(150 mg/daily, once weekly) in patients who achieved CR of the disease during a one-year follow-up period [26]. Forty-two patients (35 males, seven females) with a median age of 75.2 years, and complete regression of their advanced BCC after treatment with vismodegib, were included. Of these, 27 (64%) patients received a once-weekly maintenance dosage of 150 mg vismodegib for one year, and 15 (36%) patients decided not to take the maintenance dosage due to severe AEs. Patients who continued to receive the low-dose vismodegib treatment did not present any BCC recurrence during the one-year follow-up period. Furthermore, no AEs were reported with the exception of mild dysgeusia in 48% (13/27) of patients and mild muscle pain in 29.6% (8/27). In the group of patients who discontinued treatment, a BCC recurrence rate of 26.6% (4/15 patients) was reported. The retrospective design of the study and the fact that the control arm comprised a small number of patients were considered limitations. In conclusion, these results demonstrate that the maintenance dose of vismodegib effectively eliminated skin tumour recurrence and reduced the severity of common adverse events, therefore increasing patient compliance. ■

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Dermpath & Clinic: Where the shoe pinches – painful plantar plaque

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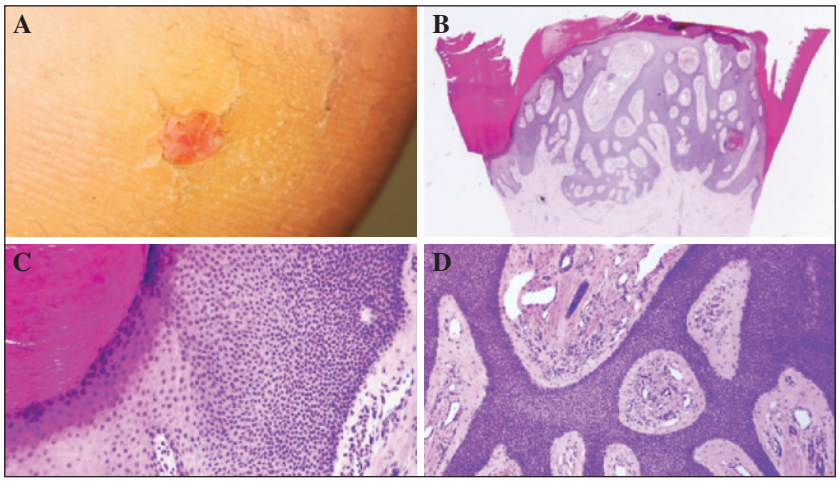

Figure 1. A) A 5-mm painful plaque with a vesicular pattern on closer examination. **B**) Well-circumscribed benign proliferation of small monomorphic, cuboidal cells arising from the lower portion of the epidermis and extending to the dermis (H&E; 2x). **C**) Higher magnification highlights the uniform basophilic cells, which differ from the overlying keratinocytes; there is no palisading or clefting (H&E; 20x). **D**) Ductal differentiation in the dermal compartment of the lesion (H&E; 10x).

A 62-year-old patient presented to our department with a plaque in the heel area that had been slightly painful and slowly growing for about a year. The skin-coloured lesion was 0.5 cm in diameter and showed a vesicular pattern on closer view. To exclude amelanotic melanoma, the plaque was excised.

Histopathologically, the lesion showed a polypus growth pattern with basophil staining (*figure 1*) and originated from the epidermis with an intradermal part. Higher magnification revealed a regular epidermis without cellular atypia. A sharp transition from the regular epidermis to an area with much smaller, monomorphic, small cuboidal cells without peripheral palisading could be seen. Ductal differentiation was present. Tumour cells were Ber-Ep4-negative and epithelial membrane antigen-positive (*data not shown*). A diagnosis of eccrine poroma was established.

Eccrine poroma (EP) is a benign adnexal neoplasm first described by Pinkus *et al*. in 1956 [1] and is also known as hidroacanthoma simplex, dermal duct tumour, and eccrine hidroadenoma. It originates from the intraepidermal portion of the sweat gland duct, the acrosyringium. More recent data suggests that apocrine components may be present as well [2]. The malignant counterpart of EP, porocarcinoma, may arise *de novo* or may develop from a pre-existing poroma, the latter in roughly 18% of cases [3]. Clinically, poroma manifests at a mean age of 65 years with a male predominance as a solitary, asymptomatic, dome-shaped papule, plaque, or nodule with slow growth that mainly affects the palmoplantar skin [4]. Multiple EPs, also known as poromatosis, are a rare condition associated with previous radiotherapy, chemotherapy, and hormonal changes such as pregnancy [5, 6]. Since poroma is known to mimic a number of conditions, dermatoscopically [7, 8], differential diagnoses includes a wide range of benign and malignant lesions such as pyogenic granuloma, verruca vulgaris, melanocytic nevus, basal cell carcinoma, and even amelanotic melanomas [2, 4]. Therefore, diagnosis is usually made based on histopathological grounds.

