Combination of Hypertrophic Pachymeningitis, PR3-ANCA-positive Vasculitis, and Relapsing Polychondritis

To the Editor:

Relapsing polychondritis (RP) is a rare connective tissue disease characterized by inflammation and destruction of cartilaginous tissue[1]. Although the exact underlying pathologic mechanism is unknown, it is widely accepted that there is a role of an autoimmune response in most cases[2]. Patients may have lung, renal, ocular, joint, and vascular compromise. Central nervous system (CNS) involvement is rare, and few cases have been described. We describe 3 patients with RP and CNS involvement manifested as hypertrophic pachymeningitis (HP), an inflammatory process that thickens the dura mater. These 3 cases additionally presented with an anti-proteinase 3-antineutrophil cytoplasmic antibody (PR3-ANCA)-positive vasculitis. We reviewed the clinical records of 18 patients with RP diagnosed according to the criteria established by McAdam, *et al*[3] treated between 2001 and 2009 in a tertiary care center in Cali, Colombia. Three patients had the association of HP and PR3-ANCA-positive vasculitis.

Case 1. A 50-year-old woman presented with episcleritis, arthralgias, intense occipital headache, marked tenderness in the tracheal and ear cartilage, and hypoesthesia in the left side of her face. A lumbar puncture showed no abnormalities; magnetic resonance imaging (MRI) scan showed hyperintense meningeal thickening in the left cerebellopontine angle (Figure 1). Urinalysis showed proteinuria, hematuria, and urinary casts. Antinuclear, anti-DNA, anti-SSA, anti-SSB, anti-Sm, and anti-RNP antibodies were negative; PR3-ANCA analyses were positive. Ear cartilage biopsy showed changes related to polychondritis and a renal biopsy revealed leukocytoclastic vasculitis (Figure 2). Her clinical progression showed multiple relapses and difficulty in tapering the steroid dose.

Case 2. A 48-year-old woman was admitted complaining of diplopia, hypoacusia, headache, arthralgias, and ear and nose chondritis. Urinalysis showed proteinuria, leukocyturia, and hematuria. Cerebral MRI showed diffuse enhancement of the dura mater (Figure 1). A renal biopsy showed vasculitis. A test for PR3-ANCA was positive. Treatment was based on steroids and oral cyclophosphamide, with a good clinical response.

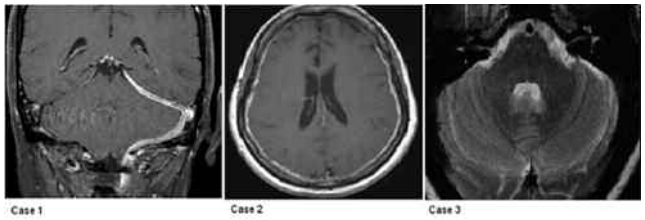

Figure 1. Cerebral MRI. Case 1: meningeal thickening in the left cerebellopontine angle; Case 2: diffuse pachymeningitis; Case 3: thickening of dura mater in the pontine zone.

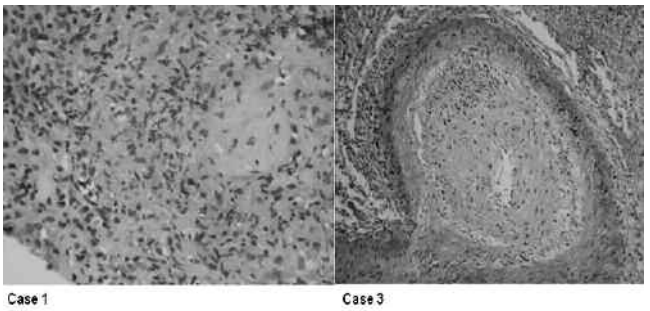

Figure 2. Biopsies showing renal (Case 1) and meningeal (Case 3) vasculitis.

Case 3. A 50-year-old woman with history of trauma in her right ankle developed fever, chondritis in her ears, nose and trachea, weight loss, arthralgias, episcleritis, severe headache, and multiple cranial nerve palsy. Cerebral MRI showed thickening with gadolinium enhancement of dura mater in parietal and pontine zones (Figure 1). A cerebral and meningeal biopsy revealed HP with granulomatous vasculitis (Figure 2). PR3-ANCA analysis was positive. The clinical condition had a poor response to steroids, and required cyclophosphamide and rituximab treatment.

