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Funding sources: The Ministry of Health, Labour and Welfare of Japan to H.N. Research for Intractable Diseases and a grant from Keio University to J.K.

Conflicts of interest: None declared.

Urticaria-like neutrophilic dermatosis in association with IgA gammopathy: a new entity

DOI: 10.1111/bjd.12771

DEAR EDITOR, IgA gammopathy and multiple myeloma have been associated with multiple neutrophilic dermatoses including subcorneal pustular dermatosis,^{1–4} erythema elevatum diutinum,⁵ urticarial vasculitis,⁶ Sweet syndrome⁷ and pyoderma gangrenosum.⁸ We report an unusual urticaria-like neutrophilic dermatosis as the presenting sign of IgA myeloma. An 84-year-old woman with cardiomyopathy, atrial fibrillation, rectal cancer in remission, and hypertension was admitted for syncope. She reported bone pain and an intermittent rash over the preceding months. Laboratory studies were notable for normocytic anaemia, normal white blood cell count, negative serologies for HTLV-1, RPR, hepatitis and HIV, widespread osteolytic lesions on skeletal survey, elevated serum IgA (1080 mg dL⁻¹, normal: 70–350), decreased serum IgG (599 mg dL⁻¹, normal: 700–1700) and IgM (< 6.5 mg dL⁻¹, normal: 50–300) and a monoclonal IgA kappa on serum protein electrophoresis consistent with plasma cell dyscrasia and confirmed with bone marrow biopsy, demonstrating 15% atypical plasma cells.

The patient had noticed a mildly pruritic rash on the back and legs for the preceding 2 months; individual lesions lasted 3–4 days. On examination, she had annular and round erythematous plaques, some with central clearing, on the back, buttocks and proximal extremities, as well as pink-brown patches, corresponding to resolved lesions (Fig. 1). Several lesions were marked in pen and noted to persist for a minimum of 3 days.

Skin biopsy demonstrated a moderate superficial interstitial infiltrate of predominantly neutrophils with some nuclear debris.



Fig 1. Clinical image showing lesions.

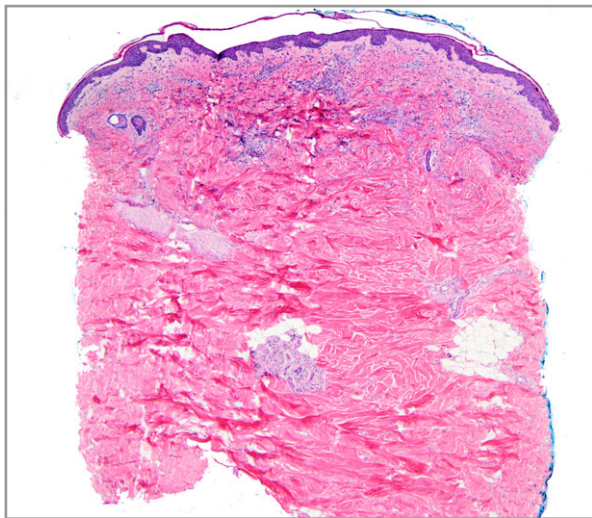


Fig 2. Skin biopsy at low power (original magnification $\times 4$).

ris (Fig. 2). Gram and PAS stains were negative. The distribution and extent of neutrophilic infiltrate did not fit well with any of the known histopathological entities. She was diagnosed with IgA multiple myeloma with extensive bony metastases. She and her family declined treatment and she was placed on comfort care. She died 3 months after her diagnosis due to complications from her disease. During this period, her rash persisted.

The histopathology in this case was unique. The moderate infiltrate consisted predominantly of neutrophils with some nuclear debris. The pattern was interstitial, rather than the perivascular pattern seen in leukocytoclastic vasculitis. Neutrophilic dermatoses seen in association with bowel disease and with arthritis are well described but are characterized by a much denser interstitial infiltrate than that seen in this case. Still disease is characterized by a very sparse neutrophilic interstitial infiltrate. The unique and difficult to classify histopathological findings in this case prompted a literature review that uncovered two cases with similar clinical and histopathological features. This case is the third report of an urticaria-like neutrophilic dermatosis in association with IgA gammopathy.^{1,9}

In 2004, Zhang *et al.*¹ described a case of urticaria-like erythema in a 79-year-old Japanese man with IgA myeloma. He had several months of recurrent urticaria-like erythematous plaques that individually lasted approximately 1 week. Histopathological examination demonstrated 'leukocytoclasia as well as perivascular leukocytic infiltration, being consistent with urticarial erythema'. They reported that the rash correlated with disease activity: with treatment the eruption resolved and with relapse it returned.¹ In 2008, Demitsu *et al.*⁹ reported a case of 'urticaria-like erythema' in a 70-year-old Japanese man with IgA monoclonal gammopathy. Similarly, the patient was reported to have had an eruption for several months that was described as erythematous, indurated plaques persisting for 3–5 days. Histopathological examination demonstrated a diffuse

interstitial neutrophilic infiltrate with no vasculitis. The patient was treated with chemotherapy and the eruption persisted.⁹

Our patient is unique in that she represents the first reported case in the U.S.A. and the first report of this new entity in a female. The two previously described cases occurred in Japanese men. We propose that urticaria-like neutrophilic dermatosis in association with IgA gammopathy represents a new distinct entity. There is a similarly named entity in the literature, 'neutrophilic urticarial dermatosis', recently reviewed by Kieffer *et al.* in 2009.¹⁰ It is characterized by true urticarial lesions that last < 24 h. Our case and the two previously reported papers describe lesions which resemble urticaria morphologically, but by definition are not true urticaria, because the lesions persist for at least 3 days. Thus, nomenclature aside, urticaria-like neutrophilic dermatosis and neutrophilic urticarial dermatosis are distinct conditions.