Histopathologically, poroma is a well-circumscribed tumour composed of proliferative cuboidal or poroid cells that commonly extend from the basal epidermis into the dermal layer [7, 8]. Within the epidermis, poroid cells can be sharply differentiated from the adjacent keratinocytes by their cuboidal appearance with monomorphous nuclei. Mitotic figures, foci of necrosis *en masse*, and a highly vascularized stroma may occur. The aggregates of poroid and cuticular cells in a poroma may show ductal or tubular formation [9]. The solid tumour masses correspond to each other by anastomoses creating an epithelial network. In contrast to basal cell carcinoma, no palisading occurs in the periphery and Ber-EP4 stains negative in poroma. Carcinoembryonic antigen (CEA) immunostaining can identify the presence of both eccrine and apocrine ducts [7, 8]. Tubular foci lined with columnar cells with holocrine secretion are highly suggestive of apocrine aetiology of the poroma [9]. Porocarcinoma is described as a collection of anaplastic, glycogen-rich cells spanning the epidermis and extending into the dermis. The dermal part frequently shows mitotic figures and areas of necrosis [7-9]. As EP is a benign adnexal lesion, surgical removal is curative. In contrast to its malignant counterpart, recurrence of EP is rare. ■

Disclosure. *Conflicts of interest: none*

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Case of the month: a case of IgG4-related skin disease

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A 50-year-old male patient presented with an 18-month history of an intensely pruritic rash. He was otherwise fit and well and took no regular medications. Ultra-potent topical steroids and high-dose antihistamines were ineffective. Examination of the skin revealed multiple non-scaly erythematous papules and nodules on the head, trunk and limbs (*figure 1A, B*). These lesions coalesced to form plaques on the back (*figure 1C*). There was no organomegaly, but lymph nodes were palpable in bilateral axillary and inguinal regions.

Blood tests revealed a mild eosinophilia of 0.84 (normal <0.5) and a raised serum IgE level of 825 kU/L (normal <120). Serum IgG level was raised at 26.22 g/L (normal <15). Serum kappa and lambda light chains were also elevated, but protein electrophoresis revealed a polyclonal pattern and there was no evidence of Bence Jones Protein in the urine.

Skin biopsies taken from the left forearm and left upper back both revealed superficial and deep infiltrates of lymphocytes, histiocytes and eosinophils with prominent plasma cells (*figures 1D, E*). Staining for spirochetes was negative. The plasma cells were polytypic with no light chain restriction on immunohistochemistry. Subsequent blood tests for syphilis and Lyme serology were negative.

The prominence of plasma cells on skin biopsy raised the possibility of a diagnosis of IgG4-related disease. Serum IgG4 levels were markedly elevated at 15.53 g/L (normal <0.86) on serology testing for IgG4 subclasses. Immunohistochemistry for IgG4 was positive in both skin biopsies with high IgG4/IgG ratios of ≥0.84 (*figure 1F*).

Cross-sectional computed tomography imaging revealed significant lymphadenopathy in inguinal, pelvic and axillary regions. Discussion of the patient's case at the regional IgG4 multidisciplinary team meeting concluded that the findings were consistent with a diagnosis of IgG4-related skin disease. Core biopsy from an inguinal lymph node showed a marked plasmacytosis within and around follicles. As was the case in the skin biopsies, immunohistochemistry for IgG4 was positive with an IgG4/IgG ratio of close to 1.00, thereby further supporting a diagnosis of IgG4-related disease with lymph node involvement. The patient was treated with oral prednisolone (40 mg once daily) and reported symptomatic relief within 48 hours, with improvement of his rash over one week. It is likely that he will require maintenance therapy using a steroid-sparing agent such as methotrexate.

IgG4-related disease is defined as a systemic, multi-organ, fibro-inflammatory condition with lesions sharing similar histopathological findings and often a raised serum IgG4. It may have cutaneous and systemic manifestations, predominantly affecting middle-aged men [1, 2]. Clinically, cutaneous disease presents with papules, nodules and plaques and less so with macules, although the latter has also been described [3]. It is often pruritic with nodular prurigo-type lesions. The histological findings include a perivascular to nodular dermal lymphoplasmacytic infiltrate, subcutaneous nodules, interface reaction, lymphoid follicles and a "B-cell pseudolymphoma"-like appearance. Findings resembling Kimura's disease, angiolymphoid hyperplasia with eosinophilia, Rosai-Dorfman disease and xanthogranulomas have been reported and are sometimes also seen clinically. The defining histological criteria for the diagnosis of IgG4-related disease include a triad of features: dense lymphoplasmacytic infiltrate, concentric fibrosis and obliterative phlebitis. However, obliterative phlebitis is almost never seen in some types of involved tissue. Fibrosis may not be present in non-chronic lesions and its absence does not preclude the diagnosis. Elevated levels of serum IgG4 support the diagnosis. An allergic phenotype may be seen with a peripheral eosinophilia and raised serum total IgE level.

Systemic manifestations can occur prior to, subsequent to, or concurrently with cutaneous presentations of the disorder, highlighting the importance of the dermatologist maintaining a high index of suspicion in patients presenting with a clinical and histological picture consistent with IgG4-related skin disease. Rarely, no extracutaneous lesions are found [4, 5] and these cases are reported to represent types of cutaneous pseudolymphoma that respond to thalidomide. The prototype of IgG4-related disease is type 1 autoimmune pancreatitis [6]. Other common presentations include salivary gland, orbital and retroperitoneal disease. A consensus has been published with diagnostic criteria for IgG4-related disease [7]. Umehara *et al.* proposed a different set of diagnostic criteria (*summarised in figure 1G*) which includes organ involvement or dysfunction, serological parameters and histopathological features [8].

Systemic corticosteroids are the first-line agents in the treatment of IgG4-related disease and patients typically show a swift response. Options for maintenance therapy include low-dose prednisolone, azathioprine, mycophenolate mofetil, methotrexate, leflunomide and cyclophosphamide [9]. Some success has also been seen with the B-cell depleting agent, rituximab, with one study showing disease response in 29 out of 30 patients with IgG4-related disease [10]. Disease relapse can occur, and further research is required to investigate other treatment options. As this is most often a multi-system disorder, management in a multi-disciplinary setting is essential to minimise organ dysfunction. ■