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Recurrent lymphocytic meningitis and progressive dementia: manifestations of relapsing polychondritis: a case report

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Abstract

Background Recurrent polychondritis is an immune-mediated systemic disease that affects cartilaginous and non-cartilaginous structures. Despite being rare, multiple neurological manifestations have been described, such as involvement of cranial nerves; headache; ataxia; seizures; confusional syndromes; meningitis; limbic encephalitis; cerebral infarcts; psychosis; and dementia. We present a case report of patient with atypical manifestation of recurrent polychondritis.

Case presentation A 71-year-old man with history of three episodes of meningitis who was admitted due to headache, walking difficulties, disorientation, loss of sphincter control and prostration. These symptoms were attributed to recurrent lymphocytic meningitis and progressive dementia secondary to relapsing polychondritis with excellent response to treatment with glucocorticoids and methotrexate.

Conclusion The accurate identification of atypical manifestations in relapsing polychondritis is essential for the timely implementation of appropriate therapeutic interventions, thereby enhancing the overall quality of life for individuals affected by this pathology.

Keywords Recurrent polychondritis, Aseptic lymphocytic meningitis, Neurological manifestations, Progressive dementia, Case report

Introduction

Recurrent polychondritis (RP) is an immune-mediated systemic disease primarily affecting cartilaginous and non-cartilaginous, structures rich in proteoglycans [1]. Approximately 80% of patients have auricular chondritis and polyarthritis, disease onset is variable and heterogeneous, with periods of remission and relapse, which can delay the diagnosis by up to 2.9 years [2, 3].

Pathophysiology or Recurrent polychondritis (RP) involves mechanisms of autoimmunity and autoinflammation. Antibodies against types II, IX, and XI collagen; matriline I; and, more rarely, anti-labyrinthine, anti-cornea, and anti-desmin antibodies have been evidenced. Up to 30% of RP cases are associated with autoimmune diseases such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and vasculitis. Additionally, there is an increase in interleukin-8, tumor necrosis factor (TNF), and macrophage inflammatory protein 1B. On histology, a pleomorphic inflammatory infiltrate is identified, with predominance of $CD4^+$ T lymphocytes,

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macrophages, and plasma cells. Inflammation begins in perichondrium and is present in hyaline and elastic cartilage but not in fibrocartilage, which explains the absence of manifestations in intervertebral discs or symphysis. Later, it expands to all cartilage, with predominance of the Th1 response over Th2, activation of cathepsin K, cathepsin L, and matrix metalloproteinase-3 (MMP3) with progressive destruction of the extracellular matrix [4].

Clinically, RP involves (in order of frequency) auricular, nasal, articular, and tracheobronchial cartilage. Characteristic manifestations are cauliflower ear or saddle nose. Complications such as hearing loss (46%) and collapse of the nasal bridge (11%) may occur. Ocular (scleritis, conjunctivitis, uveitis, retinitis), skin, cardiac, blood vessel (for example, infiltration or aortic dilation with aneurysms), renal, or neurological alterations are less frequent. Association of symptoms of Behçet's disease and RP in MAGIC syndrome (mouth and genital ulcers with inflamed cartilage) has been described [1], also hematological manifestations, myelodysplastic syndrome and neutrophilic dermatoses in patients with mutations of gene encoding for ubiquitin activating enzyme 1 causing VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome [5, 6].

