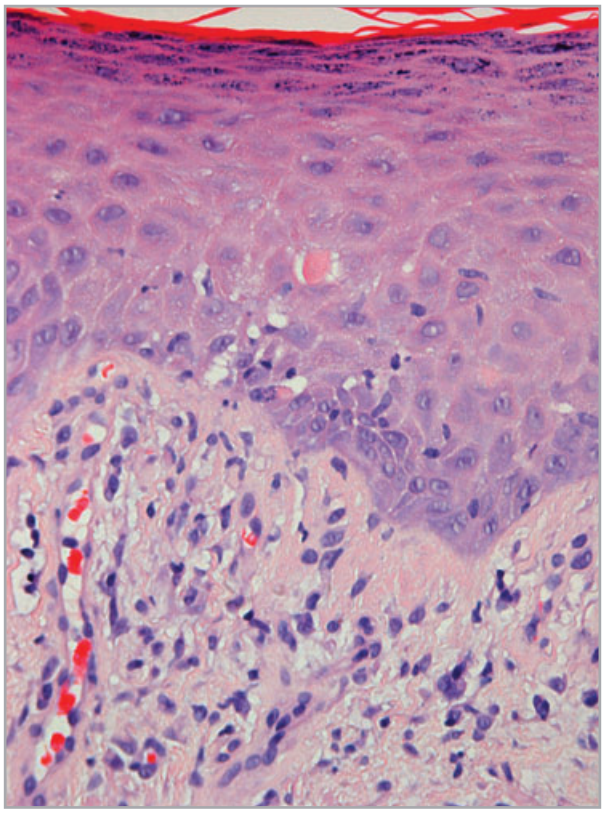

Fig 2. Punch biopsy showing a band of lymphocytic infiltrate and a few eosinophils in the papillary dermis. Apoptotic keratinocytes are seen at the basal layer and at the midepidermis. A few lymphocytes infiltrate the epidermis, associated with vacuolar change. Haematoxylin and eosin, original magnification × 400.

findings that are more common in LDE include the presence of eosinophils, focal parakeratosis, focal interruption of granular layer, cytoid bodies and a cellular infiltrate around deep vessels.[1,3]

Identification of the offending drug causing LDE can be difficult, complicated by factors like different drug dosages, multiple medications, drug interactions, and different latent periods, reported to range from a few months to 1–2 years.[1] The duration for resolution of LDE can range from a few weeks to 2 years after drug cessation, and the eruption has been reported to disappear and reappear intermittently, even when the drug had not been discontinued.[5,6] Further treatment of LDE is similar to that of LP. Challenge tests for patients with LDE are controversial and generally not recommended.[1]

Terazosin is an α1-adrenoceptor-blocking agent that causes relaxation of smooth muscle in the bladder neck and prostate. It undergoes minimal first-pass metabolism and has a half-life of approximately 12 h, with plasma clearance rates decreased in older patients. Significant adverse reactions that have been reported include asthenia, postural hypotension, dizziness, somnolence, nasal congestion and impotence. Adverse cutaneous reactions to terazosin are mild and uncommon,[7,8] and severe reactions are rare.[9] Although other α1-adrenoceptor blocking agents, like prazosin and doxazosin have been reported to cause LDE,[10] currently, to our knowledge, there have been no reports of terazosin as a cause of LDE.

In conclusion, based on the time–event relationship, morphology, distribution and histopathological findings, we conclude that our patient developed a LDE to terazosin. As the use of this drug for patients with BPH is increasing, clinicians should be aware of the possibility of LDE occurring as a rare adverse effect.

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Key words: *Terazosin, lichenoid eruption, lichen planus*

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A case of bromoderma and bromism

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Sir, Halogenodermas are rare dermatoses that develop following exposure to bromides, fluorides and iodides. Bromide-containing drugs have been used therapeutically since 1835. Potassium bromide was widely used as an antiepileptic drug before the advent of phenobarbital and, therefore, many cases of bromoderma were reported in the 1900s. This entity is

now rarely seen by the dermatologist. We report a patient who demonstrated the classical features of bromoderma and bromism following treatment for polycythaemia vera with a bromide-containing drug.

