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Letter

Update on Sweet Syndrome in Eosinophilic Granulomatosis With Polyangiitis

To the Editor:

I read the article entitled, "Sweet Syndrome in Eosinophilic Granulomatosis with Polyangiitis," published in the July issue of *The Journal*[1], with great interest. However, it is important to mention concerns and issues with regard to investigations, diagnosis, differential diagnosis, and treatment of Sweet syndrome with vasculitis as presented by the authors. It is relevant to place these issues for the knowledge of the readers of this article.

In these patients, it is pertinent to take family history due to genetic association with the presence of HLA-B54[2]. The patient presented in the Murphy, *et al*[1] case report is asthmatic, and eosinophilia on blood investigations is usually seen in such patients because eosinophils are granulocytes with a major role in allergic reactions and parasitic infections. It has been hypothesized that vasculitis in Sweet syndrome may represent an epiphenomenon with secondary vessel wall damage due to toxic metabolites released by activated neutrophils rather than a primary immune complex–mediated disease. A possible role for bacterial, viral, or tumor antigens, as well as circulating autoantibodies, immune complexes, or cytokines has been postulated. Sweet syndrome may occur as a hypersensitivity reaction following the use of antibiotics (e.g., cotrimoxazole, minocycline, fluoroquinolones), nonsteroidal antiinflammatory drugs (e.g., diclofenac), granulocyte colony-stimulating factor, levonorgestrel/ethinyl estradiol, all-trans retinoic acid, antineoplastic agents, biologic agents, and subsequent radiotherapy, all of which have been implicated in the onset of these lesions; these lesions stimulate your body to make neutrophils, a type of immune system cell[3,4,5].

Several myeloid hematologic malignancies have been associated with Sweet syndrome apart from chronic myeloid leukemia, which includes myelodysplasia, acute myeloid leukemia, and other nonmyeloid hematologic malignancies like mycosis fungoides, Hodgkin disease, cutaneous T cell lymphoma, non-Hodgkin lymphoma, hairy cell leukemia, and multiple myeloma.

Other important factors to consider are the differential diagnoses. Well syndrome, also known as eosinophilic cellulitis, is a subtype of hypereosinophilic syndrome. B cell non-Hodgkin lymphoma has shown clinical and histological features similar to Sweet syndrome, including deep and massive infiltration of eosinophils with leukocytoclastic vasculitis[6]. Also, clinicians should remember the diagnosis of eosinophil-rich acute febrile neutrophilic dermatosis in patients with enteropathy-associated T cell lymphoma, type 1, can have presentation similar to Sweet syndrome[7].

The literature describes cases of extreme eosinophil infiltration occurring in this disease that could be misleading[8]. Murphy, *et al*[1] should have emphasized the need to undertake relevant blood investigations in this disorder since anemia and thrombocytopenia are common in patients, especially those with underlying malignancy. A complete blood cell count and cytology, along with differential blood count that shows neutrophils as predominant cell types (up to 70 %) helps in assessing the presence of minor criteria in patients of Sweet syndrome and in ruling out hematologic disorder or malignancy where leukopenia may be present. Erythrocyte sedimentation rate and C-reactive protein levels as acute-phase reactants may be elevated and should be done. Patients with myeloperoxidase (MPO) antibodies often develop MPO–antineutrophil cytoplasmic antibodies and may present with azotemia secondary to glomerulonephritis (pauciimmune necrotizing glomerulonephritis). Therefore, it is very important to simultaneously rule out any associated renal dysfunction by relevant investigations. It is also important to perform a serologic evaluation for antistreptolysin O antibody, rheumatoid factor, and thyroid function because streptococcal infection, rheumatoid arthritis, and thyroid disease have been found to be associated with Sweet syndrome.

Potency topical steroids like 0.05% clobetasol propionate or intralesional glucocorticoids like triamcinolone acetonide may also be useful in localized lesions[9]. Several reports describe biologic agents like etanercept, adalimumab, and infliximab, apart from rituximab, in successfully treating Sweet syndrome in recalcitrant cases[10]. If corticosteroids are contraindicated, antiinflammatory medications such as potassium iodide, colchicine, or dapsone can be used. The efficacy of anakinra, which is an interleukin 1 inhibitor, has been found to be effective in refractory cases. Of note, in most patients, skin lesions heal without scarring.

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