In summary, urticaria-like neutrophilic dermatosis is characterized by (i) relatively asymptomatic urticaria-like erythematous plaques, with a predilection for the trunk, which persist for days and may resolve with hyperpigmentation; (ii) histopathological findings of a moderate interstitial neutrophilic infiltrate, distinct from urticarial vasculitis and the other known neutrophilic dermatoses; and (iii) the presenting sign of an IgA gammopathy or IgA multiple myeloma, with the presence and severity of the lesions reflecting the extent of underlying disease activity, improving with treatment and recurring with relapse of disease. At present there are too few cases to draw definitive conclusions. Additional case reports are needed to better characterize the features of this entity, as recognition of this condition may allow for earlier diagnosis and treatment of the underlying multiple myeloma.

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Funding sources: no external funding.

Conflicts of interest: none declared.

Needle-free anaesthesia, a promising option for the needle-phobic patient

DOI: 10.1111/bjd.12784

DEAR EDITOR, Needle phobia and pain during injection with a needle is often an overlooked obstacle that may impede access to effective healthcare in dermatological procedures. Needle phobia, defined as an intense, persistent and unreasonable fear of needles, affects more than 20% of the population.

Needle injection on the thick skins of the palms requires an effective pain management method, particularly during onabotulinumtoxinA (BTX-A) injections to control intractable palmar hyperhidrosis.¹

Peripheral nerve blockade of the wrist, an effective method of alleviating pain during palmar injection may have serious drawbacks, particularly when used repeatedly.² Moreover, it is time consuming and may affect hand dexterity for many hours. The Bier block technique is also effective, but systemic effects could occur.³ Vibration anaesthesia has been used with inconsistent results.⁴ Cryoanalgesia can freeze the needle, slowing down the diffusion of the injectate.⁵

Needle-free injection, also known as jet injection, is a needle-free drug delivery method in which a high-speed stream of fluid penetrates the skin. The use of jet injectors in routine

dermatological practice remains low owing to several factors, including the risk of infection, pain and bruising. In our practice, a versatile, low-pressure needle-free injector (such as the Med-Jet[®] MBX manufactured by MIT Canada, Montreal, QC, Canada) has many applications. Here we describe two cases that illustrate the effective application of a needle-free injection device for local anaesthesia.

Firstly, we have treated a patient's severe palmar hyperhidrosis on an annual basis, with BTX-A injections, 100 units per palm: 2% lidocaine is delivered subepidermally to allow subsequent painless BTX-A injection with a needle. Approximately 40 intradermal anaesthetic weals with 2% lidocaine were induced with the jet injector on each hand: one for each phalanx and 26 on each palm. Each anaesthetic weal was injected with 2–3 units of BTX-A. The patient who, at a different time, has received the same BTX-A dose without jet anaesthesia was previously dissatisfied for two reasons: (i) the pain induced by needle puncture (7 on a severity scale of 0–10), and (ii) the same quantity of BTX-A injection had a shorter effect (2 months compared with 1 year with jet injection) (see Supplementary Video S1).

Secondly, we have painlessly excised a naevus on a needle-phobic patient. The patient, who agreed to the biopsy only when needle-free anaesthesia was offered, described the pain of the local anaesthetic administration as 1 and the shave biopsy of the mole as 0 on a severity scale of 0–10 (Fig. 1).

In both cases we used the following parameters: the volume of injectate delivered was between 0.07 and 0.1 cc per spurt, the nozzle diameter 0.12 mm and a 1-mm spacer to keep a stand-off distance between the skin surface and the nozzle. The driving pressure was set at 140 psi and further increase was not needed as the anaesthetic papules were visible.

In our practice, we use the Med-Jet[®] device manufactured by MIT Canada, which is approved by Health Canada and the European Union, and is pending U.S. Food and Drug Administration approval. We use this low-pressure device for jet injection of triamcinolone to treat alopecia areata, localized psoriasis, lichen simplex chronicus, granuloma annulare, necrobiosis lipoidica, hypertrophic scars and keloids. Our most recent application includes needleless injection of triamcinolone into the nail matrix for the treatment of nail psoriasis,⁶ which obviated the need for preliminary digital-block anaesthesia. Controversies pertaining to the severity of pain during

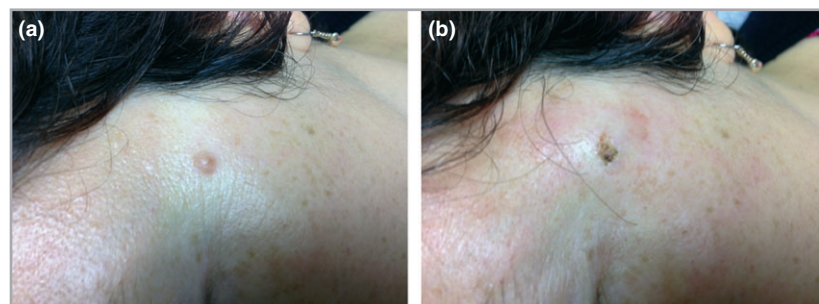


Fig 1. Case 2. (a) Before excision of the mole. Note its inconvenient location on the patient's temporal region. (b) After painless shave biopsy of the mole. Note that there is an almost imperceptible scar, measuring the same size as the excised mole.