

An unusual cause of glycosuria in a 5-year-old child

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Case presentation

A healthy 5½-year-old child was assessed together with her parents for an immigration medical. A thorough clinical examination was done and the child's height and weight were plotted on growth charts. All findings were unremarkable. As part of the medical a urine dipstick test was routinely performed.

The urine dipstick test alarmingly showed +++ glucose, but was negative for all other substances routinely tested for on urine multi-dipstick testing (leucocytes, nitrites, urobilinogen, blood, protein, etc.), and, importantly, was negative for ketones.

The examining physician requested a blood sample for analysis of glucose and glycosylated haemoglobin (HbA_{1c}). The glucose level was 4.0 mmol/l and the HbA_{1c} 4.9% (both normal). These were subsequently checked, with results of 4.0 mmol/l and 5.0% respectively. The glucose concentration in urine was also measured quantitatively, as 33 mmol/l.

The possibility of contamination of the sample with bleach from toilet water was considered, as bleach can interfere with urine dipstick testing and cause false-positive results for glucose.¹ Another urine sample was therefore requested, with similar results obtained on dipstick testing (+++ glucose, ketones negative).

Further enquiry about the child from her mother revealed that she was a well and healthy 5½-year-old, with normal development and milestones.

Additional investigations were then performed. Serum was analysed for urea, creatinine, electrolytes and uric acid, all of which were within normal limits, and the urine was also analysed for phosphate, creatinine and sodium, all of which were within normal limits. The fractional excretion of sodium and phosphate was calculated, also both normal, and proteinuria was excluded on dipstick testing, as well as measured quantitatively in the laboratory.

Urine was analysed for reducing substances (Clinitest strongly positive) and the reducing sugar was identified as glucose on thin-layer chromatography.

Both parents were also tested for glycosuria, which was absent on dipstick testing.

The diagnosis of renal glycosuria was made.

Discussion

With normal renal tubular function, glucose will only be excreted in urine when blood glucose concentrations are

elevated, and the renal tubular reabsorptive capacity for glucose is exceeded. Glucose transport in the human kidney and intestine is mediated by sodium-coupled glucose transporters, termed SGLT, and glucose transporters, termed GLUT. Glucose is transported across the brush border into the epithelial cell via SGLT, and across the basolateral aspect out of the epithelial cell by GLUT (Fig. 1). The intestine and kidney share high-affinity Na⁺/glucose co-transporters (SGLT1), but a low-affinity Na⁺/glucose co-transporter (SGLT2) is kidney specific. In the normal nephron, filtered glucose is reabsorbed in the proximal convoluted tubule (PCT), about 90% being reabsorbed in the first segment of the PCT by high-affinity SGLT1, and the remainder in the second and third segments of the PCT by low-affinity SGLT2.²

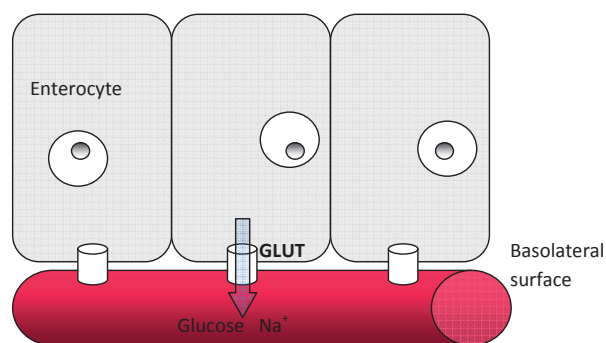


Fig. 1. Diagrammatic illustration of glucose transport in the kidney and intestine. See text for explanation.

Renal glycosuria (also known as benign glycosuria or non-diabetic glycosuria) is a benign, inherited condition in which glucose is excreted in the urine despite normal blood glucose concentrations.³ The condition is asymptomatic and self-limiting, and is usually only discovered incidentally. However, glycosuria may be associated with other tubulopathies, such as Fanconi's syndrome, cystinosis, Wilson's disease, hereditary tyrosinaemia, and oculocerebrorenal syndrome (Lowe's syndrome). These other tubulopathies, however, are associated with growth failure, muscle dystonia, polyuria, polydipsia, dehydration or ocular defects (glaucoma, cataracts). In renal glycosuria no other renal tubular dysfunction is present.⁴

Benign glycosuria can be of two types:

Type A: Classic glycosuria caused by a reduced tubular threshold and maximal reabsorptive rate for glucose.

Type B: Normal maximal reabsorptive rate for glucose, but reduced tubular threshold.

Plasma glucose, glucose tolerance, insulin and HbA_{1c} are all

normal, and all other renal tubular abnormalities are absent in both types.⁴

The molecular mechanism giving rise to benign renal glycosuria has been discovered to be due to a defect in the low-affinity SGLT2 in the proximal convoluted portion of the renal tubules.^{5,6} Inheritance is autosomal recessive,⁷ but because the condition is asymptomatic, a family history is often non-contributory.

Suggested investigations for suspected cases of renal glycosuria include blood tests for urea, creatinine and electrolytes, calcium, phosphate, uric acid, glucose, and measurement of the HbA_{1c}. Urine should be sent for urinalysis and microscopy, and measurement of phosphate, and the tubular maximum of phosphate reabsorption should be calculated. In cases where another tubulopathy is suspected on the basis of abnormal laboratory results or clinical findings, a 24-hour urine specimen should be collected and sent for amino acid analysis. Referral to a paediatric nephrologist is then recommended.⁴

Renal glycosuria requires no treatment or special dietary restrictions, and the prognosis is excellent. Once diabetes mellitus and other renal tubular disorders are excluded, all that remains is to explain the condition, and reassure the parents.⁴

Conclusion

The case illustrates an unusual cause of glycosuria, the commonest cause of which is uncontrolled diabetes mellitus.

In young non-obese children, type I diabetes mellitus is the commonest type of diabetes, where the absence of insulin production and secretion from the beta cells in pancreatic islets causes hyperglycaemia and ketosis. Renal glycosuria is a benign autosomal recessive condition caused by a defect in SGLT2 in the PCT of the nephron, which allows renal glycosuria to occur in the absence of a raised serum glucose level. Benign renal glycosuria is not associated with other renal tubular abnormalities. The condition is benign, and asymptomatic, and no treatment or dietary restriction is necessary.

References

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