when an IgM serum protein is identified. The costs of these tests should be weighed against those of delayed identification of a more aggressive disease, and the potential side effects (or even increased costs) of a bone marrow biopsy to detect an underlying systemic lymphoid or plasma cell neoplasm.

While the aforementioned symptoms are well recognised features of LPL with Waldenström macroglobulinaemia, cutaneous infiltration is not. Therefore, definite diagnosis of cutaneous LPL, even in the presence of a *MYD88* mutation, should be deferred until SPEP and bone marrow assessment have been performed. The bone marrow biopsy revealed involvement of the bone marrow by LPL in all of our cases (Fig. 2C,D), which also harboured the typical chromosomal aberration of LPL in one case (Fig. 2E).

While the small number of cases described herein constitutes a limitation, they do represent an expansion upon the small number of confirmed reports of cutaneous LPL in the literature. In addition, we offer a detailed description of the histopathological findings, clinical management, and follow-up, and document that progression of the disease (including with cutaneous involvement) is a common feature, warranting early recognition and distinction from other more indolent entities. All cases showed a serum paraprotein of the same light chain subtype, as well as bone marrow involvement by the same neoplastic process. These findings highlight the need for complete haematopathological and clinical assessment of these patients, in order to avoid under-diagnosis of LPL in patients with *MYD88* L265P mutated cutaneous small B-cell lymphomas.

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Isolated IgG4-related cutaneous pseudo-lymphoma with crystal-storing histiocytosis

To the Editor,

IgG4-related disease (RD) is a multi-organ immune-mediated condition that mimics many malignant, infectious and inflammatory disorders.¹ It can present with cutaneous and/or systemic manifestations including IgG4-positive plasma cell organ infiltration with accompanying elevated levels of circulating IgG4.² There are many other fibrosing conditions which are pathologically similar to IgG4-RD.² This poses a diagnostic challenge, and with very limited literature surrounding this rare disease, consistent clinical and demographic history to help guide diagnosis is sparse. Typically, IgG4-RD encompasses middle-aged to elderly males; however, for reasons not yet clear, gender predilection appears to change dependent on the location of the IgG4-RD.¹

Rarer still are isolated cutaneous manifestations of IgG4-RD^{2,3} and in extremely rare instances, cutaneous IgG4-RD can be accompanied by a phenomenon known as crystal-storing histiocytosis (CSH). Very few cases in the literature exist for this entity alone with fewer still for cutaneous IgG4-RD with CSH.⁴

CSH is a rare condition in which crystalline material accumulates within the cytoplasm of macrophages.⁵ CSH can be localised or generalised and, in 90% of cases, is associated with lymphoplasmacytic neoplasms such as multiple myeloma, lymphoplasmacytic lymphoma and monoclonal gammopathy of undetermined significance.⁵ Most of the remaining cases of CSH that are not associated with underlying malignancy appear to show an association with diseases that have an inflammatory background.⁶ The cause of the crystalline deposits is hypothesised to be from histiocytic ingestion of the secreted immunoglobulins which are most commonly kappa light chain, with lambda light chain being a rarer occurrence.^{5,6}

The patient was an 84-year-old male with the only pertinent medical history of a basal cell carcinoma recently excised from his face. He presented to an outpatient clinic for follow up of this excision. On examination a mid-back lesion clinically suspicious for another basal cell carcinoma was

noted and an excision planned. At the time of the operation, the lesion was described grossly as well circumscribed, pearly with possible ulceration centrally.

On histological examination, there was an ulcer with an underlying superficial dermal infiltrate consisting of large numbers of plasma cells with smaller numbers of lymphocytes, eosinophils and neutrophils (Fig. 1). Within the cellular infiltrate, there were cells containing tightly packed non-refractile, non-polarisable elongated crystals (Fig. 1). The plasma cells were polyclonal and expressed both kappa and lambda light chains. They were almost entirely IgG-secreting cells (Fig. 2) with only occasional cells expressing IgM and IgA. A large percentage of the cells, approximately 40%, expressed IgG4 (Fig. 2). The crystals expressed lambda light chain (Fig. 2).

Recent literature has provided some diagnostic guidance surrounding the cutaneous manifestation of IgG4-RD with clinical features related to size and location of masses, serum IgG4 concentration and the following histological features: marked lymphocyte and plasma cell infiltrate and fibrosis and infiltration of IgG4-positive plasma cells with a ratio of IgG4

to IgG being greater than 40% as well as greater than 10 IgG4-positive plasma cells per high power field.² The diagnostic criteria continue to be debated and adapted within the literature.^{7,8} Efforts to identify a criterion using clinical markers such as serum concentration of IgG4 have been purported as having low sensitivity and specificity with contrasting opinions within the literature.⁷ This emphasises the lack of universal criteria for diagnosis; however, there is some histopathological consistency with a hallmark feature of enhanced infiltration of tissue by IgG4-positive plasma cells.

