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CASE REPORT

Relapsing Polychondritis with Central Nervous System Involvement at Onset: A Case Report

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Abstract

Relapsing polychondritis (RP) is a rare autoimmune disease characterized by the inflammation of cartilaginous tissues, particularly ears, nose, respiratory tract, eyes, and joints. Central Nervous System (CNS) involvement is a rare presentation of RP. We report a case of RP in a 44-year-old male who initially presented as seizures, headache, bilateral red eye, fever and disorientation in time and space.

Keywords: Relapsing polychondritis, cerebrospinal fluid, meningoencephalitis, seizures

Background

RP is an autoimmune disease characterized by the inflammation of cartilaginous tissues. The disease can affect several organs, including proteoglycan rich tissues, particularly ears, nose, respiratory tract, eyes, and joints.[1] The incidence and prevalence of RP are not exactly known, but a recently study reported that the calculated prevalence is 4.5 cases/million in population.[2] Neurological involvement in RP is rare but confers a high morbidity and mortality.[3] The most common neurologic features are cranial neuropathies of the second, sixth, seventh, and eighth nerves. However, miscellaneous neurological conditions can occur such as hemiplegia, seizures, organic brain syndrome, dementia, and cerebral dysfunction.[4,5]

There have been previous reports on CNS involvement of RP but they are few in number and are only sporadic.[6] Here, we report a case of RP with CNS involvement which presented as seizures, headache, fever, bilateral red eye, and disorientation in time and space.

Case Report

44-year-old man, who previously worked as a driver and who had no relevant hereditary background; he had been previously diagnosed with hypertension 8 months ago, for which he was being treated with losartan and metoprolol. History of allergies, tattoos, and transfusions were denied. He had an open right nephrolithotomy 9 years ago without major eventualities. He reported smoking 6 cigarettes a day during a period of 6 years, alcohol consumption every week without inebriation, he denied drug use. Infectious-contagious diseases were denied, as well high-risk sexual behavior and recent trips. He had a history of transient ischemic attack of the right middle cerebral artery 4 months ago, in secondary prevention with acetylsalicylic acid. He had an episode of acute meningitis without isolation of etiological agent 3 months before his admission, for which he was treated with ceftriaxone and vancomycin. He reported having multiple events of red eye syndrome, for which he was diagnosed with bilateral papillitis and treated with topical corticosteroid. Two months before his admission, he presented tonic clonic generalized seizures, for which he was being treated with phenytoin.

He began his current illness with intense oppressive frontal headache and diaphoresis, of 2 days of evolution, fever, bilateral red eye, and disorientation in time and space. On admission his vital signs included a heart rate of 100 beats per minute, respiratory rate of 22 breaths per minute, temperature of 38 °C, blood pressure of 140/100 mmHg. On physical examination, a general appearance with pallor of teguments, without any other lesion. Both eyes with cornea and transparent conjunctiva, white sclerotic, moderate to severe ciliary hyperemia (figure 1A), a positive Tyndall phenomenon, cloudy vitreous, effacement of papilla edges. Nose without deformities, right ear with moderate edema, as well as generalized erythema, painful on palpation (figure 1B), bilateral otoscopy without alterations. Mouth with adequate salivary lake, without ulcers. Neck and axillary region without palpable adenopathies. Heart sounds were rhythmic of good intensity and frequency, without murmurs, lung fields with vesicular murmur present, without adventitious. Hypotrophic limbs, right knee phlogosis, rest without synovitis, no livedo reticularis, no Raynaud phenomenon, capillary filling of 2 seconds. On neurological examination alert, disoriented in time, place and person, hypofluent speech, partial understanding. Visual acuity of the right eye to hand movement, left eye to counting fingers, bilateral hypo-reactive photomotor reflex, rest of the cranial nerves without abnormalities. Extremities with preserved tone, with generalized hypotrophy, strength in thoracic and pelvic limbs 4/5 proximal and distal. Normal osteotendinous reflexes. Bilateral plantar flexor response. Respected superficial and deep sensitivity. Dysmetry in a bilateral manner with greater right predominance. Presence of bilaterally non-exhaustible nystagmus. No neck stiffness.