A 56-year-old woman with polycythaemia vera (PCV) presented with a 2-month history of pruritic, tender, erythematous nodules affecting her forehead, upper trunk and limbs with development of asymptomatic haemorrhagic lesions on her hands. In addition, her husband commented that lately his wife had displayed bizarre behaviour necessitating hospital admission 4 months previously. A diagnosis of psychotic depression was made at the time and treated accordingly, together with community psychiatric follow-up. Her PCV had been recalcitrant to a variety of treatments including regular venesections, hydroxycarbamide (Hydrea®, Bristol-Myers Squibb, Uxbridge, U.K.), interferon alfa (IntronA®, Schering-Plough, Welwyn Garden City, U.K.) and anagrelide (Xagrid®, Shire, Basingstoke, U.K.). She was therefore commenced on pipobroman (Vercyte®, Abbott Labs, Maidenhead, U.K.) 75 mg once daily and she had been taking this for the previous 7 months.

On examination, she had a symmetrical erythematous, papulonodular eruption with erosions and pustulation affecting her forehead, upper back and both upper and lower limbs (Fig. 1). Smaller haemorrhagic lesions with necrotic-looking areas were also noted on the pulps of her fingers. Laboratory testing showed a mildly elevated white blood cell count ($12{\cdot}8 \times 10^9\ L^{-1}$) and a microcytic anaemia (haemoglobin $8{\cdot}6\ g\ dL^{-1}$). The inflammatory markers were raised (erythrocyte sedimentation rate 28 mm in the first hour; C-reactive protein 77 mg L^{-1}) and serum bromide level was significantly elevated at 48·8 mg L^{-1} (upper limit of normal <10 mg L^{-1}). Antineutrophil cytoplasmic antibody was positive with a perinuclear staining pattern (pANCA) but ANA, dsDNA, complement levels, renal and liver function tests were all normal. Multiple skin swabs revealed no growth and a computerized tomography scan of her brain revealed no abnormalities. An incisional biopsy from her left arm (Fig. 2) revealed a normal epidermis but an extensive neutrophilic infiltrate within the dermis, forming abscesses. Gram and PAS stains for microorganisms were negative.

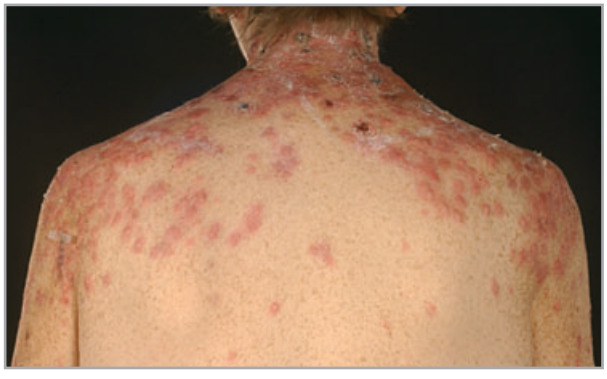

Fig 1. Marked erythematous papulonodular eruption on posterior aspect of trunk.

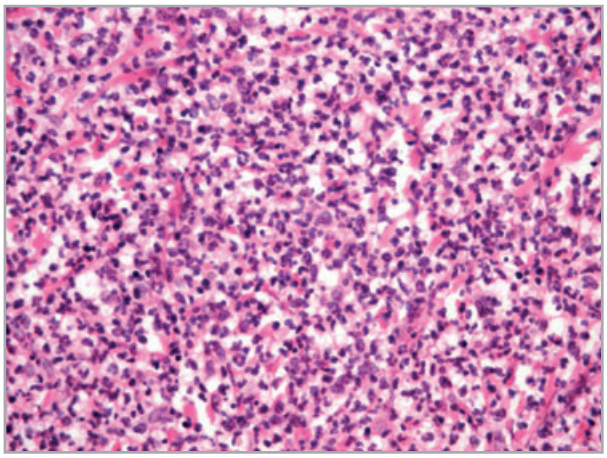

Fig 2. Normal epidermis but an extensive neutrophilic infiltrate within the dermis forming abscesses. No evidence of vasculitis. (Original magnification × 200).

The pipobroman was discontinued and the patient was placed on a high sodium chloride and fluid diet. She was treated topically with clobetasol propionate (Dermovate NN®, GSK, Uxbridge, U.K.). Within 4 weeks there was significant improvement of the skin eruption with complete resolution within 8 weeks; this correlated well with a reduction in her serum bromide level (16·8 mg L^{-1}). Her mental state returned entirely to normal.

