oral prednisolone. Thereafter tacrolimus was introduced to provide ongoing control of her eye disease.

The cornea comprises five layers: epithelium, basement membrane zone, stroma, Descemet’s membrane and endothelium. Within the stromal layer is a dynamic process of repair and regeneration.

Modified fibroblasts constantly remodel the cornea, and their activities are regulated by the presence of MMPs, produced by stromal fibroblasts that degrade the extracellular matrix, and their tissue inhibitors, e.g. tissue inhibitor of metalloproteinases-1, and other non-specific protease inhibitors [3]. PUK is hypothesized to occur when this balance is upset [2].

Another study [3] suggests that PUK is due to a cell-mediated process, as MMP-1, in particular, is strongly associated with a mononuclear cell infiltrate as described in ulcerating corneas. It is possible that PUK is triggered by the release of MMPs from fibroblasts in response to pro-inflammatory cytokines, e.g. IL-1 produced by activated macrophages. Alternatively, MMPs could be produced by the macrophages themselves [3].

There is also evidence for HLA-DR expressing cells, along with helper and cytotoxic T cells, in the cell infiltrate [3]. This finding may explain why PUK is a recurring pathology when the cornea is damaged by any other reason. In this case, there had been a long history of keratoconjunctivitis sicca and recurrent episcleritis.

As far as we are aware, this is the first case report of PUK following treatment with rituximab. At the time of her corneal melt, our patient did not have any obvious trigger such as cataract surgery, but her cornea might be vulnerable from her previous pathology. Could B-cell depletion cause disequilibrium within the cellular network? Interestingly, rituximab has actually been found to be a useful treatment for PUK, although these cases were associated with WG rather than RA [4, 5].

**Rheumatology key message**

- We highlight a possible link between rituximab and PUK.

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**References**


is responsible for hypokalaemia and metabolic alkalosis, hypocalciuria and secondary hyperaldosteronism, which is characterized by hypomagnesaemia, musculoskeletal symptoms.

6-methylprednisolone with satisfactory control of symptoms at 12.4 mg/day. Therapy with colchicine (2 mg/day) was started, but colchicine induced profuse diarrhoea. In other cases, treatment of hypomagnesaemia can be efficacious, and it has a laxative effect. In fact, in our patient, repeated intravenous infusions of potassium and magnesium were required. Moreover, the association with CPPD deposition disease secondary to hypomagnesaemia, the stabilization of magnesium and potassium levels can reduce the deposition of CPPD crystals in the synovium and SF, reducing the frequency of attacks of articular pain [5]. In other cases, treatment of hypomagnesaemia can be difficult because oral supplementation alone is inadequate, and it has a laxative effect. In fact, in our patient, repeated intravenous infusions of magnesium and potassium were required. Moreover, the association with colchicine induced profuse diarrhoea.

The development of acute neck pain and stiffness induted to perform a CT scan of the cervical spine, which showed diffuse calcifications of the peri-odontoid tissues (transverse ligament of the atlas and cruciate ligament), indicative of CDS. The term CDS was first proposed by Bouvet et al. in 1985 [7]. In a recent report conducted by Salaffi et al. [12], in 5 out of 49 patients (51%) affected by CPPD deposition disease, axial CT

| TABLE 1 | Laboratory values at different times of evolution |
|----------------|-----------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Plasmatic K (nv 3.5–5.5 mmol/l) | 2.9                   | 3.7               | 3.7             | 3.3             | 3.7             | 3.3             | 3.6             |
| Plasmatic Mg (nv 1.4–2.4 mg/dl) | 0.5                   | 1.4               | 1.2             | 0.8             | 1.2             | 0.9             | 0.9             |
| Urinary Ca (nv 100–300 mg/24 h) | 9.6                   | 40                | 40              | ND              | 19              | 26.6            | 33.8            |
| Renin activity (nv supine: 0.20–2.70 ng/ml/h; upright: 1.50–6.00 ng/ml/h) | Supine: 4.8          | ND                | Supine: 2       | ND              | ND              | ND              | Supine: 6       |
| Aldosterone (nv supine: 30–150 pg/ml; upright: 70–350 pg/ml) | Supine: 183          | ND                | Supine: 40      | ND              | ND              | ND              | Supine: 110     |
|             | Upright: 434         | Upright: 6        | Upright: 12.4   | Upright: 370    |                 |                 |                 |

aThe reported values are the most representative for each year. ND: not determined.

bicarbonate 31.8 mmol/l) and hyperreninaemic hyperaldosteronism in both the supine and upright position. Genetic testing showed two different mutations in the NCCT gene. The diagnosis of GS was made. Treatment with high doses of oral magnesium carbonate (average dose 9 g/day) and potassium (70 mmol/day) was begun; however, electrolyte balance and clinical symptoms remained poorly controlled. Therefore, repeated intravenous infusions of potassium and magnesium were administrated with a discrete response. Laboratory values at different times are shown in Table 1.