The following laboratory tests were performed: Hb 10.8 g / dl, hematocrit 33%, mean corpuscular volume 87 fl, corpuscular hemoglobin mean concentration 32.6%, platelets 409,000 / mm3, leukocytes 5.880 / mm3, lymphocytes 1.140 / mm3 (19.4%) , neutrophils 4.110 / mm3 (69.8%), monocytes 500 / mm3 (8.5%), eosinophils 20 / mm3 (0.4%), basophils 30 / mm3 (0.03%), elevated erythrocyte sedimentation rate (30 mm / h) , elevated C reactive protein (60.6 mg / l), normal procalcitonin (0.34) ng / ml, glucose 83 mg / dl, urea 23.98 mg / dl, creatinine 56 mcmol / l, uric acid 169.3 mcmol / l, gamaglutamyl transferase 399 U / l, total bilirubins 0.4 mg / dl, total protein 5.8 g / dl, albumin 3.0 g / dl, globulins 2.9 g / dl, alanine aminotransferase 53 U / l, aspartate aminotransferase 23 U / l, alkaline phosphatase 150 U / l, phosphorus 1.4 mmol / l, calcium 2.1 mmol / l, chlorine 100 mmol / l, sodium 139 mmol / l, magnesium 0.7 mmol / l, lactic dehydrogenase 312 U / l.

Clinical data was compatible with an infection of the central nervous system, so empirical antibiotic therapy was started with ceftriaxone, vancomycin, ampicillin and fluconazole. The patient was treated with intravenous boluses of methylprednisolone and ophthalmic prednisolone due to the presence of panuveitis of both eyes. Lumbar puncture was performed, obtaining a clear cerebrospinal fluid with leukocytes 50 / mm3, polymorphonuclear cells 0%, mononuclear cells 100%, glucose 38 mg / dl, proteins 41 mg / dl, Gram, BAAR and nigrosine stains were negative. Microbiology studies were carried out to rule out chronic bacterial or fungal infections, HIV ELISA test was negative, blood and cerebrospinal fluid cultures were negative, polymerase chain reaction for Mycobacterium, VDRL and febrile reactions (typhi H, typhi O, Huddleson Brucella abortus, bengal rose) were negative; and IgG and IgM antibodies against Borrelia burgdorferi were also negative. Chronic infectious processes were ruled out, and the patient continued with fever despite the broad-spectrum antibiotics; relapsing polychondritis was suspected due to physical examination findings. A right ear cartilage biopsy was performed, showing the findings presented in figure 2. We established a diagnosis of aseptic meningoencephalitis with RP. Complementary immunological studies were performed to rule out associated systemic diseases resulting negative, with immunoglobulin G 1120 mg / dl, immunoglobulin A 212 mg / dl, immunoglobulin M 86.9 mg / dl, C3 132, C4 39.5, rheumatoid factor <11.5, anti-citrullinated peptide antibodies <0.5 U / ml, ANCA-weak positive, negative ANCA-c, antinuclear antibodies positive 1:80 mottled fluorescence pattern, negative anti-DNA antibody, anti-Smith antibody 4.24 U / ml, anti-La 2.9 U / ml antibody ml, anti-Ro antibody 3.137 U / ml.

Due to the presence of neurological focalization, a CT scan of the head was performed, which did not present alterations. Given the suspicion of vasculitis of the central nervous system, magnetic resonance imaging of the head with

gadolinium was performed, finding multiple compatible ischemic lesions (figure 3).

Treatment with prednisone and azathioprine was started, however, it was suspended days later due to respiratory deterioration and development of hospital-acquired pneumonia, dying 5 days later.

Discussion

RP is a rare multisystem autoimmune disease of unknown origin characterized by recurrent episodes of inflammation and a progressive destruction of cartilaginous tissues. Elastic cartilage of the ears and nose, hyaline cartilage of the peripheral joints, vertebral fibrocartilage, and tracheobronchial cartilage, as well as the proteoglycan-rich structures of the eye, heart, blood vessels or inner ear may all be affected. In most patients RP manifests as a fluctuating but progressive course which eventually results in a significant shortening of life expectancy.[7] Although RP can occur at all age groups, like in this case, the starting age of the disease is the fifth decade of life. The etiopathogenesis of RP is still unknown. Nonetheless, it seems to be a combination of constituents comprising genetic predisposition, a triggering factor (chemical, toxic, and infectious agents, or direct trauma), and presence of autoimmunity.

