

Case Report

Nonparaneoplastic Limbic Encephalitis in a Patient with Relapsing Polychondritis

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Submitted: 20 January 2014

Accepted: 24 February 2014

Published: 03 March 2014

ISSN: 2333-7087

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Abstract

Relapsing polychondritis is a rare immune mediated systemic disorder which destroys cartilaginous structures such as the auricles, eyes, nose, joints and other parts of the body. Many cases of relapsing polychondritis are associated with other systemic autoimmune diseases particularly various vasculitides. Neurological involvement is rare and the pathogenesis is currently unknown. We present a case of a patient with diagnosed polychondritis who presented with memory disturbance and MRI revealed bitemporal signal change. Workup was negative for infection, malignancy, or paraneoplastic antibodies. Treatment with high-dose steroids resulted in improvement in symptoms.

Keywords

- Limbic encephalitis
- Polychondritis
- Paraneoplastic

ABBREVIATIONS

RPC: Relapsing Polychondritis; CSF: Cerebrospinal Fluid; EEG: Electroencephalogram

INTRODUCTION

Relapsing Polychondritis (RPC) is a systemic disorder, thought to be immune-mediated which results in inflammation and destruction of cartilaginous structures. The diagnosis is established via clinical findings and can be supported with biopsy. Auricular inflammation is the most common presenting feature but can involve many other structures throughout the body such as eyes, nose, large airways, joints, heart valves, kidneys [1]. Nervous system involvement is a rare manifestation of the disease. There are case reports of cranial nerve abnormalities [2,3], rhombencephalitis [4], meningoencephalitis [5], and limbic encephalitis [6,7]. The etiology of polychondritis is unknown but is hypothesized to begin with an unknown insult to connective tissue or cell membrane epitopes leading to an inflammatory response in people with genetic susceptibility. The pathogenesis of neurologic sequelae is speculated to be due to vasculitis. Approximately one third of RPC cases occur in association with another systemic autoimmune disease including vasculitis and can involve large, medium and small vessels. We describe a case of a patient with recently diagnosed polychondritis who presented with memory problems and was found to have limbic encephalitis.

CASE PRESENTATION

39yo M presented to the emergency department of our hospital

with bilateral ear pain, eye pain and throat pain for a period of several months. He was given a diagnosis of polychondritis at an outside hospital. Patient was also complaining of intermittent memory loss which had been going on for several months. He reported forgetting conversations, appointments, asking the same question over and over again etc. On exam was noted to have mildly erythematous bulbar conjunctiva, thickened auricular cartilage bilaterally with the R being slightly distorted. Initial neurologic exam did not reveal any deficits. Patient was fully oriented and had no obvious cognitive deficits. However, a more detailed inquiry revealed that he had poor memory and recognition of iconic famous historic events. He was afebrile and vitals were stable. Lab work on admission was significant for mild leukocytosis of 13, and ESR of 30.

MRI Brain was done and showed T2 FLAIR hyperintensities involving bilateral hippocampi and occipital lobes that did not enhance with gadolinium. Lumbar puncture was done and CSF revealed; glucose of 52, protein 56, WBCs 46 with lymphocytic predominance and negative cultures. The patient was started on acyclovir but shortly after CSF viral PCR came back negative and acyclovir was discontinued. CSF IgG, IgG index and IgG synth rate were all elevated at 16.5, 2.01 and 59.5 respectively. There were no oligoclonal bands. CSF was negative for mycobacteria, VDRL, and west nile virus. CSF ACE was elevated at 55. CSF cytology and NMDA antibody was negative. Serum labwork included ANA, dsDNA, SSA, SSB, anti-smith antibody all of which were negative. Serum ACE was wnl. Anti-mitochondrial and anti-thyroglobulin antibodies were negative. Paraneoplastic antibody screen was negative. CT chest, abdomen and pelvis did not

reveal any malignancy. EEG was done and revealed bitemporal sharp waves. The patient was started on twice daily solumedrol 500mg IV. He received a total of three days of treatment with significant improvement in his ear pain, eye and throat pain. The patient reported that he felt that his thinking was clearer; however examination revealed that he was still having difficulty remembering important events. The patient was discharged with prednisone 60mg daily to take for one month followed by a taper. He was also started on keppra 500mg BID.