Over the following 10 years, the patient developed acute episodes of arthritis of the wrists, elbows and knees. She was referred to our Rheumatology Department. Laboratory data revealed an increase in the ESR and CRP, hypomagnesaemia (0.9 mg/dl), hypokalaemia (3.3 mmol/l) and hypocaliuria (26.6 mg/24 h). Joint X-ray showed huge calcific deposits in the menisci of both knees and in the triangular cartilage of both wrists (Fig. 1A). Sonographic examination documented the presence of marked enlargement of the suprapatellar puch of the right knee and confirmed the presence of widespread calcifications (Fig. 1B and C). Knee arthrocentesis was carried out and CPPD crystals were observed in the SF by polarizing light microscopy. After 2 weeks, she complained of acute neck pain associated with marked neck stiffness. X-ray of the cervical spine was normal, whereas a CT of cervical spine showed diffuse calcifications of the peri-odontoid and a small erosion of the odontoid process (Fig. 1D–F). The diagnosis of CDS was made. The term CDS was first proposed by Bouvet et al. in 1985 [7]. In a recent report conducted by Salaffi et al. [12], in 25 out of 49 patients (51%) affected by CPPD deposition disease, axial CT
scanning of the cervico–occipital junction revealed periodontoid calcification. The mean age in this study was 70.4 years. Our patient is notably younger, probably because the CPPD deposition disease was secondary to GS. Further cases are needed in order to improve knowledge of the pathophysiology and prevalence of this entity in patients with CPPD deposition disease secondary to hypomagnesaemia.

We suggest that rheumatologists bear in mind the clinical association between GS, CPPD and CDS in order to avoid misinterpretations and carry out the correct clinical approach. Particular attention must be paid to young adult patients with a history of hypomagnesaemia and/or hypokalaemia associated with musculoskeletal symptoms, frequently reported in rheumatologic daily clinical practice.

Rheumatology key message

- In patients with GS associated with CPPD disease, the occurrence of CDS should be considered.

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Comment on: New insights into the epidemiology of gout

Sir, The recent article by Michael Doherty [1] lists three dietary risk factors for gout: higher intakes of red meat, beer and fructose. Benjamin Franklin’s celebrated meaty diet and love for Madeira wine aptly illustrates a historical recognition of meat and alcohol as legitimate risk factors for gout. The addition of fructose to this list by Doherty is completely unwarranted, however, because it lacks adequate justification and proof in real-world diets.

First, all United States Department of Agriculture-defined macronutrient categories—added sugars, added fats, flour/cereal, vegetables, fruits, dairy and milk/eggs/nuts—have increased more or less in parallel with total energy intake (±24%) since the introduction of high-fructose corn syrup (HFCS) 35 years ago [2]. As all macronutrients contribute energy to the diet, a focus on fructose is misleading, because it cavalierly dismisses other macronutrients and misses the greater issue that we eat too much of everything.

Secondly, Doherty’s speculation about fructose differences in sucrose vs HFCS contradicts the growing consensus on caloric sweeteners. There is now general agreement that sucrose and HFCS are metabolically equivalent among scientific experts: expert scientific panels like those convened by Experimental Biology (Federation of American Societies for Experimental Biology) [3] and the International Life Sciences Institute–United States Department of Agriculture [4]; and professional organizations like the American Medical Association [5] and the American Dietetic Association [6]. Recent human studies by Melanson et al. [7], Angelopoulos et al. [8] and Havel et al. [9] directly comparing HFCS and sucrose for metabolic markers of obesity confirm no substantive differences in serum glucose and insulin, ghrelin and leptin, hunger and satiety, triglycerides and uric acid.

Finally, experimental data used in support of fructose as a dietary risk factor is inappropriately applied from extreme diets that bear no resemblance to real-world human exposures. Rat studies commonly use fructose at 60–66% of energy; human studies use fructose at 20–50% of energy [2]. The most recent estimate for fructose intake [10] reports the mean whole-population value at 9.1% of energy and the 95th percentile (males and females aged 19–22 years) value at <18% of energy. Human studies thus test unrealistic fructose levels, whereas animal studies use highly exaggerated exposures that not only do not remotely resemble human intakes, but may well approach toxic conditions. It is indeed possible that the experimental diet is itself inducing an extreme variant of human metabolism not in evidence at typical fructose exposures.

At the current state of scientific understanding, it is decidedly premature and unjustified to include fructose on the same list of well-established dietary risk factors for gout as red meat and beer.

Disclosure statement: J.S.W. is a consultant to the food and beverage industry in nutritive sweeteners, including HFCS and sucrose. His professional associations, past and present, include individual food industry companies as well as such organizations as the American Chemical Society, American Council on Science and Health, Calorie Control Council, Corn Refiners Association, and Institute of Food Technologists and International Life Sciences.

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