Halogens may induce acneiform eruptions, pustules and less commonly, granulomatous or vegetative plaques, ulcers and even bullae. Cutaneous lesions often appear after long-term exposure and can be associated with bromism – a syndrome characterized by weakness, ataxia and personality changes including delusions, hallucinations and depression,[1] as seen in this case. Halogenodermas may persist for weeks after drug withdrawal because of the slow elimination rates of iodides and bromides.

Our patient developed both bromoderma and bromism secondary to pipobroman, a piperazine derivative with a chemical formula related to alkylating agents. Although the exact mechanism of action remains to be defined, this drug has established efficacy for treating myeloproliferative disorders,[2] and is more commonly used in Europe. Common side-effects are gastrointestinal effects, myelosuppression, leukaemia and rarely skin rashes, the latter occurring in <25% of cases following chronic ingestion.[3] Although most cases of bromoderma have occurred after ingestion of bromine-containing sedatives, such as potassium bromide,[4] ingestion of soft drinks containing brominated oil (ruby red squirt and cola) have been reported.[5,6] Other reported causative factors include the pesticide methyl bromide, brominated pool disinfectants and photographic films. Whilst even more rare, bromoderma and bromism, manifesting as hypotonia and weakness has been reported in the newborn and infant arising from excess

maternal ingestion of bromide-containing drugs.[7] The clinical and histological differential diagnosis includes Sweet's syndrome (acute febrile neutrophilic dermatosis), although cANCA is found in up to 85% of cases of Sweet's syndrome, but not with pANCA,[8] as in our case. Furthermore, our patient was not febrile on presentation.

Some authors have suggested that halogenodermas represent hypersensitivity reactions;[9] however, accumulation of the halogenide appears to be important. Bromoderma can occur without symptoms of bromism and are thought to represent hypersensitivity reactions, whilst the symptoms of bromism are thought to be a toxic reaction. The mainstay of treatment, in addition to stopping the offending agent, is topical and systemic steroids, high fluid intake and, in severe cases, immunosuppressive agents such as ciclosporin (Neoral®, Novartis, Camberley, U.K.) which have been used in iododerma.[10] In acute bromide intoxication, infusion of 0·45% sodium chloride together with diuretics may hasten bromide excretion. This case illustrates that bromoderma and bromism are rare but important side-effects of therapeutic agents that are still in use today.

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Confirmed cancer trends in families of patients with multiple cancers including cutaneous melanoma

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Sir, Patients developing multiple primary cancers are rare and their familial risk for cancer can give information about cancer aetiology.

In a previous hypothesis-generating study we investigated all patients (n = 44) with four or more primary tumours including at least one cutaneous malignant melanoma (CMM) in southern Sweden. Patients were screened for the *CDKN2A* mutation 113insArg[1] which might predispose also to tumours other than CMM.[2] Three subgroups were defined according to a hypothesized different aetiological genesis: (A) patients with multiple CMM (including three mutation carriers); (B) patients with single CMM and adenocarcinomas (including one mutation carrier); and (C) patients with late-onset, single CMM and multiple nonmelanoma skin cancer (NMSC). Brain and neural system tumours (NST) were found among nonmutation carriers in groups A and B.[3]

We hypothesized that it might be possible to detect the same tumour trends among relatives if the tumours were a result of shared hereditary, immunological and/or environmental factors.[4] All first- and second-degree relatives of the 44 index patients were traced through the National Swedish Tax Registry, Parish Records and the National Population Registry. Tumours and deaths were identified through the population-based National Cancer Registry and National Population Registries. All NMSC were *in situ* or invasive squamous cell carcinomas, not basaliomas. Tumour distribution was analysed and standardized morbidity ratios (SMRs) were calculated by means of the indirect standardization method (Swedish population as reference).

In this kind of association study it may be a problem that genetic associations are over-interpreted and as a registry-based study it has limitations concerning lack of information about aetiological factors such as sun exposure, smoking, etc. It is difficult to discover the relative importance of genetic and environmental influences in determining risk. We have been investigating tumours that are to an unknown extent environmentally dependent and there is also some uncertainty about carcinogenic mechanisms involved for the different tumours. Sorting out chance findings was difficult because of lack of similar data in the literature.

We identified 521 relatives and found an overall increased risk of malignant tumours, mainly due to CMM but also due to NST, NMSC, corpus uteri cancer and colon cancer but not for breast cancer. Relatives of nonmutation carriers (n = 437) had an increased risk for CMM and a slightly increased total risk (Table 1).

