

Diabetes: Approach to First Presentation

General Presentation

Diabetes mellitus (DM) is an important endocrine disorder that presents commonly in children and adolescents. There are two types of diabetes mellitus: type 1 and type 2. Type 1 DM is one of the most common chronic diseases in children and is characterized by insulin deficiency as a result of autoimmune destruction of pancreatic beta islet cells; whereas type 2 DM is the presence of high blood glucose with insulin resistance and relative insulin deficiency. Diabetes mellitus is a chronic condition that requires long-term follow-up and adequate patient (and parent) education to maintain good glycemic control to prevent long-term complications.

Epidemiology

Type 1 DM

Approximately 2/3 of all new diabetes diagnoses in patients less than 19 years of age in the United States are type 1 DM. Over 300,000 Canadians have type 1 DM, with a 3-5% increase each year; especially in children aged 5-9. Typically, the age of onset has a bimodal distribution, with the first peak in children 4-6 years old, and the second peak in children 10-14 years old (early puberty). Unlike other autoimmune diseases, the overall incidence appears to be equal in both genders. There is a higher risk of developing this condition in children with close relatives who have type 1 DM.

Type 2 DM

The incidence of type 2 DM has increased 10 fold in the last decade. There is an estimated 3600/100,000 cases of type 2 DM in Canadian adolescents and 1100/100,000 cases in Canadian children. This value may be as high as 1% in Canadian aboriginal youths and children. There is a strong association between increasing rates of obesity in the pediatric population and the development of type 2 DM.

Basic Physiology

Type 1 DM

In type 1 DM, there is autoimmune-mediated destruction of insulin-producing pancreatic beta cells that results in insulin deficiency. It is a progressive condition that occurs in genetically susceptible individuals. The autoimmune destruction can be triggered by various environmental agents. Some proposed environmental factors include pregnancy-related and perinatal influences, viruses, cow's milk and cereals. There is a long latency period (where the patient is asymptomatic and euglycemic) between the onset of beta cell destruction and clinical presentation of diabetes mellitus. A large

number of functional beta cells must be lost before clinical symptoms like hyperglycemia occurs.

Genetic polymorphisms in six genes have been shown to be associated with type 1 DM. Major Histocompatibility Complex genes and elsewhere in the genome all contribute to the risk, but only the HLA alleles seem to have a large effect.

The natural history has four stages:

1. Preclinical autoimmune destruction of pancreatic beta cells
2. Onset of clinical symptoms
3. Transient remission
4. Established diabetes with acute and chronic complications

Type 2 DM

Type 2 DM is a complex, multifactorial disease characterized by both relative insulin deficiency and insulin resistance with various environmental and behavioural risk factors. Increased hepatic glucose production, insulin resistance and progressive loss of glucose-stimulated insulin release all contribute to the development of hyperglycemia. In Type 2 DM, pancreatic beta cells retain the ability to produce insulin, but levels are not adequate to counteract the developing insulin resistance. The current theory is that insulin resistance develops first, followed and complicated by gradual destruction of beta cells. Insulin resistance worsens with obesity and physical inactivity; and improves with weight loss and increased physical exercise.

Puberty also plays a role in the development of type 2 DM in adolescents. During this period, insulin sensitivity is approximately 30% lower than that of preadolescents or adults, which results in hyperinsulinemia as a compensatory mechanism. In adolescents with both genetic predisposition and negative environmental contributors, this period of relative insulin resistance may result in a decompensated state (inadequate insulin secretion and glucose intolerance). The resulting hyperglycemic state may cause worsening abnormalities of insulin secretion and action, starting a vicious cycle that progress beyond the adolescent years.

Clinical Presentation

Type 1 DM

Childhood type 1 DM can present in the following ways:

Classic new onset:

- Hyperglycemia without acidosis
- Symptoms include:
 - o Polyuria – serum glucose > 10 mmol/L (exceeding renal threshold for glucose → increased urinary glucose excretion)
 - Can present as nocturia, bedwetting, daytime incontinence in a previously continent child

- Polydipsia – due to increased serum osmolality and hypovolemia
- Weight loss – due to hypovolemia and increased catabolism
 - Impaired glucose utilization in skeletal muscle and increased fat and muscle breakdown

Diabetic ketoacidosis

- Similar symptoms but are usually more severe
 - Clinical: polydipsia, polyuria, dehydration, hypotension, ketosis, etc.
 - Metabolic: hyperglycemia, glycosuria, metabolic acidosis, ketonemia, etc.
- Reported frequency varies between 15-67%
 - Young children (<6) from low socioeconomic backgrounds are more likely to present with diabetic ketoacidosis

Silent Presentation

- Diagnosis before onset of clinical symptoms
- Typically occurs in children with a family member with type 1 DM (close monitoring)

