small increases in height and weight. Growth charts reveal a downward trend falling below the 5th percentile. Eating habits and nutritional causes were ruled out after interviewing the parents. A gastroenterology workup was performed at 2 years old, which included an upper endoscopy and sweat chloride test. Results were negative. Bone age assessment using radiography of hand and wrist was normal.
Family history revealed that the mother has a history of gestational diabetes and occasional elevated morning blood sugars. The maternal grandfather was diagnosed with diabetes at age 20, not requiring medication until later in life. Both maternal grandparents are of short stature.
Review of systems including constitutional, cardiac, gastrointestinal, endocrine, and genitourinary was negative. There is no history of polyuria, polydipsia, or polyphagia.

DIAGNOSTIC TESTING

Laboratory tests were ordered including: comprehensive metabolic panel, urinalysis, thyroid function tests, vitamin D, complete blood count, erythrocyte sedimentation rate. Because of the mildly abnormal GTT, the endocrinologist ordered a repeat GTT, Hemoglobin A1c, insulin-like growth factor binding protein-3, insulin-like growth factor and blood karyotype.

DIAGNOSIS

Results of lab tests were negative with the exception of a Hemoglobin A1c at 7.0%. Considering the otherwise normal lab and gastrointestinal workup, the patient was diagnosed with familial short stature and a suspicion of monogenic diabetes of youth (MODY). No specific cause was identified for the poor weight gain.

DISCUSSION

Short stature is defined as a height less than 2 standard deviations below the mean or below the 2.5 percentile for sex on the growth chart. The most common cause for short stature in a well-nourished child with no apparent genetic abnormalities is familial.
A positive family history of diabetes and one mildly elevated Hemoglobin A1c is insufficient to diagnose monogenic diabetes, however, the concern for developing this condition remains. Monogenic diabetes, or "MODY" - "maturity onset diabetes of youth" is a group of rare genetic mutations that causes diabetes. MODY-2 makes up 32% of patients with genetic diabetes. This dominantly-inherited mild hyperglycemia is associated with multiple mutations in GCK, the glycolytic enzyme.
Common presenting complaints include weight loss (44%), polyuria, nocturia, or polydipsia (82%) and gastrointestinal symptoms (59%).1 Onset is earlier than in typical non-insulin-dependent diabetes. The age at diagnosis of MODY is younger than in type-2 diabetes mellitus (T2DM) patients (mean 13.6 (11.5-15.3); $P < 0.01$), but older than in T1DM patients (mean 8.2 (4.6-11.4); $P < 0.01$).2 While short stature is not common with MODY, there is a newly described variant in which growth retardation is part of the presentation.3 With increased affordability of genetic testing, early identification of MODY in at risk individuals may be available in the future.4
What usually initiates the workup for MODY is an incidental finding since patients do not present with typical signs and symptoms of insulin resistance or uncontrolled hyperglycemia. This patient's delayed growth can be considered the incidental finding that resulted in a workup revealing a mildly elevated A1c. The patient's parents were reassured and regular follow-up visits were scheduled to detect early development of MODY.

CONCLUSION

The most common cause for short stature is familial so providers should always inquire about the height of others in the family. Although metabolic causes for short stature are rare, MODY-2 should be considered in the differential if a patient has an unusual presentation, "mild" diabetes and positive family history of diabetes.

REFERENCES

1. Pihoker C, Gilliam LK, Ellard S, et al. Prevalence, Characteristics and clinical diagnosis of maturity onset diabetes of the young due to mutations in HNF1A, HNF4A, and glucokinase: results from the SEARCH for diabetes in youth. *J Clin Endocrinol Metab*. 2013 98(10):4055–62.
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