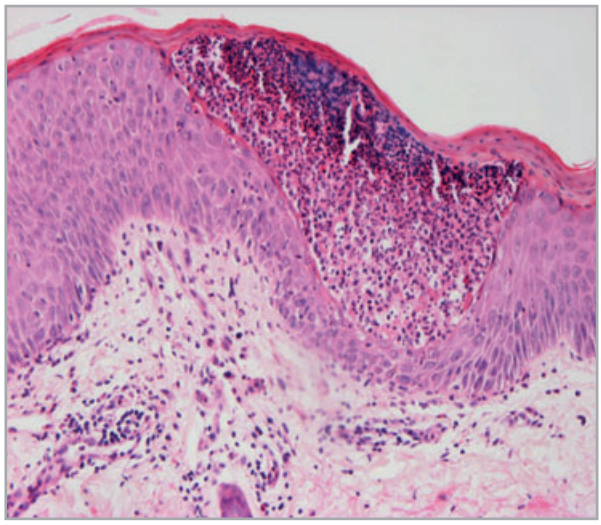

Fig 3. Histology showing epidermal hyperkeratosis, parakeratosis, subcorneal pustule filled with neutrophils and mixed dermal inflammatory infiltrate of lymphocytes, neutrophils and eosinophils.

Over 100 cases have been reported to date of which 50 have been drug induced.[2] One of the most commonly implicated drugs is penicillin. These are the first reported cases, to our knowledge, of SDRIFE associated with the atypical antipsychotic clozapine. Various cutaneous side-effects have been reported with clozapine ranging from eczematous reactions, pustular eruptions and photosensitivity to Stevens–Johnson syndrome. Personal communication with the manufacturer confirmed they had no similar reports to date.

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Funding sources: no external funding.

Conflicts of interest: none declared.

Successful treatment of cutaneous venous malformations in a patient with blue rubber bleb naevus syndrome by Nd:YAG laser

DOI: 10.1111/j.1365-2133.2011.10751.x

Madam, Blue rubber bleb naevus syndrome (BRBNS) is a rare disorder with only about 200 cases reported in the literature. It is a syndrome characterized by multiple venous malformations in the skin and the gastrointestinal tract. It was first described in 1860 by Gascoyen and, in 1958, Bean fully characterized it and named it 'blue rubber bleb naevus syndrome'.[1] BRBNS is important because of potentially severe or even fatal gastrointestinal bleeding; in addition, the mucocutaneous vascular malformations pose a severe problem socially for patients. These malformations are varieties of haemangioma found particularly on the trunk and upper arms. We present a case of an 18-year-old patient with multiple cutaneous and mucosal lesions who was treated successfully by long-pulsed Nd:YAG laser.

An 18-year-old man presented in our outpatient clinic for treatment of multiple cutaneous and mucosal haemangiomas. He was referred to us by paediatricians where he had been in regular care because of a previously diagnosed BRBNS. Until then no treatments for the cutaneous and mucosal lesions had been performed. On physical examination an uncountable number of mostly eruptive haemangioma-like lesions were found. Prior to laser treatment lesions were anaesthetized by local lidocaine/tetracaine application. We treated the cutaneous haemangiomas with Nd:YAG laser (1064 nm, 250 J cm^{-2}, 50 ms, 4-mm spot size, cryogen cool tube). Immediately after treatment the patient felt pain for a few minutes, and the lesions showed a discrete swelling. Shortly after the treatment we found marginal tissue sloughing. Retraction occurred in nearly all treated lesions after a few weeks, and each treatment led to significant shrinking. Newly developing, small lesions diminished after only one treatment. Larger, eruptive haemangiomas needed several treatments at 4-week intervals to disappear. Some lesions, for example, the big lesion on the chin, were located too deeply to be treated with laser (Fig. 1). We followed the patient for 4 years; to date we have not seen any relapse of the treated lesions, but new lesions occur as expected in the natural course of the disease.

BRBNS is a very rare disorder characterized by distinctive vascular malformations of the skin and gastrointestinal tract. The genetic inheritance follows an autosomal dominant pattern with high penetrance. However, there are also many cases of sporadic mutations. In 1995 Gallione *et al.*[2] suggested that BRBNS is identical to the familial venous malformation syndrome, which is caused by a mutation in the *TEK* (tyrosine kinase, endothelial) gene.