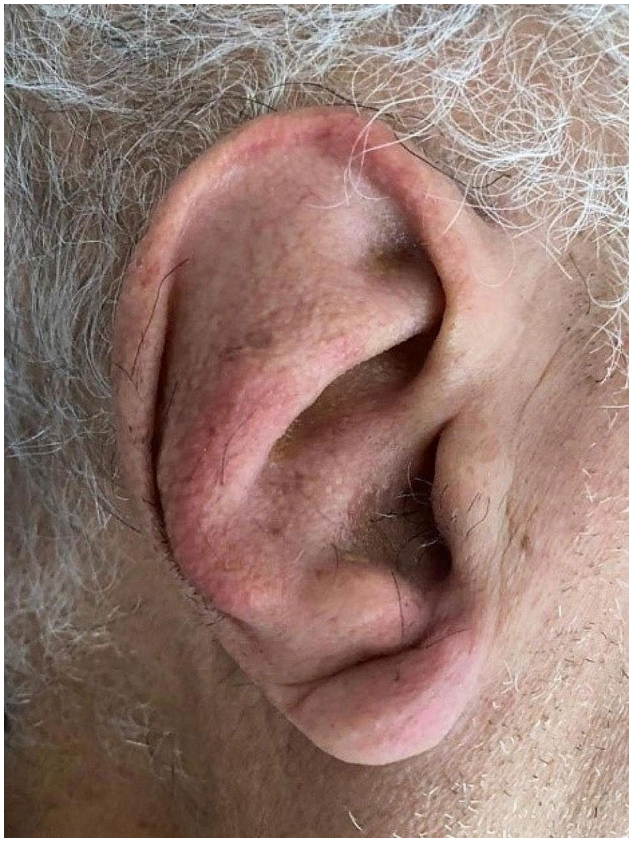

Fig. 1 Auricular alterations in the described patient

Clinical criteria defined by McAdam were related to cartilaginous impairment, modified by Damiani-Levine including histological characteristics and good response to steroids or dapsone and later, Michet added ocular, vestibular and articular manifestations [7]. The Relapsing Polychondritis Disease Activity Index (RPDAI) scale allows to evaluate severity and activity of the disease, considering disease symptoms over 28 days [8]. Survival rates of 95% and 91% at 5 and 10 years, respectively, have been reported in previous series [9]. In this report, we present one case of RP with recurrent episodes of aseptic meningitis and progressive dementia, an atypical neurological manifestation.

Case description

A 71-year-old man with history of three episodes of meningitis (first episode at 58 years of age, with diagnosis of tuberculous meningitis without microbiological confirmation; second and third episodes at 66 and 70 years, respectively, both aseptic lymphocytic meningitis) and secondary progressive cognitive decline, was admitted due to bitemporal and frontal headache with mandibular irradiation, walking difficulties, low-grade fever, disorientation, temporary loss of sphincter control, dependence for activities of daily living and prostration. He had arterial hypertension treated with losartan and at the age of 56, he received a diagnosis of RP, fulfilling Michet's criteria [7], (3 major criteria for auricular, nasal, and laryngotracheal chondritis), without follow-up or treatment for several years.

Upon admission, he was drowsy, his temperature was 100.2 °F, other vital signs were normal, and deformity was observed in the right ear (Fig. 1). Laboratory results were: leukocytes 13,400/μL, neutrophils 10,600/μL, lymphocytes 1,900/μL, hemoglobin 12.4 g/dL, platelets 350,000/μL, increased C-reactive protein (1.14 mg/dL), and erythrocyte sedimentation rate (ESR) 10 mm/h with normal electrolytes. Blood and urine cultures were negative. Contrast brain magnetic resonance imaging (MRI) showed supra- and infratentorial nodular enhancement, increased volume of the supratentorial ventricular system, and foci of subcortical and periventricular nodular enhancement (Fig. 2). Lumbar puncture showed lymphocytic pleocytosis similar to previous episodes of meningitis. Microbiological studies and PCR of cerebrospinal fluid for multiple microorganisms were negative, including herpes viruses (Mollaret meningitis was ruled out). The cytology and flow cytometry of the cerebrospinal fluid were negative for neoplastic infiltration, and there were no suspicious lesions of neoplasia in chest or abdominal tomography.

The patient had antinuclear antibodies 1:160 with homogeneous pattern (AC-1), tests for SLE, RA, vasculitis, sarcoidosis, IgG4-related disease, Sjögren´s