The pathogenic characterization of RP remains incomplete. Nonetheless, a role for the immune system has been established based on the frequent association with other autoimmune diseases (> 30% of patients); the existence of autoantibodies; and the presence of autoreactive CD4 lymphocytes, immunoglobins, C3, and plasma cells in cartilage biopsies[1]. This immune response is partly explained by the presence of autoantibodies against type II collagen. RP is characterized by intense pain and tenderness, along with erythema and edema in the ear cartilage, with progressive tissue destruction. Other sites of cartilage involvement include joints, airway, and nose. Eye, lung, heart, hematologic, renal, and skin involvement have been described. CNS and peripheral nervous system involvement is infrequent, and although some form of vasculitis has been suspected as the underlying mechanism, this hypothesis has not been demonstrated[4]. CNS involvement has been reported in less than 10% of patients[5], including stroke[6] and aseptic meningitis[7,8,9] (in some cases, with a migratory[6] or relapsing pattern[8] or purulent expression[9]).

On the other hand, cases of RP have been described in association with primary systemic vasculitis, mainly Wegener's granulomatosis (WG)[10]. In these cases, RP has been considered as a secondary phenomenon during an acute phase of a primary vasculitic entity. Symptoms of WG may include chondritis (in up to 15% of the patients). However, if nasal and tracheal chondritis are classical in WG, ear inflammation is exceptional. In our cases, the initial clinical picture has been the RP, and ear chondritis was present in all 3 cases. Pachymeningitis has also been described as a rare manifestation in patients with WG. RP and HP in our patients are probably the consequence of primary systemic vasculitis, with PR3-ANCA-positive test, without the classical clinical picture of WG.

We describe 3 cases with RP and HP, a rare condition associated with diverse infectious, autoimmune, and neoplastic disease. Our patients additionally had PR3-ANCA-positive tests with evidence of renal or cerebral vasculitis, without the full clinical expression of WG. The observation of PR3-ANCA in RP should encourage clinical and laboratory research of primary systemic vasculitis.

This complex presentation of these cases raises the possibility of a new clinical syndrome recognizable in the spectrum of PR3-ANCA-positive autoimmunity.

CARLOS A. CAÑAS, MD, Rheumatology Unit; JUAN C. DÍAZ-MARTÍNEZ, MD, Internal Medicine; GABRIEL J. TOBÓN, MD, MS, Rheumatology Unit, Fundación Valle del Lili, Cra. 98 18-49, Cali, Colombia. Address correspondence to Dr. Cañas;
E-mail: cacd12@hotmail.com

REFERENCES

1. Rapini RP, Warner NB. Relapsing polychondritis. Clin Dermatol 2006;24:482-5.
2. Hansson AS, Heinegard D, Piette JC, Piette JC, Burkhardt H, Holmdahl R. The occurrence of autoantibodies to matrilin 1 reflects a tissue-specific response to cartilage of the respiratory tract in patients with relapsing polychondritis. Arthritis Rheum 2001;44:2402-12.
3. McAdam LP, O'Hanlan MA, Bluestone R, Pearson CM. Relapsing polychondritis: prospective study of 23 patients and a review of the literature. Medicine 1976;55:193-215.
4. Kothare SV, Chu CC, Van Landingham K, Richards KC, Hosford DA, Radtke RA. Migratory leptomeningeal inflammation with relapsing polychondritis. Neurology 1998;51:614-7.

5. Zeuner M, Straub RH, Rauh G, Albert ED, Schölmerich J, Lang B. Relapsing polychondritis: clinical and immunogenetic analysis of 62 patients. J Rheumatol 1997,24:96-101.
6. Hsu KC, Wu YR, Lyu RK, Tang LM. Aseptic meningitis and ischemic stroke in relapsing polychondritis. Clin Rheumatol 2006;25:265-7.
7. Brod S, Booss J. Idiopathic CSF pleocytosis in relapsing polychondritis. Neurology 1988;38:322-3.
8. Berg AM, Kasznica J, Hopkins P, Simms RW. Relapsing polychondritis and aseptic meningitis. J Rheumatol 1996;23:567-9.
9. Ragnaud JM, Tahbaz A, Morlat P, Sire S, Gin H, Aubertin J. Recurrent aseptic purulent meningitis in a patient with relapsing polychondritis. Clin Infect Dis 1996;22:374-5.
10. Small P, Black M, Davidman M, de Champlain ML, Kapusta MA, Kreisman H. Wegener's granulomatosis and relapsing polychondritis: a case report. J Rheumatol 1980;7:915-8.

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