The clinical picture of the RP changes with severity and duration of the disease. The most common and characteristic feature is auricular involvement, as presented in our patient, but other sites of the body and tissues may be involved as well. Auricular involvement is present in 90% of the patients with RP. Ocular inflammation can affect any part of the eye and may affect 20%−60% of the cases. Most common ocular manifestations are episcleritis, peripheral ulcerative keratitis, scleritis, and uveitis.[1] The patient presented both clinical manifestations. Central and peripheral nerve system involvement in RP occurs in approximately 3% of patients. Various cranial neuropathies as well as headaches, encephalopathy, seizures, hemiplegia, and cerebral aneurysms have been reported.[8] Although the frequency of these is not well established at onset, as in the patient, whose initial symptoms were neurological manifestations.

The diagnosis is usually established by clinical features, whose criteria are proposed by McAdam,[9] and Damiani.[10] Modifications to the criteria of McAdam were made by Damiani and Levine due to the variability of clinical manifestations during the course of this disease. The present patient fulfilled the criteria for Damiani, not for McAdam.
The neurological symptoms in the present case were aseptic meningoencephalitis, seizures and ischemic events.

Cerebral vasculitis has been proposed many times as the mechanism of encephalitis, meningitis and meningoencephalitis in cases of RP. There is currently not enough evidence to definitively confirm that hypothesis.[11] As in other cases of central nervous system (CNS) involvement, magnetic resonance imaging revealed multifocal gray- and white-matter high intensities. This pattern is consistent with cerebral arteritis as described in other systemic vasculitis.[12]

As many as one-third of the patients with RP have a concomitant disease including systemic vasculitis, dermatologic or hematologic disease, or other systemic rheumatic disease.[4] Coexisting autoimmune diseases have been reported to include rheumatoid disease, lupus erythematous, Sjogren's syndrome, Behcet's disease, ankylosing spondylitis, psoriatic arthritis, and polymyalgia rheumatic,[13] all of which were excluded in the patient.

Improvement in the survival of patients with RP have been achieved in recent years. Survival rates were reported to be increased from 55% to 91% at 10 years.[14,15] Main causes of death in patients with RP are specific organ involvements such as airways, blood vessels, concomitant diseases, and infections in which development is facilitated by the treatment itself.[1] In this case, a hospital-acquired pneumonia was the cause of death of the patient, which is the main cause of death in patients with RP.[14]

Since the initial symptoms in our patient were neurological, it is important to recognize that meningitis, encephalitis, meningoencephalitis, and stroke can be present at onset in a patient with RP, thereby should be considered in the differential diagnosis.

Conclusion

CNS involvement is a very rare complication of RP. Here, we report a case of RP with several neurological manifestations at onset, even preceding chondral inflammation. The diagnosis of this condition can be quite challenging. Early suspicion and prompt management may prevent disability and mortality, specially when the CNS is compromised. It’s important to include PR with meningoencephalitis in the differential diagnosis of acute meningoencephalitis as suggested by previous studies. More case reviews and research studies are needed to uncover the pathogenesis of RP and its rare neurological involvement.

