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# IgA vasculitis associated with chronic myelomonocytic leukemia

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**Abstract**

IgA vasculitis is a predominantly pediatric autoimmune disease characterized by IgA deposit in small vessels. Chronic myelomonocytic leukemia (CMML) is a rare hematological malignancy classified within myelodysplastic syndromes. Here, we present a previously unrecognized case of CMML associated with IgA vasculitis. A 62-year-old woman presented with necrotic and infiltrated purpura and mild arthralgia, primarily affecting the knees and wrists, without gastrointestinal or kidney involvement. A comprehensive screening for other etiologies was unremarkable. Blood tests showed an increase of monocyte count and circulating monocyte phenotyping was consistent with CMML. Bone marrow analysis showed no blast cells or karyotypic abnormalities. Genetic testing identified an NRAS mutation. Autoantibody screening and viral serologies were negative. A skin biopsy revealed small-vessel vasculitis with IgA immune deposits. CMML can be associated with autoimmune diseases, such as polyarteritis nodosa and cutaneous leukocytoclastic vasculitis. However, this is the first report of IgA vasculitis occurring in the context of low risk CMML.

**Keywords** Purpura, Chronic myelomonocytic leukemia, IgA vasculitis, Autoimmune disorders

Dear Editor,

IgA vasculitis, also known as Henoch-Schönlein purpura (HSP), is a small-vessel vasculitis characterized by predominant IgA immune deposits [1]. In adults, IgA vasculitis is rare, with an annual incidence ranging from 0.1 to 1.8 per 100,000 individuals. It is more common in males and is characterized by vascular purpura, arthralgia, and gastrointestinal and kidney involvement. While often idiopathic, IgA vasculitis can also be associated with solid neoplasia [2, 3] and hematologic malignancies [4–6].

Chronic myelomonocytic leukemia (CMML) is a clonal hematopoietic stem cell disorder characterized by persistent blood monocytosis. The median age at diagnosis is 70 years, with an incidence of approximately 1 per 100,000 individuals. Most CMML patients have somatic mutations in hematopoietic cells, particularly in the *TET2*, *SRSF2*, *ASXL1*, *RUNX1*, and *CBL* genes [7]. Standard treatments for aggressive or progressive CMML include hypomethylating agents, hydroxyurea, or allogeneic stem cell transplantation [8]. CMML has been associated with autoimmune and autoinflammatory disorders, including various forms of systemic vasculitis [9, 10].

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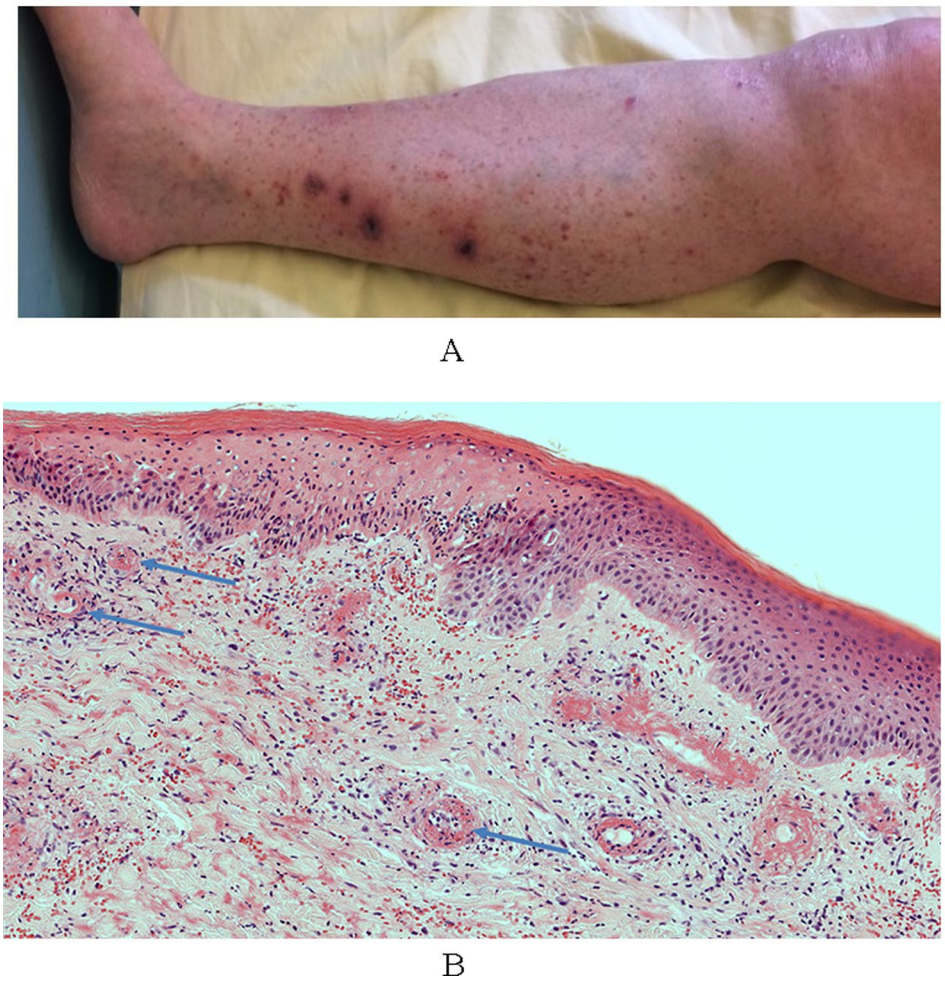

