Figure 2 A recurrent conjunctival granuloma in the left lateral canthus.

There are only two reports of conjunctival granulomatosis in IBD, both in patients with Crohn's disease and not UC.[4,5] In one case the lesions were similar in appearance to this case but in the other bilateral conjunctival circumlimbal nodules are described, neither had a prolonged course. In our case, the ophthalmic findings started 10 years before any bowel symptoms and it is possible that they are unrelated. However, extensive investigations failed to identify any other cause and it is worth noting that during treatment for his UC the eyes were quiescent. It is also interesting to note that although granulomata are classically found in Crohn's disease, they occasionally occur in UC.[6] This would suggest that it is plausible that the conjunctival granulomata seen in this case are due to the same underlying disease process that caused the UC. Our case is the first in the literature to describe conjunctival granulomatosis in a patient with UC.

Conflict of interest

The authors declare no conflict of interest.

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Sir,

Reactivation of Darier's disease following Azathioprine treatment for thyroid eye disease

Azathioprine is an immunosuppressive agent commonly used for treating active thyroid eye disease (TED). Documented side effects include gastrointestinal intolerance, bone marrow suppression, and hepatic toxicity.[1] We describe an unusual side effect of Azathioprine treatment.

Case report

A 51-year-old woman was referred for management of active TED. Past medical history included inactive Darier's disease. Her thyroid function tests were controlled and she stopped smoking following our advice. The active TED was controlled with oral Prednisolone 40 mg. Azathioprine was gradually introduced in the treatment as a steroid-sparing agent with gradual tapering of Prednisolone after ensuring normal thiopurine methyltransferase levels (106 mU/l, normal; 68-150 mU/l).

At Azathioprine 150mg daily, the patient reported sudden reactivation of a florid, brown papulomatomatous rash on her forehead and chest consistent with reactivation of her Darier's disease (Figures 1a and b). Azathioprine was discontinued and she was treated with oral acitretin (retinoid) by dermatologists with complete recovery (Figures 1c and d).

Comment

Darier's disease or keratosis follicularis is a dermatological condition affecting seborrheic areas of the skin. Patients present with yellow–brown papules, which have a greasy and warty texture. It is an autosomal dominantly inherited disorder that has been associated with mutations in the gene *ATP2A2*.[2]

To our knowledge this is the first reported case of reactivation of Darier's disease, following the use of Azathioprine treatment. Anolik and Rudolph[3] describe a case of a transplant patient being treated with azathioprine and prednisolone who developed a papular rash consistent with Darier's disease; however, the cause was thought to be secondary to scabietic infestation. In our case scabietic infestation was not identified.

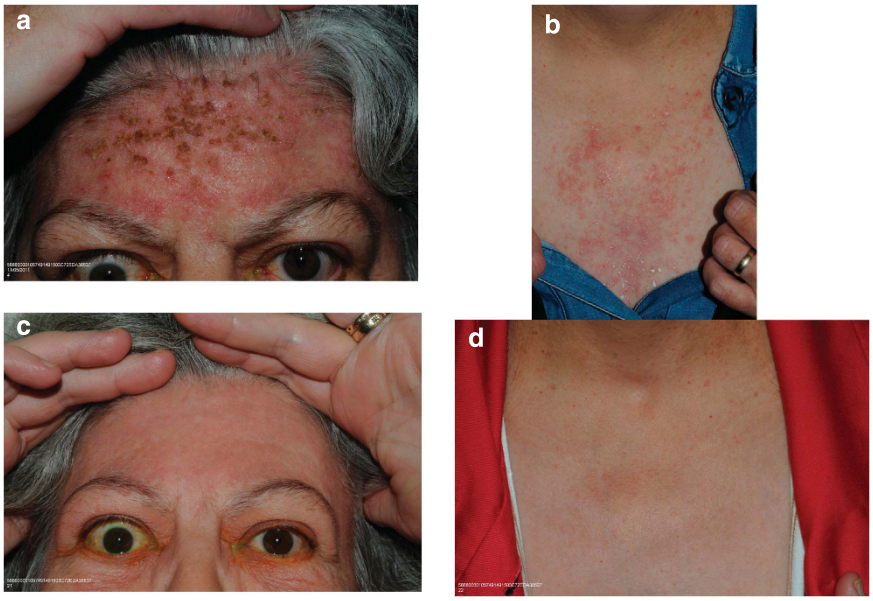

Figure 1 Composite pictures showing reactivation of Darier's disease after commencing Azathioprine treatment (a, b), with resolution following cessation of Azathioprine and treatment with acitretin (c, d).

Azathioprine is a purine analog and results in a reduced number of leukocytes owing to disruption of DNA and RNA synthesis.[4] A specific gene mutation, known to encode for a calcium pump located on the endoplasmic reticulum, has been identified in relation to Darier's disease.[2] The cause for reactivation of Darier's disease in our patient may be due to Azathioprine's pharmacological action within the endoplasmic reticulum, stimulating the Darier's disease process.

We recommend that Azathioprine is avoided in patients with known Darier's disease.

Conflict of interest

The authors declare no conflict of interest.

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Sir,

Combined inhibition of tumor necrosis factor (TNF) and vascular endothelial growth factor (VEGF) for the treatment of macular edema of various etiologies: a short-term pilot study

The aim of this study is to report the 6-month anatomic and Early Treatment Diabetic Retinopathy Study (ETDRS) best-corrected visual acuity (BCVA) response after the combination of intravitreal adalimumab and bevacizumab (IVBA) in patients with macular edema of various etiologies.

Case report

We reviewed the clinical records of consecutive patients with macular edema of various etiologies, which were treated with at least one off-label combined intravitreal injection of 1.25 mg/0.05 ml of bevacizumab and 2 mg/0.08 ml of adalimumab (Figure 1). Five consecutive patients (7 eyes), and at least 6 months of follow-up were identified and included for this analysis.

Our results are depicted in Table 1. Eyes 1 and 7 were previously treated with intravitreal bevacizumab (3 doses with 6-week intervals), with no anatomical or functional response $\geq$12 weeks from last injection. Four (57.1%) of seven eyes gained $\geq$3 ETDRS lines of BCVA. None of the patients developed systemic complications such as thromboembolic events or a cerebral vascular accident, and none developed any ocular complication.