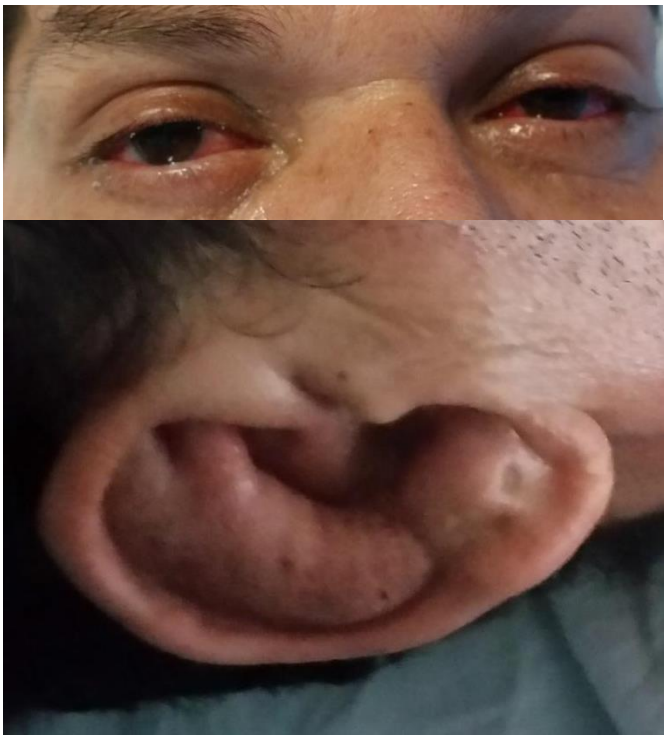

Figure 1.
A. Bilateral red eye syndrome in the patient
B. Inflammation and deformation (cauliflower ear) of the right ear

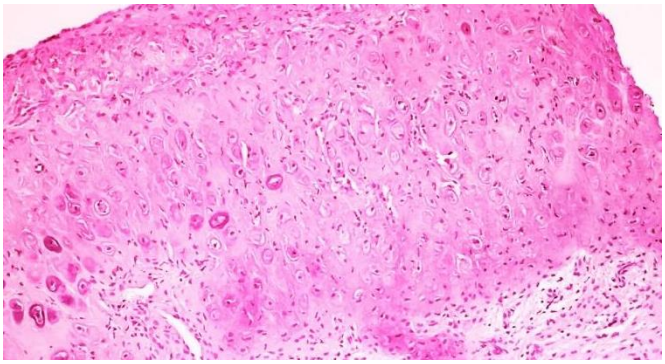

Figure 2. Biopsy sample of the right ear cartilage shows eosinophilia and perichondral inflammation with predominance of neutrophils, as well as degenerative changes and apoptotic cells (hematoxylin and eosin stain x100).

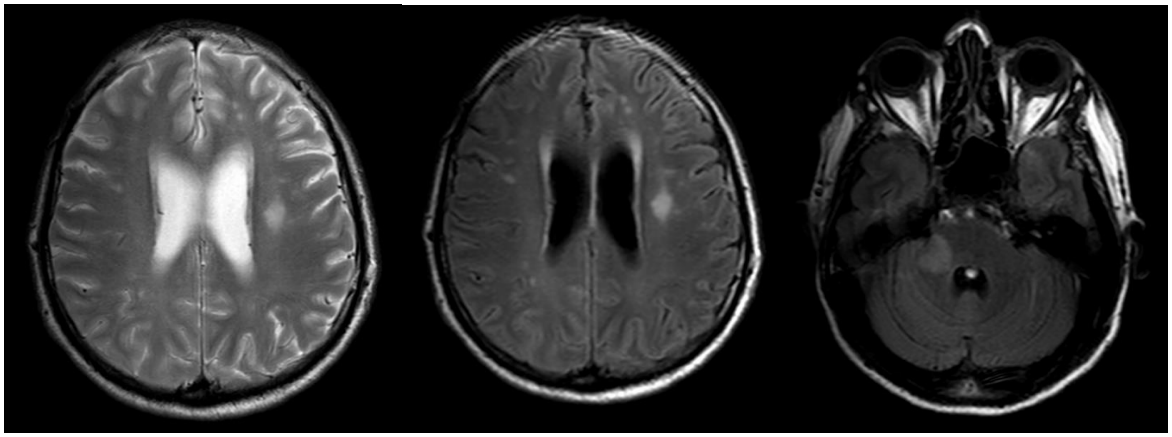

Figure 3. Magnetic resonance imaging of the head showing hyperintense lesions in T2 and FLAIR sequences, homogeneous, with defined borders, in the right cerebellar peduncle and left periventricular region. In addition, the presence of lesions of smaller size were observed in the subcortical matter of the frontal lobe, with a greater right predominance.

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Conflicts of Interest

None.

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