Relapsing polychondritis in a patient treated with Dupilumab

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We present the case of a 45-year-old female with severe asthma and chronic rhinosinusitis with nasal polyps, who was treated with Dupilumab with clinical response. One year after initiating treatment, she presented episodes of thoracalgia and dyspnea, as well as deformity of the bridge of the nose (Figure 1), left third metacarpophalangeal, left fourth interphalangeal and cuneonavicular joint arthritis. Thoracic computed tomography scan showed bronchial and tracheal wall thickening with luminal narrowing (Figure 2) and involvement of costochondral and thyroid cartilages, suggesting polychondritis. Immunological study including anti-nuclear antibodies, anti-myeloperoxidase and anti-proteinase 3, anti-neutrophil cytoplasmic antibodies, rheumatoid factor, and anti-cyclic citrullinated peptide antibody were negative. Erythrocyte sedimentation rate and C-reative protein were elevated. Given the risk of respiratory compromise, Prednisolone 1 mg/kg and Methotrexate were initiated. During the following months, respiratory symptoms worsened. After Rheumatology's observation, diagnoses of relapsing polychondritis (RP) and vasculitis were considered. Nasal septum biopsy showed inflammation with no signs of vasculitis and systemic involvement of other organs was excluded. Immunophenotyping revealed increased Th17A lymphocytes.

To summarize, our patient presented episodes of thoracalgia and dyspnea, chondritis of nasal cartilage with "saddle nose" deformity, chondritis of respiratory tract, arthralgias and inflammatory arthritis, and cartilaginous inflammation of ribs and thyroid, meeting criteria for the diagnosis of RP, according to Michet *et al*.[1] Dupilumab was suspended by the allergist after the diagnosis without asthma or nasal polyp worsening. Treatment with Cyclophosphamide was initiated, with respiratory symptoms improvement.

RP is a rare immune-mediated multisystem disease involving cartilaginous and proteoglycan-rich structures. It is characterized by recurrent episodes of progressive cartilage inflammation predominantly affecting the ear, nose, and laryngotracheobronchial tree. The etiology of RP is unknown and its mechanism is poorly understood. It is suggested that a genetic predisposition may exist and multiple inciting factors have been hypothesized like infection, chemical or toxic exposure or trauma. The diagnosis is based on a combination of clinical features, imagiological findings and/or biopsy of a cartilaginous site, and several diagnostic criteria have been proposed. It is mandatory to search for differential diagnosis and associated inflammatory disease. The main differential diagnosis are ANCA-associated vasculitis, especially eosinophilic

granulomatosis with polyangiitis. Treatment includes corticosteroids and immunosuppressants such as methotrexate, azathioprine, cyclophosphamide and cyclosporine[2].

Dupilumab is a human monoclonal antibody that inhibits IL-4 and IL-13 pathways and is currently approved for the treatment of Type 2 inflammatory diseases such as severe asthma and chronic rhinosinusitis with nasal polyps. With the increased use in clinical practice, rheumatologic conditions have been associated with Dupilumab, namely T Helper 17-driven inflammatory diseases like seronegative arthritis and enthesitis/enthesopathy, but not to humoral autoimmune diseases[3]. By antagonizing both IL-4 and IL-13, it may skew immune responses toward IL-23/IL-17 pathway-related conditions[3]. However, the mechanism of RP is poorly understood and we did not find any case report associating RP with Dupilumab. The authors hypothesize that Dupilumab may have unveiled RP in a genetically predisposed patient and suggest close monitoring of non-humoral autoimmune diseases in patients treated with this monoclonal antibody.

Tables and Figures

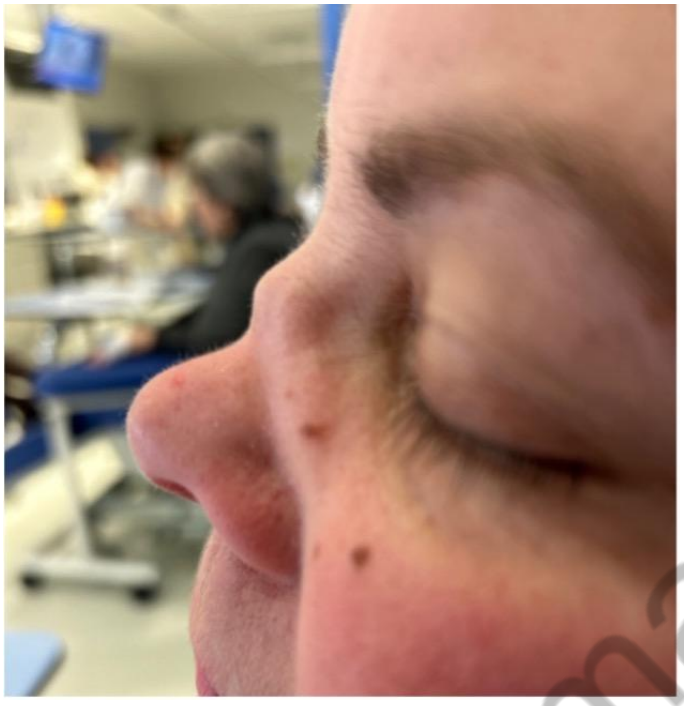

Figure 1. “Saddle nose” deformity

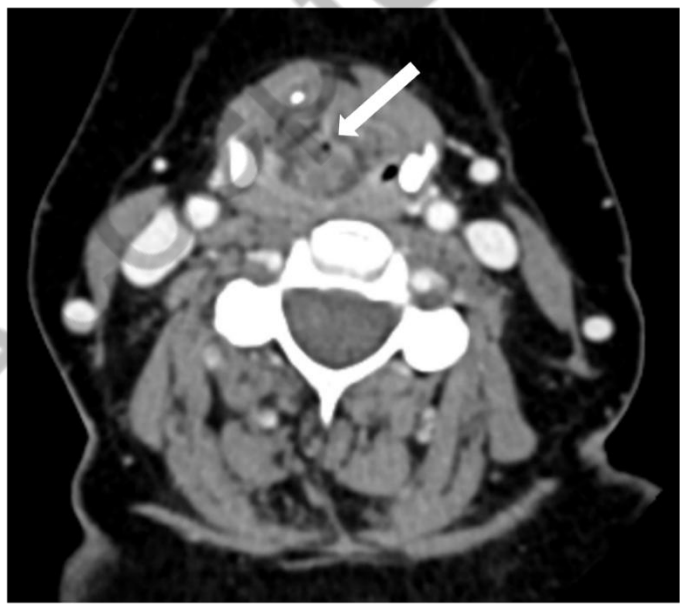

Figure 2. Computed tomography scan revealing tracheal narrowing (*arrow*)

References

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