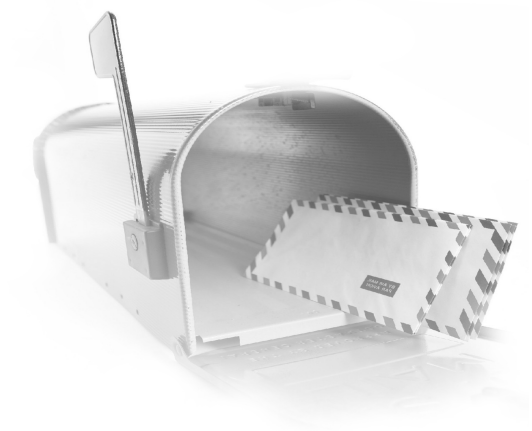

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Letters to the Editor

Primary mixed-type autoimmune hemolytic anemia concomitant with acute splanchnic venous thrombosis of idiopathic origin in a young woman: an unexplained association

TO THE EDITOR: Mixed autoimmune hemolytic anemia (AIHA) is defined by the presence of both warm and cold types of autoantibodies [1, 2]. The diagnosis is based on the detection of these autoantibodies by using a monospecific direct antiglobulin test; a positive test result shows a pattern of IgG and complement C3d along with the presence of cold agglutinins. Mixed AIHA may be of idiopathic origin or associated with an underlying disease [1]. Venous thromboembolism is a common complication of AIHA, although it is not often identified [3, 4]. In some instances, its occurrence may be related to coexistent antiphospholipid antibodies. However, the association of primary mixed AIHA with idiopathic acute splanchnic venous thrombosis (SVT), as we recently observed, represents an exceptional occurrence; thus far, it has been reported for AIHA only in conjunction with splenectomy [5], but has never been reported as a concomitant manifestation.

In the present report, we describe the case of a 19-year-old woman who presented with diffuse abdominal pain and severe anemia. At admission, she presented with life-threatening medical conditions due to severe anemia and critical abdominal features. Her medical history was unremarkable. Findings on clinical images and laboratory parameters were consistent with an acute and severe hemolytic disorder; her Hb level had decreased to 3.9 g/dL, whereas the reticulocyte count, indirect bilirubin level, and lactate dehydrogenase concentration were elevated. On admission, the patient was transfused with packed red blood cells (12 units). A strongly positive result on direct antiglobulin test (IgG3 and C3d) was detected; the indirect antiglobulin test indicated a positive result at 4°C and a negative result at 22°C and 39°C in the presence of a cold panagglutinin antibody (IgM). The concomitant acute abdominal condition was investigated by a comprehensive radiological work-up, including an abdominal echography and a body computed tomography scan, and revealed complete thrombosis of the portal and splenic veins as well as partial occlusion of the superior mesenteric vein. A diagnosis of mixed AIHA associated with SVT was made, and treatment with prednisone (1 mg/kg body weight/day) was promptly initiated; in addition, therapeutic subcutaneous Fraxiparine injections with warfarin were also administered. Additional laboratory investigations revealed no other causes of anemia and ruled out the presence of autoimmune disorders, infections, and liver diseases. Investigations into the possible causes for the development of the thrombosis, including all genetic and acquired abnormalities associated with hypercoagulability states, as well as those aimed to identify a possible underlying neoplastic etiology, did not provide any useful findings. Similarly, the presence of a paroxysmal nocturnal hemoglobinuria clone or abnormal Hb chains was ruled out.

The patient was discharged with continued warfarin treatment with a fraxiparine bridge. However, based on the patient's decision, the warfarin treatment was subsequently discontinued, whereas the fraxiparine was maintained for only 6 months, after which a careful reevaluation showed complete SVT resolution and full vein recanalization in the splanchnic area. Moreover, based on the clinical response, the prednisone dose was adjusted and tapered until the minimal effective maintenance dose was reached; immunohematological evaluations were regularly repeated and indicated completely negative results. However, an AIHA recurrence was observed 6 months after the reduction of prednisone to the lowest dosage. At this time, a second line treatment of rituximab (375 mg/m^2, 4 weekly courses) was given. A complete response by rituximab was achieved. At approximately 1 year after the primary diagnosis was made, the patient is doing well. As AIHA and acute SVT may have been the initial manifestations of underlying occult disorders, the patient is carefully and regularly evaluated

to promptly diagnose any recurrence of her hematological complaints. Thus, we report a rare and unexplained association of primary mixed AIHA with acute SVT, both of idiopathic origin that simultaneously occurred in a young patient.

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Successful treatment of steroid resistant hypereosinophilic syndrome with low-dose CsA

TO THE EDITOR: Although much is known about hypereosinophilic syndrome (HES), the notable discovery of a few genetic rearrangements, such as *FIP1L1/PDGFRA* (*F/P*) and *TEL/ PDGFRB*, and the identification of a phenotypically aberrant clonal T lymphocyte brought a new paradigm to HES. As a result, multidisciplinary groups of hematologists and scientists have created more stratified treatment guidelines for patients with HES.

However, more than half of patients with HES are still classified as undefined under the current diagnostic criteria and the best course of treatment for these patients remains unclear, especially after initial steroid treatments fail. Here, we present two cases of undefined HES who were successfully treated with cyclosporine A (CsA) after corticosteroid treatment failed.

CASE 1

A 41-year-old man visited our emergency room with rashes on both legs and his trunk area.

On physical examination, only a skin lesion was found. His complete blood count (CBC) showed hypereosinophilia (eosinophils 4,730/mm^3). Although he had no history of allergies, a previous CBC reports showed persistent hypereosinophilia over the previous 6 months.

Subsequent analyses did not reveal any evidence of secondary HES including any autoimmune disease or parasitic infestation. Bone marrow aspirate and biopsy showed marked eosinophilia without dyspoiesis. *FIP1L1-PDGFRA, TEL-PDGFRB,* or *BCR-ABL* rearrangement was not detected on fluorescence *in situ* hybridization. *JAK2 V617F* mutation analysis performed with a reverse transcription polymerase chain reaction technique was negative. Serum immunoglobulin E (IgE) level (1,599 mg/dL) and eosinophilic cationic protein level (163.35 ng/mL) were elevated.

Skin biopsy of the leg rash showed perivascular lymphohistiocytic infiltration and many eosinophils. Flow cytometric analysis to evaluate the associated aberrant T-lymphocyte found no abnormal phenotypes such as CD3-CD4+ or CD3+CD4-CD8-, but the T cell receptor (TCR) gene rearrangement was not checked. Although we could not confirm the subclass of HES, clinical findings indicated a lymphocytic variant of HES (L-HES). The patient initially responded well to a high-dose glucocorticoid treatment, but after reducing prednisone, the eosinophil count and IgE level rebounded. Thus, we administered a low dose of CsA (100 mg bid), and his eosinophil count returned to normal after just 1 week of treatment. Prednisone was then tapered to 10 mg per day (Fig. 1A).

CASE 2

A 41-year-old man who had been suffering from intractable eosinophilic pustular folliculitis for 5 years was referred to our hospital. Skin biopsy from the lesion showed perivascular and periadnexal eosinophilic infiltration. He had no history of allergies. Although he had been taking dapsone, prednisone, and an antihistamine since 2008, his skin lesion had waxed and waned and the CBC showed persistent hypereosinophilia for over 1 year. The laboratory results showed an eosinophil count of 1,790/mm^3 and a serum IgE level of 119 IU/mL. Nevertheless, there was no evidence of secondary HES. Sequentially performed bone-marrow aspiration and biopsy showed hyperplasia of the eosinophilic lineage,