Sir,

Angiolymphoid hyperplasia with eosinophilia (ALHE) is an uncommon benign vasoproliferative disorder of unknown origin characterized by erythematous or violaceous multiple papulonodular lesions typically located on the head and neck, first described in 1969 by Wells and Whimster.\[1\] It typically occurs between the third and fourth decades of life, although there are a few cases reported in infants. Histopathology is required to make a differential diagnosis with Kimura’s disease (KD), given the common characteristics they share. KD is a rare and chronic allergic inflammatory disorder of unknown etiology characterized by painless subcutaneous masses, blood and tissue eosinophilia, and markedly elevated serum immunoglobulin E (IgE) levels.\[2\]

Overlap between Angiolymphoid Hyperplasia with Eosinophilia and Kimura’s Disease in a Child with Immune Thrombocytopenic Purpura

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Figure 1: Erythematous papulonodular lesions with erosive center located on the head and neck (a and b), trunk (c), and upper right limb (d)
A 20-month-old Afro-American male infant with a history of chronic immune thrombocytopenic purpura (ITP) refractory to treatment with corticosteroids, immunoglobulins, and anti-D immunoglobulin, presented with erythematous papulonodular lesions with erosive center [Figure 1] after starting treatment with rituximab for chronic ITP. The lesions were located on the head and neck [Figure 1a and b], trunk [Figure 1c], and upper right limb [Figure 1d], appearing after the first dose of the drug and increasing after the second. The marrow biopsy supported a peripheral origin thrombocytopenia, with an increased number of eosinophils (8%). Skin biopsy showed a lymphohistiocytic infiltrate with eosinophil accumulation surrounding a vascular proliferation with cuboidal endothelium [Figure 2]. CD4+ lymphocytes predominated with some presence of CD8+ cells and CD20+ [Figure 3]. No increase in S100/CD1a or CD30 cells was observed. A lymphoid follicle was noticeable. Dermal collagen was moderately increased. Renal function and proteinary excretion were normal; he showed a mild eosinophilia (6.6%) and a mild increase in IgE (97.1 UI/ml). The study of lymphocyte populations and autoimmunity was normal. The patient was treated with prednisolone 0.7 mg/kg/day for a month with tapering resulting in regression of the cutaneous lesions though no improvement in ITP, which finally responded to eltrombopag.

Figure 2: Cutaneous biopsy. (a) Superficial and deep perivascular dermal inflammation with normal epidermis and focal hypodermal involvement (H and E, ×40). (b) A lymphohistiocytic infiltrate can be observed (H and E, ×100). (c) Prominent endothelial cells are surrounded by this dense infiltrate (H and E, ×200). (d) Abundant eosinophils and prominent endothelial cells (H and E, ×400)

KD is very similar to ALHE but is no longer used synonymously. The typical characteristics of each entity are summarized in Table 1. The origin of ALHE is unclear: it has been attributed to hyperestrogenemia in cases occurring during pregnancy, to prior trauma, infectious agents, or a history of atopy. Furthermore, some cases could represent a CD4+ T-cell lymphoproliferative disorder. In our case, we believe that concomitance of immune thrombocytopenia (which would suggest an autoreactivity of B-cells) and the use of rituximab both played an important role in the pathogenesis, creating an imbalance in the regulatory role of Th2 cells, with increased production of certain cytokines that are associated with ALHE and KD pathogenesis. We postulate that the altered B-cell cytokine milieu allows an exacerbation of the patient’s concomitant T-cell response. Although considered a benign proliferation, ALHE has been associated with various lymphoproliferative T-cell processes. It is possible that there are other reasons for the exacerbation of the skin lesions in our patient, but the temporal sequence makes rituximab the most likely etiological factor.

Regarding the treatment of ALHE, surgical excision is the most accepted therapeutic intervention and the one which has a lower relapse rate. However, there are other local therapeutic modalities (laser, intrallesional corticosteroids, or cryotherapy) or systemic (oral corticosteroid therapy) that have been successfully used.

Figure 3: Cutaneous biopsy. Immunohistochemistry. (a) Marked with CD20; (b) marked with CD4
In our case, the latter option was preferred for the age of the patient and number of lesions. So far, and after 24 months of follow-up, the lesions have not recurred.

Histology of our case presents characteristics of both entities without being able to perform a specific anatomopathological diagnosis. The presentation as a systemic disease with analytical alterations is more typical of Kimura’s disease. However, the presentation as dermal nodules without lymphadenopathy orients more to ALHE, in which eosinophilia is rare. Some authors, where we include ourselves, consider that both entities are part of the same clinicopathological spectrum while others are in favor of the separation of both entities.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient’s parents have given their consent for images and other clinical information to be reported in the journal. The patient’s parents understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

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**Table 1: Typical characteristics of each entity**

| Characteristic                  | KD                                             | ALHE                                          |
|--------------------------------|------------------------------------------------|-----------------------------------------------|
| Typical age                    | Younger people                                 | Third and fourth decades of life              |
|                                | Second and third decades of life               |                                               |
| Sex                            | Males                                          | Males=females                                 |
| Typical morphology             | Deep masses                                    | Grouped nodules                               |
| Most frequent location         | Head and neck                                  | Head and neck                                 |
| Symptoms                       | Asymptomatic                                   | Pruritus, pain                                |
| Lymphadenopathy                | Frequent                                       | Infrequent                                    |
| Lymphoid follicles             | Frequent                                       | Rare                                          |
| Vascular proliferation         | Mild                                            | Profuse                                       |
| Endothelium                    | Flat/low cuboid                                | Cuboid/epithelioid/histiocytoid               |
| Eosinophilic infiltrate        | Abundant                                       | Scarce, moderate                              |
| Eosinophilic abscesses         | Present                                        | Rare                                          |
| Eosinophilia                   | Frequent                                       | Rare                                          |
| Increased IgE                  | Very frequent                                  | Rare                                          |
| Proteinuria and nephrotic syndrome | Frequent                                   | Described (one case)                          |
| Eosinophilia in bone marrow    | Described                                      | Not described                                 |
| Association with immune thrombocytopenic purpura | Described                                    | Described (one case)                          |

Highlighting in bold the ones of our case. *Especially in the second decade of life, *Especially in the third decade of life, KD: Kimura’s disease, ALHE: Angiolymphoid hyperplasia with eosinophilia