Type 2 DM

Childhood type 2 DM can present in the following ways:

Diabetic ketoacidosis

- Hyperglycemia, ketonuria, acidosis
- Frequency varies between 5-25%

Hyperosmolar hyperglycemic state

- Marked hyperglycemia (>33.3 mmol/L) and severe dehydration but no ketonuria
- Less common in adolescents

Symptomatic

- Due to hyperglycemia and include: polyuria, polydipsia, and nocturia
- Recent weight loss is less frequent
- Adolescent girls: vaginal discharge due to candida infection may be initial presentation

Asymptomatic

- Identified based on screening (for type 2 DM or urinalysis as part of a regular physical exam)

Questions to Ask

Historical Investigation

Presenting condition:

- Have you been very thirsty? Do you drink a lot?
- Have you been urinating more than usual?
- Has the child had any bedwetting episodes?
- Has there been any recent weight loss?
- Have you been feeling tired lately?

- Have you noticed an increased appetite lately?
- Has the child had more frequent minor skin infections?

Predisposing factors:

Type 1 DM:

- Have you had any viral infections recently?

Type 2 DM:

- What kinds of exercise do you participate in on a regular basis? How frequent do you exercise? How long do you exercise each time?
- How many hours a day do you spend watching TV, using the computer, and play video games?
- What do you normally eat? What is the portion size? How many meals do you have per day? Do you normally eat out or home cooked meals? Do you eat as a family? Do you eat at the table or in front of the tv?

Family history:

Type 1 DM:

- Are there any family members with insulin-dependent diabetes mellitus?
- Are there any family members with autoimmune conditions?

Type 2 DM:

- Does your mother or father have diabetes?
- Are there any other family members with diabetes? (grandparents, aunts, uncles, brothers, sisters, etc.)

Physical Examination

Do a complete physical exam with particular attention to the following:

Type 1 DM:

- Assess hydration status
- Assess circulation: HR, BP, capillary refill
- Temperature: coexisting infection
- Use growth chart to check for weight loss
- Neck examination: look for thyroid abnormalities
- Respiratory: respiratory rate (hyperventilation – DKA), auscultation (respiratory infection), ketones on breath (DKA)

Type 2 DM:

- Measure body weight and height, calculate BMI
- Measure lying and standing BP
- Inspect skin for acanthosisnigricans
- Examine feet to look for decreased sensation and circulation (pulses)
- Measure visual acuity

Differential Diagnosis

- DM types 1 and 2

- Diabetes insipidus
- Urinary tract infection
- Malabsorption (e.g. Celiac disease)
- Secondary diabetes
- Maturity-onset diabetes of the young

Procedure for Investigation

Diagnostic Criteria

- Fasting plasma glucose >7 mmol/L (no caloric intake for at least 8 hours)
- Symptoms of hyperglycemia, random venous plasma glucose >11.1 mmol/L
- Abnormal oral glucose tolerance test – plasma glucose >11.1 mmol/L measured 2 hours after a glucose load of 1.75 g/kg (max 75g)
- Glycated hemoglobin (A1C) ≥ 6.5%

Other Investigations

- Urinalysis for glucosuria and ketonuria
- Urinalysis for microalbuminemia

References

1. Alemzadeh R, Wyatt DT. Section 6 - Diabetes mellitus in children. In: Kliegman: Nelson Textbook of Pediatrics. 18th ed. Saunders, Pennsylvania. 2007
2. Eisenbarth GS, McCulloch DK. Pathogenesis of type 1 diabetes mellitus. In: UpToDate, Basow, DS (Ed), UpToDate, Waltham, MA, 2011
3. Laffel L, Svoren B. Epidemiology, presentation, and diagnosis of type 2 diabetes mellitus in children and adolescents. In: UpToDate, Basow, DS (Ed), UpToDate, Waltham, MA, 2011
4. Levinson P, Nelson BA, Scherger JE. Diabetes mellitus type 1 in children. [Online]. 2007. Available from: FirstConsult, MDConsult. [cited 2011 Jan 15]
5. Levitsky LL, Misra M. Epidemiology, presentation, and diagnosis of type 1 diabetes mellitus in children and adolescents. In: UpToDate, Basow, DS (Ed), UpToDate, Waltham, MA, 2011
6. McCulloch DK, Robertson RP. Pathogenesis of type 2 diabetes mellitus. In: UpToDate, Basow, DS (Ed), UpToDate, Waltham, MA, 2011
7. Panagiotopoulos C. Type 2 diabetes in children and adolescents. BCMJ. 2004;46(9): 461-466
8. Scherger JE, McIntire SDC, Escobar O, Heinzman DM. Diabetes mellitus type 2 in children. [Online]. 2007. Available from: FirstConsult, MDConsult. [cited 2011 Jan 15]