A case of Henoch-Schönlein Purpura with underlying TRAPS (Tumour necrosis factor Receptor-Associated Periodic Syndrome)

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Rheumatology key message: Consider alternative diagnosis with recurrent HSP attacks and partial response to steroids.

DEAR EDITOR, a 22-year-old Caucasian man with no previously diagnosed illness presented to the emergency department with a one week history of bilateral lower limb rash. Past history was pertinent for recurrent non-specific childhood abdominal pain persisting into early adulthood. The rash was non-blanching, purpuric, palpable and maculopapular in nature, extending up to the knee with associated arthralgia (see figure 1). Routine blood tests revealed neutrophilia, raised inflammatory markers, elevated serum IgA with preserved renal function. Florid leukocytoclastic vasculitis affecting dermal blood vessels with prominent neutrophilic micro-abscesses was evident on skin biopsy. Immunofluorescence was notable for moderate IgA staining of dermal vessels along with fibrinogen. In view of characteristic joint and skin findings with elevated serum IgA, a diagnosis of Henoch Schönlein Purpura (Ig-A vasculitis) was firmly established.

The skin rash and arthralgia promptly dissipated on initiation of topical steroids. However, inflammatory markers were less responsive, and he developed persistent mild proteinuria and microscopic haematuria requiring multiple courses of oral steroid therapy. Over a course of five years, he had a total of seven inpatient stays with relapse of rash on steroid taper, recurrent abdominal pain and persistently raised C-reactive protein (CRP). In each instance, he was treated as a flare up of his HSP. Several incidental findings accumulated including low-grade colitis, gastritis, cryofibrinogenenaemia, hypoalbuminemia & microcytic anaemia. These features were thought to be consistent with underlying autoimmune vasculitis. Eventually declining steroid responsiveness culminated in acute presentation of worsening abdominal pain, moderate reactive ascites, limb swelling and pleuro-pericardial effusion. The possibility of a multisystem autoinflammatory disorder was entertained. Genetic testing conducted at a specialist unit confirmed TNFRSF1A Tyr38Cys (Y38C) heterozygote, and diagnosis of TRAPS was established. He subsequently began treatment with
interleukin-1 antagonist Anakinra. Marked and sustained improvement was noted in clinical and inflammatory parameters, with no further hospital admission or steroid requirement.

In retrospect, the episodes of non-specific childhood abdominal pain were likely related to repeated TRAPS flare up. A total of ten documented contacts with medical care were made, with presumptive diagnoses of dairy allergy, abdominal migraine, psychogenic abdominal pain, gastroenteritis, and anxiety attack. At time of presentation, a skin biopsy revealed features of leukocytoclastic vasculitis and IgA staining. Whilst several differentials for leukocytoclastic vasculitis exist, the presence of IgA deposits is highly suggestive of HSP [1]. Whilst, cutaneous manifestations are also common in TRAPS syndrome, they tend to present as migratory erythema with dermal infiltration from T cells and monocytes [2] as opposed to the neutrophilic infiltrates seen in this case. The HSP course was atypical due to resistant vasculitic rash and inflammatory markers. An isolated cryofibrinogen band was detected on two separate occasions with no cryoprecipitate, this was deemed to be of unclear significance. A historical case report has documented presence of cryofibrinogen during the active HSP phase [3]. Moreover, cryofibrinogaemic vasculitis could be a reasonable differential. Isolated cryofibrinogenaemia is commonly associated with cutaneous purpura, leukocytoclastic vasculitis and fibrinogen in dermal vessels as seen in this case. However, there is no well accepted criteria for cryofibrinogenaemia, and it was deemed less likely in view of positive IgA staining, absence of cold sensitivity and vasocclusive disease. Eventually on developing worsening abdominal pain, unexplained ascites, limb swelling and serositis, a diagnosis of underlying autoinflammatory disease was considered. Retrospectively, he fulfilled the Eurofever proposed diagnostic criteria for TRAPS syndrome [4] based on the following: episode durations greater than 6 days, migratory erythematous patches, myalgia, and absence of vomiting or aphthous stomatitis. TRAPS is a rare autosomal-dominant periodic syndrome resulting from missense mutation in the TNF-1 receptor. Characteristic features include long-lasting febrile episodes, limb pain, abdominal pain, ocular
inflammation, serositis and rash. Of note, prolonged fevers and associated family history were not prominent features in his presentation.

This case follows a unique course with a biopsy confirmed diagnosis of adult-onset Henoch Schönlein Purpura later revealing underlying TRAPS syndrome on genetic testing. The rarity of co-existing vasculitis and autoinflammatory syndrome may suggest co-incidental causation, but an exaggerated innate immune response may explain the interlink [5]. HSP has been documented in up to 7% of patients with Familial Mediterranean Fever [6], whilst its link with TRAPS is less well established. Genetic studies have implicated TNF signalling defects in several autoimmune diseases including Crohn’s disease, type I diabetes and Sjogren’s syndrome [7]. In particular, TNFRSF1A mutation has also been associated with the development of multiple sclerosis [8]. In conclusion, we highlight that both conditions may present in adulthood, and furthermore co-exist with underlying immunogenic link leading to repeated attacks of vasculitis unmasking florid manifestations of autoinflammatory syndrome. The possibility of autoinflammatory syndrome should be considered in the setting of unexplained, episodic, or persistent multi-system inflammation, repeated hospital admissions and recurrent abdominal or limb pain. Furthermore, an alternative diagnosis should be evaluated in cases of recurrent HSP with partial response to steroids.

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_Data availability statement_

There is no relevant data other than the confidential patient file.
References:


**Figure 1:** Vasculitis appearing rash affecting ankle and shin at initial presentation.
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914x685mm (72 x 72 DPI)