Correspondence

Flatulence and carpopedal spasm: more than social embarrassment

Sir,

A 61-year-old female of mixed Asian and African descent was admitted to our institution in December 2001, because of carpopedal spasms. She had been well until 13 months prior to admission, when she began to lose weight progressively, to a total of 20 pounds. She denied any loss of appetite, change in vision or bleeding. On examination, her vital signs were stable. Her abdomen was unremarkable. There were spasms of her hands and feet, and slight ankle oedema. Her stools were negative for occult blood on many occasions. Her blood results were as follows: sodium 134 mmol/l, chloride 104 mmol/l, potassium 3.6 mmol/l, bicarbonate 20 mmol/l, blood urea nitrogen 2.28 mmol/l (8 mg/dl), creatinine 26 μmol/l (0.3 mg/dl), calcium 1.35 mmol/l (5.4 mg/dl), albumin 26 g/l, haemoglobin 87 g/l with an MCV of 62 fl, white blood cell count 7000/mm³, phosphate 1.23 mmol/l (3.8 mg/dl), and a prothrombin time of 15 s (N 11–13).

An electrocardiogram revealed sinus bradycardia at 60 bpm and a prolonged QT interval. Intravenous calcium gluconate was administered. Serum 25-hydroxy vitamin D was 12.48 nmol/l (N 20–200). Vitamins D and K were administered. The patient denied ever having diarrhoea or any loose bowel movements. She had severe flatulence that was persistently foul-smelling, causing social embarrassment. She was evaluated for coeliac sprue. Her serum antigliadin antibodies, both IgG and IgA, were markedly elevated. Endoscopic evaluation of her gastrointestinal tract revealed a normal colon and stomach. A proximal jejunal biopsy (Figure 1) showed severe villous flattening with crypt hypertrophy, and chronic inflammatory infiltrate in the lamina propria. No granulomas, parasites or malignant cells were seen. The patient was placed on a gluten-free diet. Her clinical response to treatment was dramatic: 18 months after discharge, she had gained 35 pounds, had little flatulence that was no longer malodorous and her laboratory values had returned to the normal range.

Coeliac sprue is a relatively common disease in patients of Northern European ancestry, with a prevalence rate of 1:300, but its epidemiology is not well established in patients of African or Asian origin.¹ It is strongly associated with selected HLA class II antigens HLA-DR3 and HLA-DQw2. In the genetically-susceptible host, gluten (found in wheat, rye, barley and oats but not rice and corn) triggers both humoral and cell-mediated inflammatory responses that result in mucosal destruction. The diagnosis is often delayed because of the variable presentation.² The diarrhoea and weight loss often seen in children is rarely seen in adults.² In a series of 30 consecutive patients, 25 had no gastrointestinal complaints and anaemia was the most frequent presentation.³ Coeliac-related antibodies are now readily available, and should help in screening patients before jejunal biopsy. Treatment of coeliac sprue is of course life-long abstention from gluten-rich foods. Coeliac sprue can be complicated by malignancies, with intestinal T-cell lymphoma occurring in more than 10% of patients, and other autoimmune diseases such

Figure 1. Proximal jejunal biopsy showing severe villous flattening with crypt hypertrophy and chronic inflammatory infiltrate.
as lupus, Graves disease and type 1 diabetes. Our patient presented with late-onset coeliac sprue with only flatulence as her initial symptom before developing carpopedal spasms as a result of hypocalcaemia.

Flatulence is usually a benign symptom when it is secondary to compulsive aerophagia. It is usually of low volume, composed of nitrogen and responds to non-specific modifications in diet and behavior. However, flatus that is malodorous and of large volume suggests the presence of methane, hydrogen and carbon dioxide, which are produced (together with the characteristic sulphides) by the action of colonic bacteria on unabsorbed polysaccharides and glycoproteins.4,5 Such patients should not have their symptoms flatly dismissed, but rather should be evaluated for possible malabsorption.

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References

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Familial juvenile hyperuricaemic nephropathy

Sir,
The letter of Bleyer et al.1 raised two important questions regarding our families reported in QJM,2 with the syndrome termed familial juvenile hyperuricaemic nephropathy (FJHN). The first was the questionable efficacy of allopurinol, in view of its lack of effect in ameliorating the progression of the renal lesion in the single large kindred they reported recently,3 and second, whether similar uromodulin mutations are responsible for FJHN in our families in that report.

Our QJM paper reported our findings in our first eight kindreds, studied for from 10 to 36 years. The results stressed the importance of compliance with allopurinol treatment, and we note that the propositus in the kindred described by Bleyer et al.3 was a poor complier. The importance of compliance is illustrated by one of our families (K3) studied for 20 years, in which renal function actually improved on allopurinol—except for the one very poor complier whose renal function fell by 50% before being lost to further study. This family also provides an answer to their second question—do the mutations differ in our families? K3 has a proven mutation in hepatocyte nuclear factor-1ß on chromosome 17q.4

The two children of our UK kindred K1, studied since their Austrian mother (and uncle) presented with gout and died of renal disease in 1974, aged 36 years, have been on allopurinol since 1989. They were followed up annually, and with hindsight would have been treated from the start had we then recognised that the low FEur was the hallmark of FJHN, rather than a raised plasma urate as Bleyer et al. imply. Since taking allopurinol, both siblings have maintained a stable, if slightly reduced, renal function.2 This kindred does have a linkage to chromosome 16q,5 and interestingly is a branch in the UK of the Innsbruck family mentioned by Lhotta,6 and reported by Turner et al.7 as having a heterozygous 481T-C mutation in the uromodulin gene. The case history of this Austrian branch of our kindred—the sister and nephew of our propositus—also underlines the importance of early recognition and treatment with allopurinol. FJHN was unrecognized and untreated until the GFR had fallen to 38 ml/min in the mother, that of the son being 58 ml/min at diagnosis.3 A combination of benz-bromarone and allopurinol has stabilized the renal function in both, despite the very low GFR in one.6 Importantly, none of the other members of our families in the QJM paper now studied for up to 36 years have, like the kindred of Bleyer et al.,3 progressed to ESRD.

Regarding mutations, only one other kindred in the QJM paper has shown linkage to 16q,5 but a similar linkage has also been found in two of our other kindreds not listed in QJM. It remains difficult to understand how a defect in a protein located only...