Several studies have shown the ratio of IgG4-positive plasma cells to IgG-positive plasma cells to be dependent on the organ location of the infiltrate⁸ with a diagnostic cut-off ratio of $\geq 30\%$. However, this number is adapted to suit disease affecting the thyroid⁸ and so a leading paper in comprehensive diagnostic criteria of IgG4-RD adapted the criteria put forth to reflect the diagnostic difficulty, as well as the variability, in histopathological staining, biopsies and sensitivity and specificity of clinical markers.⁹ This current case does not meet all the criteria outlined in the literature⁹ for definitive

Fig. 1 (A) H&E at low power of the superficial dermal infiltrate underlying a centrally ulcerated epidermis. The prominent mixed inflammatory infiltrate is easily visible. (B) H&E at higher power displaying abundant plasma cell infiltrate. (C,D) H&E at high power of elongated crystals within histiocytes.

Fig. 2 (A) IgG staining plasma cells within the inflammatory infiltrate. (B) IgG4 staining plasma cells within the inflammatory infiltrate. (C) Higher power of the crystals staining positively for lambda light chain (stained dark brown/black).

diagnosis of IgG4-RD, in that there is no known or described serum elevation of IgG4. Further notable histopathological additions to the criteria include storiform fibrosis and obliterative phlebitis⁹ which were not readily observed within this case. However, even these features may be more likely to manifest in older lesions and so absence of these may be insufficient to rule out the diagnosis of IgG4-RD.²

Still, this current case displayed numerous histopathological findings that were most consistent with an IgG4-related cutaneous pseudo-lymphoma with crystal-storing histiocytosis.

The more commonly used treatment for the cutaneous manifestation of IgG4-RD is systemic steroids alongside surgical excision.² The relapse rate appeared high with systematic review of case studies within the literature reporting roughly only 11% of patients achieving complete resolution of disease without a relapse.² There is currently no clear consensus for treatment of cutaneous IgG4-RD. However, further studies have reported successful treatment with agents such as topical corticosteroids, rituximab, azathioprine and methotrexate.²

The crystal-storing histiocytosis has been described in a variety of inflammatory and neoplastic conditions of plasmacytic cells. This phenomenon within this case, clinically and histologically at this point in time has an inflammatory association, however close patient follow-up will be pertinent nonetheless. A suggestion has been made for consideration of serum IgG4 levels and the patient is for follow-up in the respective clinical outpatient department.

This report provides further insight into an extremely rare condition with an associated rare finding of CSH. Temporally, the isolated cutaneous finding is rarer still and adds important clinical (demographic) and histopathological findings to the current paucity of literature surrounding cutaneous IgG4-RD and CSH.

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Multicentric EBV-associated smooth muscle tumour with involvement of the pituitary gland

To the Editor,

We report the unusual presentation of a multicentric Epstein–Barr virus (EBV)-associated smooth muscle tumour (EBV-SMT) in a renal transplant patient, occurring in the pituitary gland, and with apparent progression in histological appearance. EBV-SMTs are rare neoplasms occurring almost exclusively in the setting of immunosuppression, including in primary immunodeficiency, post-transplant, and HIV-associated immunodeficiency. They may occur anywhere in the body, but are most frequently reported in the liver, lungs, and gastrointestinal tract in post-transplant patients.

A 27-year-old female presented in 2020 with secondary amenorrhoea, 6 months after the removal of her contraceptive progesterone implant. Her medical history was significant for congenital abnormalities, including a hypoplastic right kidney and left-sided vesicoureteric reflux resulting in recurrent urosepsis and end-stage renal failure. Renal transplant was performed in 2014 with no immediate complications or rejection. In 2015, she presented with lymphadenopathy and was diagnosed with stage IV EBV-positive diffuse large B-cell lymphoma. During chemotherapy, new liver lesions were detected on routine imaging, with multiple biopsies demonstrating a bland spindle cell neoplasm with no mitoses or necrosis. Smooth muscle actin (SMA), caldesmon and EBV-encoded RNA *in situ* hybridisation (EBER-ISH) were diffusely positive and Ki-67 was 5%. These findings were consistent with EBV-SMT. In 2016, EBV-SMT was again diagnosed in a biopsy from a left cervical node. Biopsies in 2017 and in 2019 of bladder lesions also showed EBV-SMT.

She was referred to endocrinology for investigation of her amenorrhoea. Clinical examination demonstrated an incomplete third nerve palsy with decreased pupillary light response and a mild superior temporal quadrantanopia in the left eye. A pituitary panel was performed to investigate her amenorrhoea, showing hyperprolactinaemia [1132 mIU/L (reference interval 71–566 mIU)]. FSH was 10.9 IU/L (1.7–21.5), LH was 1.7 IU/L (1.0–96.0), and oestradiol was 51 pmol/L (45–1461). Other hormone levels were not significantly abnormal in the context of transplant-related steroid immunosuppression. Imaging revealed a 35 mm pituitary fossa lesion with bilateral cavernous sinus invasion and left-sided optic chiasm compression. Radiological findings favoured a pituitary macroadenoma, but differentials also included lymphoma. A biopsy was performed, with histology showing EBV-SMT. She proceeded to a debulking procedure, with histology confirming a moderately cellular EBV-SMT associated with