**Fig. 1** **A** Photograph of the patient's leg displaying infiltrated and necrotic purpura. **B** Skin biopsy showing leucocytoclastic vasculitis with prominent IgA deposits

A 62-year-old woman with a history of psoriasis was admitted to our university hospital in March 2018 with recent unexplained purpura and arthralgia. She had a history of psoriasis that had been limited to less than 10% of her body surface several years prior, without relapse or specific treatment. She had no history of medications, recent vaccinations, or infectious triggers preceding the onset of symptoms. Clinical examination was notable for infiltrated and necrotic purpura on the legs (Fig. 1a), but she exhibited no fever or synovitis. She reported mild arthralgia, primarily affecting the knees and wrists, without axial involvement. There were no gastrointestinal or kidney symptoms.

Previous blood tests had documented persistent monocytosis (2,280/mm$^3$) since 2015, without associated cytopenia. Serum creatinine and liver enzyme levels were normal. Autoantibody screening, including antinuclear antibodies and antineutrophil cytoplasmic antibodies, as well as cryoglobulinemia and viral serologies, were all negative. Serum IgA levels were elevated at 3.4 g/L (normal range: 0.80–2.56 g/L) and there was no monoclonal gammopathy. Urinalysis showed no proteinuria or hematuria. Circulating monocyte phenotyping revealed that over 94% of monocytes were $CD14^+CD16^-$, consistent with CMML. Genetic testing identified a NRAS mutation. Bone marrow analysis revealed no blasts, and the karyotype was normal. A skin biopsy confirmed leukocytoclastic vasculitis (Fig. 1b) with IgA deposits, consistent with IgA vasculitis.

The patient was diagnosed with type 1 CMML and IgA vasculitis and there was no specific treatment need for CMML. The IgA vasculitis resolved rapidly with symptomatic management, including NSAIDs and analgesics, and she remained relapse-free over a three-year follow-up period.

Limited data exists on the association between CMML and autoimmune or inflammatory diseases, which could occur in 10–20% of CMML cases. The most frequently reported associations include vasculitis, connective tissue diseases, and neutrophilic dermatosis [9, 11]. Among

vasculitis, polyarteritis nodosa and cutaneous leukocytoclastic vasculitis are the most common in CMML patients [9–12]. While IgA vasculitis has been reported in a few cases of myelodysplastic syndromes (MDS), it has not previously been documented in CMML [2, 9–12]. Approximately one-third of autoimmune disorders may reveal underlying MDS or CMML [2, 9], often in patients with low-risk disease, as seen in our case.

IgA vasculitis has also been associated with malignancies as a paraneoplastic phenomenon, as well as with drug-induced vasculitis. The importance of cancer screening should be raised in all patients with unexplained IgA vasculitis, although standardized screening protocols have yet to be established.

Interestingly, monocytes and macrophages play a significant role in glomerular infiltration in idiopathic IgA nephropathy [13]. Gene expression studies have identified altered monocyte/macrophage profiles in IgA nephropathy patients [14]. Additionally, the IgA receptor (FcαRI), which is involved in endocytosis and recycling of IgA, is expressed on myeloid cells, and plays a key role in IgA vasculitis pathogenesis via circulating IgA-FcαRI complex formation [15]. In the subset of clonal diseases, increased monocyte counts may alter functional properties or induce FcαRI changes involved in pathogeny of IgA vasculitis, even if the mechanisms could be different in IgA vasculitis without kidney involvement, and this remains a hypothesis, as many other monocytes related disorders are not linked to IgA vasculitis.

While our patient had a history of mild, non-relapsing psoriasis, psoriasis itself has also been associated with CMML. Thus, a potential link between psoriasis and CMML in this case cannot be entirely ruled out.

In conclusion, we present the first reported case of IgA vasculitis associated with CMML. This case highlights the need for heightened awareness of underlying hematologic malignancies in patients presenting with unexplained vasculitis. Further research is needed to elucidate the potential pathogenic links between CMML and IgA vasculitis.

#### Abbreviations

| | |
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| CMML | Chronic Myelomonocytic leukemia |
| IgA | Immunoglobulin A |
| HSP | Henoch-Schönlein purpura |

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None.

#### Author contributions
B.R. and A.M. wrote the case report, O.F. and F.C. read the case report and gave their corrections, N.A. and P.H. provided illustrations.

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None.

#### Data availability
The data that support the findings of this study are available on request from the corresponding author.

### Declarations

#### Ethics approval and consent to participate
All persons gave their informed consent prior to their inclusion in the study. Details that might disclose the identity of the subjects under study have been omitted.

#### Clinical trial number
Not applicable.

#### Consent for publication
The patient signed a consent to publication form for their clinical details along with identifying images to be published.

#### Competing interests
The authors declare no competing interests.

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## Publisher's note