It is expected that there should be a correlation between the number of haemangiomas found on the body surface and

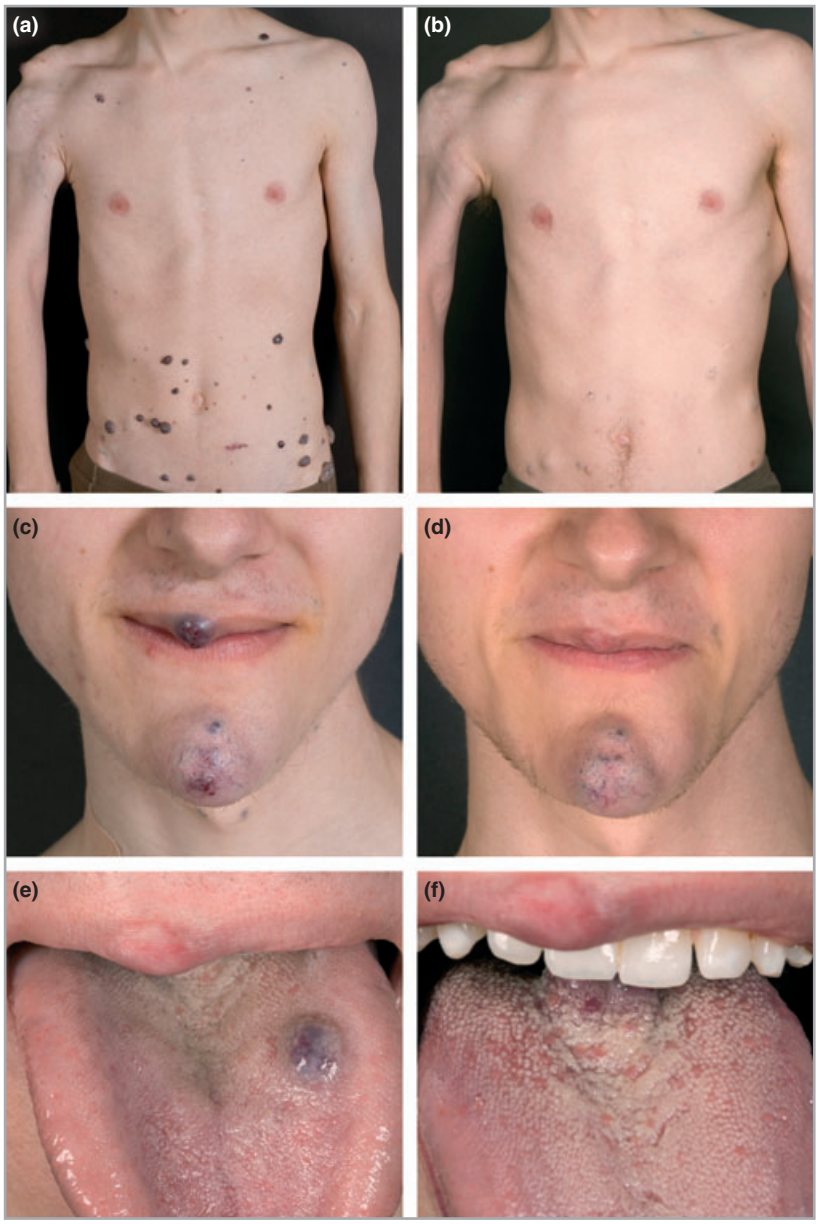

Fig 1. (a) Before treatment; (b) after five treatments; (c) before treatment; (d) after two treatments; (e) before treatment; (f) after two treatments.

haemangiomas of the gastrointestinal tract. The major complications and mortality result from severe or even fatal gastrointestinal bleedings.[3] Although most of the cutaneous haemangiomas are asymptomatic, these mechanically interfering and unaesthetic lesions pose significant physical as well as social problems for the affected patients. Therefore, an effective treatment can dramatically help to improve the life of these stigmatized patients. Several therapeutic modalities such as iron supplementation for anaemia, steroids, interferon alfa-2a, endoscopic laser photocoagulation, band ligation and polypectomy have been attempted in the treatment of BRBNS.[4] Electrodesiccation, excision, cryotherapy and sclerotherapy have been suggested as potential treatment modalities for the cutaneous lesions.[5] In our case the patient suffered from gastrointestinal haemangiomas; however, he refused treatment for these, but desired the treatment of his mucocutaneous lesions.

