A 19 year old female with obesity

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Case Presentation
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HPI

19 year old Hispanic female volunteering for a research study on DM2 in young adults. Study is determining prevalence of coronary artery calcium in young adults with DM2 for at least 5 years.

Past Medical History:
• DM2 dx 7 years ago, HbA1c ~10
• Hyperlipidemia
• Depression
Medical History, continued

Medications

- Metformin 850 mg bid
- Insulin
  - Lantus 30 units qAM, 30 units qHS
  - Humalog, 10 units each meal + sliding scale
- Simvastatin
- Gemfibrozil
- Fluoxetine

GynHx: G0P0, menses regular
Medical History, continued

Family History:
• No DM in other family members
• Father – had heart surgery 3 years ago after chest pain
• Overweight/obesity in siblings and parents
• Hyperlipidemia in maternal grandfather
• Hirsutism in female family members
Birth History

• Mom had been on OCP’s for about 8 years before becoming pregnant with patient. She had an “infection in kidneys and uterus” and needed to either get pregnant or have a hysterectomy. She became pregnant with patient. (2 more successful pregnancies after patient was born.)
• Born 10 days before due date
• Birth weight 4 lbs
• Siblings all born 7-8 lbs
• Was formula fed. Had emesis with breastfeeding.
Physical Exam

• Vitals signs normal
• Height 155.9 cm, Weight 67.5 kg, BMI 27.8
• General: obese female
• HEENT: thyroid palpable, not enlarged
• CV/Lungs: normal, Abd: no HSM
• GU: Tanner V breast and pubic hair, but has hair extending from pubis up midline on abdomen
• Skin: mild acanthosis, + hair on lower back
Bionutrition Data

Bioelectrical impedance
36.22% body fat (average 20-27)

Skinfold thickness
36.93% body fat (average 20-27)

Waist-hip-ratio
0.99 (normal <0.8)
Case summary

19 year old female

- DM2
- Obesity
- Features suggestive of PCOS
- No family history of DM – why our patient then?

In birth history, patient was born small for gestational age
Definition of Small for Gestational Age (SGA)
• An infant born with a birth weight less than the 10\textsuperscript{th} percentile for their gestational age
• Also known as “intrauterine growth retardation (IUGR)”

Standards for Intrauterine Growth by Gestational Age

These growth data, obtained from newborns at sea level, can be used to assess intrauterine growth by gestational age. Neonatal and infant risks, as well as postnatal growth patterns, may differ in children born small, appropriate, or large for gestational age. Thus, it is important to identify what the growth parameters were for each infant, whether term or pre-term. Postnataally, when assessing the growth of a child, returning to and plotting the neonatal data and understanding whether the child was born appropriate, small, or large for gestational age, may assist in the understanding of the postnatal pattern.

<table>
<thead>
<tr>
<th>Patient Name:</th>
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<tbody>
<tr>
<td>Date of Birth:</td>
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<tr>
<td>Gestational Age:</td>
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<td>Birth Weight:</td>
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<td>Birth Length:</td>
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Smoothed curve values (mean ± 2 SD) for birth weight and length against gestational age.

“New Thoughts on Growth” (1975)

Widdowson and McCance, Pediatr Res

“There is a critical point in development when the size of an animal, arising from its previous plane of nutrition, determines its appetite thereafter, and hence its rate of growth and dimensions at maturity.”

“The whole developmental life of an animal may be profoundly altered by events during a very short period in it. These have been termed the critical periods of development.”
Winick and Noble (1966)

- Growth took place in three stages, observations in rats after birth
- First 21 days: organs grow by cell division
- 21-42 days: growth of organs by cell division and cell enlargement
- 42-65 days: predominantly cell enlargement
- If cell division delayed beyond 65 days, cannot restart cell division
Widdowson and McCance (1960)

- Experiments on undernourishment in young rats at different ages
- Undernourishment during the suckling period leads to smaller rats, but no catch-up growth (critical period)
- Undernourishment during 9-12 weeks leads to rats that eat more later and do catch-up (similar to Winick and Noble’s third stage)
Dutch famine studies

Food rationing during WWII 1944-1945

- Higher rates of obesity were present in 19 year old men conceived during the famine than in people conceived before or after the famine
- Maternal malnutrition during early gestation was associated with higher BMI and waist circumference age 50 years in women but not in men


Early growth and death from cardiovascular disease in women

• 16,000 men and women born in Hertfordshire, England during 1911-1930 traced from birth

• Death rates from coronary heart disease were higher among those weighing < 5.5 lbs at birth than those weighing >=9.5 lbs.
The relation of small head circumference and thinness at birth to death from cardiovascular disease in adult life


- Study done in Sheffield, England
- 1586 men born between 1907-1924 were followed
- Increased death rate from cardiovascular disease among those with BW < 5.5 lbs and >8.5 lbs
- Those small at birth had failed to grow, rather than were small because of prematurity
Barker’s Hypothesis (1990’s)

- “During intrauterine life the tissues of the body grow during periods of rapid cell division, so-called ‘critical’ periods.”
- Undernutrition will slow cell division, and permanently change or “program” the body
- People exposed to an adverse environment *in utero* and then later exposed to an adverse environment in adulthood will manifest the programming effects
Conditions Found to be Related to SGA

• Coronary artery disease – Hertfordshire records, 3 times risk of mortality if failure to grow by age 1 year

• Insulin Resistance/DM2 - ?persistent glucose-sparing adaptation in the muscle

• Elevated LDL and fibrinogen levels – reduced liver size in reduced abdominal circumference
Is SGA related to PCOS or disordered timing of puberty?
Hokken-Koelaga, Best Prac Res Clin Endo, 2002
• Ibanez et al, JCEM 1998 – lower birth weight in children with precocious puberty and hyperandrogenism
• Jaquet et al JCEM 1999 and Boostra et al Horm Res 2001 – normal androgens in children born SGA

Current conclusion – not enough evidence for disordered puberty in SGA children at this time
Are there any SGA-specific therapies?

- rhGH – the only treatment approved with an indication for SGA
- rhGH increases insulin resistance
- No difference found in insulin resistance in SGA after stopping treatment with rhGH versus AGA controls
Our Patient

- Was born SGA
- Exhibited catch-up growth
- Developed obesity
- Has youth-onset DM2
- Has hyperlipidemia
- Has features of PCOS
- No coronary artery calcifications on EBCT