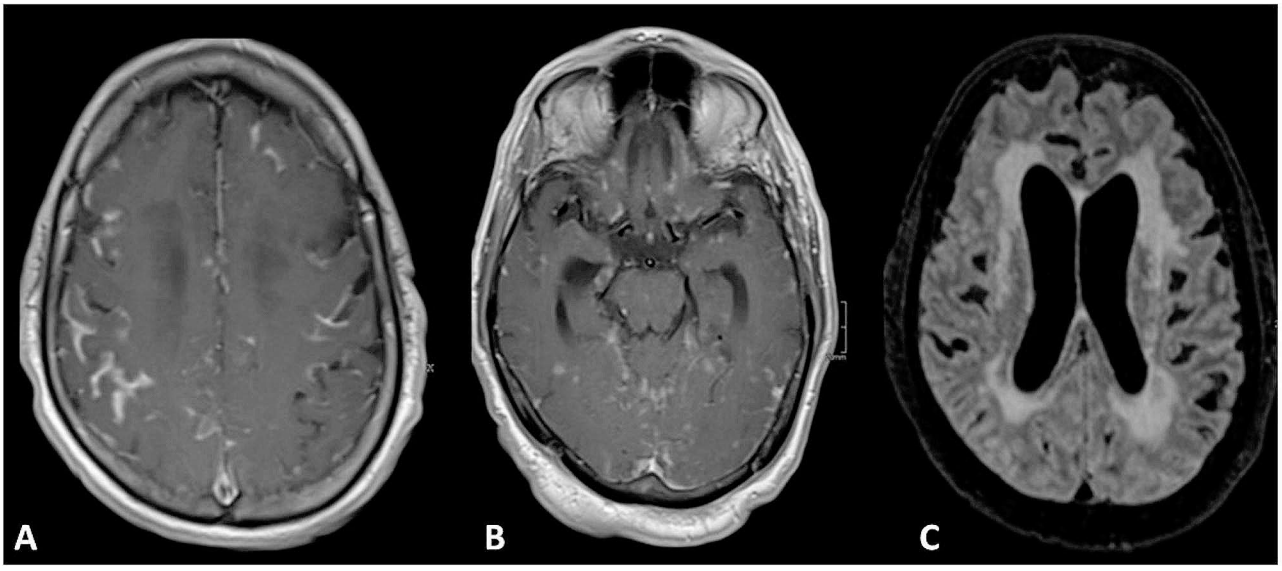

Fig. 2 Axial magnetic resonance imaging (MRI) of the described patient. **A**-**B**: T1-weighted MRI showing supratentorial and infratentorial leptomeningeal and nodular enhancement. **C**: Fluid-attenuated inversion recovery (FLAIR) showing deep white matter hyperintensities and increased volume of the ventricular system

syndrome, among other systemic immune diseases were negative. Studies for autoimmune encephalitis were not available. Aseptic meningitis was considered, and a meningeal biopsy was performed, finding a mild and focal mononuclear infiltrate as well as focal meningothelial hyperplasia. Once infectious, neoplastic, and chemical causes had been ruled out, the episodes of aseptic meningitis were deemed secondary to the baseline RP. Methylprednisolone 500 mg pulses were administered once/day for three days. This markedly improved his neurological symptoms. He continued maintenance with methotrexate and corticosteroid with progressively decreasing doses, showing a good clinical response with resolved headache and improvements in orientation, cognition, and independence for basic activities of daily life.

Discussion

Neurological manifestations of RP are rare, occurring in fewer than 3% of cases [3]. Involvement of the central nervous system (CNS) has highly variable clinical and pathological manifestations [10]. Second, third, fourth, fifth, sixth, seventh and eighth cranial nerves can be involved [3]. Other neurological manifestations are headache, ataxia, seizures, confusional syndromes, meningitis, limbic encephalitis, cerebral infarcts, psychosis, dementia [11, 12], meningoencephalitis, and intracranial aneurysms [12]. We report the case of a 71-year-old man with RP with previous auricular, nasal, and laryngo-tracheal involvement, without regular treatment and with an atypical presentation with neurological symptoms since his 58 years of age.

Aseptic meningitis has been reported in RP mainly in people between their 40s and 70s, with a mean age of 56 years [13, 14]. A review of the literature revealed 19 case reports of RP patients with aseptic meningitis or meningoencephalitis. In China, a case of a woman with RP plus recurrent aseptic meningitis with manifestations similar to those of our patient, was reported [13]. A case of encephalitis associated with antibodies against the glutamate receptor GLuR2 found in cerebrospinal fluid (CSF) and blood has also been reported [11].

According to reported cases of neurological involvement and dementia due to RP, there seem to be two clinical phenotypes, one more systemic, acute and fulminant associated with vasculitis phenomena [15], and other more progressive in which there are other histological manifestations in the CNS, such as lymphocytic infiltration of the meninges or the cortex, neuronal loss, gliosis, edema and infiltrates in the leptomeninges, and nonspecific inflammation [16], as occurred with our patient. This progressive form is associated with less constitutional or systemic symptoms [15]. According to the proposed by Elis et al. [15], there are also atrophic changes in MRI that are also present in other neurodegenerative disorders.