To our knowledge we are the first to report the successful treatment of mucocutaneous lesions in a patient with blue rubber bleb syndrome by long-pulsed Nd:YAG laser. Two aspects of the Nd:YAG laser suggest an effective treatment of these malformations. On the one hand, the 1064-nm wavelength can penetrate more deeply into lesions enabling energy delivery to a greater depth of these sometimes large, eruptive vascular structures.[6] This is the major advantage over traditional vascular lasers operating between 532 and 595 nm. At 590 nm, laser light penetrates only 1·45 mm into tissue.[7] On the other hand Nd:YAG laser light is absorbed by haemoglobin. It is used for the treatment of vascular targets such as reticular veins and port-wine stains.[6,8] Moreover, long pulse widths tend to be more damaging to larger vascular structures that shed heat poorly, while tending to spare the smaller adjacent tissue structures in addition to the thermal effects of the laser.[9]

Our patient continuously develops new lesions. Treatment was most successful in newly developing lesions. These can be completely diminished by one single treatment. But even older, more eruptive haemangiomas can be reduced and even disappear, and sometimes up to five treatments were necessary.

In conclusion, the Nd:YAG laser is an effective treatment of mucocutaneous haemangiomas in patients with BRBNS. Treatment should start as early as possible as fast and best regression is achieved in newly developing lesions.

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Funding sources: no external funding.

Conflicts of interest: none declared.

Sequential Stevens–Johnson syndrome and photo-recall phenomenon

DOI: 10.1111/j.1365-2133.2011.10734.x

Madam, A 68-year-old woman with diffuse large B-cell lymphoma of the brain was started on a chemotherapeutic regimen consisting of high-dose intravenous methotrexate (MTX) at a dose of 2·5 g m^{-2} and procarbazine at a dose of 200 mg daily. Other medications started concurrently included dexamethasone, allopurinol and omeprazole. Fourteen days later, she developed an extensive rash with mouth ulcers and fever. Clinical examination showed atypical targets that were mainly truncal in distribution associated with buccal mucositis, anogenital erosions and fever. The skin biopsy showed full-thickness apoptosis of keratinocytes, focal basal liquefactive degeneration and lymphocyte exocytosis with a chronic inflammatory infiltrate consisting of lymphocytes, histiocytes and eosinophils. A diagnosis of Stevens–Johnson syndrome (SJS) was made. An infection screen was negative. Allopurinol was deemed to be the culprit drug and was stopped. Superpotent topical corticosteroid ointment (clobetasol propionate) was prescribed with resolution of the rash 1 week later. She was readmitted electively 2 weeks later for further chemotherapy. Unfortunately, allopurinol was inadvertently reintroduced and there was a recrudescence of the rash with scattered atypical targets on the trunk. Allopurinol was immediately stopped and the target lesions settled rapidly. Two days later, she was commenced on her second cycle of chemotherapy consisting of MTX and procarbazine. Over the next 5 days, she developed a new dermatosis in a sun-exposed distribution. There was a well-defined erythema with oedema over the extensor aspects of both upper limbs and erythematous, scaly plaques over the V of the neck (Fig. 1). The autoimmune screen was unremarkable (negative antinuclear antibodies and extracted nuclear antigens, normal complement levels). A repeat biopsy of the lesional skin showed scattered apoptotic cells and focal squamatization of the basal layer overlying extensive solar elastosis and a scanty perivascular infiltrate of lymphocytes (Fig. 2). The clinical presentation and histology was suggestive of a photo-recall phenomenon which was triggered by her chemotherapy, most likely MTX. She was started on prednisolone 0·5 mg kg^{-1} with improvement and was maintained on systemic corticosteroids during her subsequent cycle of chemotherapy with no further recurrences.

Our case illustrates the sequential eruption of two uncommon adverse drug reactions: SJS and ultraviolet (UV) recall phenomenon. Although closely related temporally, we were able to dissect her clinical presentation into two separate events on the basis of discriminatory clinical features and histopathology. Recrudescence of atypical targets following inadvertent rechallenge with allopurinol helped confirm that the initial reaction was SJS.

Recall phenomenon is an unusual dermatological entity characterized by an eruption consisting of erythematous, oedematous, eczematous or vesicular lesions in areas of previous UV radiation-induced injury following drug intake.[1] The most commonly implicated drugs include MTX, other chemotherapeutic agents and antibiotics. This eruption occurs from days to years following the initial insult.[2] Our patient has had frequent episodes of sunburn in the past and prominent solar elastosis was observed on skin histology.

The pathomechanism of UV recall is poorly understood. It has been postulated that MTX inhibits anti-inflammatory path-