Neurologic syndromes in RP patients do not have unique clinical, laboratory, or neuroimaging findings that point straight to the underlying diagnosis. There should be suspicion of this entity if there are cartilaginous involvement, unexplained neurological findings, anemia of chronic inflammation and elevated ESR or C-reactive protein [12]. Aseptic meningoencephalitis is an extremely rare complication that can be misrecognized as an infection or can be secondary to other

inflammatory disorders. Shen et al., concluded that RP meningitis diagnosis is based mainly on clinical manifestations combined with CSF, MRI and adequate exclusion of infections and other etiologies, such as malignant neoplasms and other autoimmune disorders affecting CNS [13]. In accordance, our patient had history of RP fulfilling Michet's criteria, as well as neurological symptoms associated with elevated C-reactive protein in absence of infectious or other inflammatory conditions that could cause meningitis. CSF pleocytosis has been described as a hallmark of RP meningitis, literature describes a predominance of polymorphonuclear cells or mononuclear cells [13], in our case, the CSF showed predominance of lymphocytes. This was similar to that found in patients with meningoencephalitis and dementia [16, 17].

There are no guidelines for RP treatment, immunosuppressants are selected based on previous literature, severity, comorbidities, and organ involvement. Minor nasal, auricular or joint involvement may respond to glucocorticoids, colchicine or dapsone [5]. RP patients who do not respond to first-line treatment or more severe forms, can receive TNF inhibitors, tocilizumab, abatacept, cyclophosphamide, azathioprine, or methotrexate alone or in combination with dapsone and/or steroid. Rituximab and mycophenolate mofetil also have been used [5, 15]. Petitdemange et al., performed a systematic review reporting better response rates with abatacept, tocilizumab, TNF inhibitors and methotrexate: 72%, 66%, 64% and 56%, respectively. Abatacept was related to worsening of respiratory and neurological disease [5] As in the case of our patient, previous case reports have demonstrated that patients with neurological manifestations receiving methylprednisolone pulses in variable doses ranging from 250 to 1000 mg/day and combination with other immunosuppressants have favorable clinical outcomes [6, 18].

According to Shen et al., patients with meningitis and RP have a high rate of response to steroids, high frequency of recurrence and choice of treatment should be individualized [13]. Risk factors for recurrence could be tracheal involvement, high pretreatment C-reactive protein, and monotherapy with prednisolone [19]. Our patient had history of tracheal involvement (with no sequelae, current symptoms or treatment) and elevated CRP, however, neurological symptoms, including cognitive decline, improved rapidly with glucocorticoid pulse; considering excellent steroid response and absence of severe systemic involvement, methotrexate was used for maintenance therapy, the improvement was sustained in follow-ups over several months and to date. It is possible that progressive onset without systemic compromise may respond better to methotrexate than more severe forms of neurological RP.

The accurate recognition of atypical manifestations in RP facilitates the prompt diagnosis of the condition and its potential complications. This timely identification enables the implementation of appropriate therapeutic measures, ultimately contributing to the enhancement of the patients' quality of life.

Limitations

Specific test for autoimmune encephalitis antibodies were not available for differential diagnosis. As this is a case report, the information may not be generalizable to all patients diagnosed with RP. This is an infrequent disease, and its neurological manifestations are even more rare. The rarity of the disease limits conducting studies with large numbers of patients in order to establish more generalized recommendations and to date, there are no evidence based guidelines for treatment of RP or its CNS involvement, this is still a gap in knowledge to address through more studies. There is a lack of information about evolution of these patients in time, another aspect to take into account in future research.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12883-024-03657-5.

Supplementary Material 1

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Author contributions
VOP, DAV, and AHJ conceived the idea for the study. VOP, DAV, TDM and AHJ contributed substantially to the acquisition of data and the writing and critical review of the manuscript and approved its submission.

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Data availability
The dataset used and/or analyzed for the publication of this article is not publicly available in order to safeguard patient confidentiality.

Declarations

Ethics approval and consent to participate
This case report complies with current regulations on bioethical research. It was also approved by the Biomedical Research Ethics Committee of the Fundación Valle del Lili. The authors obtained written informed consent for the use of data and images from the patient described in this case report.

Consent for publication
The authors obtained informed written consent for the use of data and images from the patient described in this case report.

Conflict of interest
All authors declare that they have no conflicts of interest about the preparation of this article.

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