DISCUSSION

Relapsing polychondritis is a rare inflammatory, systemic disease, which can rarely manifest with neurologic complications. It involves cartilaginous structures of the body particularly the ears, eyes, joints and the respiratory tract. There are no known laboratory parameters specific to the disease and the diagnosis is made clinically via McAdam's criteria requiring the presence of three or more of the following features; bilateral auricular chondritis, nonerosive inflammatory polyarthritis, nasal chondritis, ocular inflammation, respiratory tract chondritis, and cochlear and/or vestibular dysfunction [1]. A biopsy can be used to confirm the diagnosis which shows perichondral infiltration by lymphocytes consisting of macrophages, polymorphonuclear cells and plasma cells, and eventual destruction of cartilage by the granulation tissue [1]. The hypothesized mechanism of RPC is an unknown insult which results in exposure of connective tissue leading to an inflammatory and immune response both humoral and cell mediated. Genetic susceptibility has been suggested due to association between RPC and certain HLA alleles.

Neurologic involvement of RPC is rare but has been reported in the literature. Most common neurologic manifestation is cranial nerve abnormalities such as trigeminal neuralgia [3], seventh nerve palsy [2], and optic neuropathy [8]. Ohta et al presented a case similar to ours of limbic encephalitis in a 57yo male who presented with symptoms diagnostic of RPC (eventually confirmed via biopsy) as well as headache and vertigo. CSF revealed pleocytosis with lymphocytic predominance and mildly elevated protein. All viral, bacterial and paraneoplastic studies were negative. About two months later the patient developed memory disturbances. Similar to our patient, his MRI revealed FLAIR hyperintensities in bilateral hippocampi. He also had lesions in several other areas, some of which enhanced with gadolinium. The patient was treated with IV methylprednisolone followed by daily oral prednisone with resolution of all his symptoms including memory loss [6]. Several other cases have been described where patients presented with various nonspecific neurological symptoms including headaches, diplopia, vertigo, memory and cognitive problems. Rhomboencephalitis [4] and meningoencephalitis [5] have been reported as well as limbic encephalitis [6,7]. Imaging typically reveals nonspecific white matter changes with involvement of the medial temporal lobes. As with our patient CSF studies tend to be similar to that of a viral infection with a pleocytosis with lymphocytic predominance and mildly elevated protein. Although there is a report of CSF findings resembling a bacterial infection with negative cultures [4]. CSF IgG index and synthesis tend to be elevated when reported. In all cases extensive workup for infectious and paraneoplastic causes is unrevealing. EEG

when done is normal⁵ or shows diffuse slowing [6,8]. Our patient had bitemporal sharp waves on his EEG. Most reported cases are successfully treated with corticosteroids either IV plus PO, or PO only. However, Erten-Lyons et al. present a case of a 51yo patient with RPC who continued to experience a progressive cognitive decline refractory to prednisone and cyclophosphamide and eventually died about ten months after the onset of neurological symptoms. Interestingly the patients CSF Tau/Amyloid levels and ratio were consistent with alzheimers disease [5]. Storey et al. describe a case of a 73yo M with a history of seropositive myasthenia gravis who developed symptoms of polychondritis and confusion. Patient was found to have limbic encephalitis on imaging and CSF with mildly elevated protein and pleocytosis. Despite several courses of high dose IV methylprednisolone , plasmapheresis and IVIG the patient's cognition worsened and he passed away five months after the onset of symptoms due to bronchopneumonia [7].

Patient s with limbic encephalitis present with short-term memory impairment, psychiatric symptoms, confusion and general cognitive decline. Complex partial seizures have also been reported. MRI findings include signal change in the mesial temporal lobes. Limbic encephalitis is frequently associated with malignancy (paraneoplastic) particularly SCLC, thymoma and germ cell tumor [9]. Associated antibodies include: anti-Hu, anti-ma2, CRMP5, amphiphysin, NMDAR, GAD, and VGKC. There are reports of antibody positivity in patients with no malignancy, particularly VGKC, NMDAR and GAD antibodies. However in one study 24% of nonparaneoplastic limbic encephalitis cases had no known antibodies and 20% of all limbic encephalitis cases had a novel antigen [10].

The mechanism of the neurologic sequelae RPC has been speculated to be a result of a vasculitic process of the central nervous system although there are only a few case reports that describe histopathological findings. The autopsy of the patient reported by Erten-Lyons et al. confirmed non-specific meningoencephalitis involving the meninges, cortical and deep parenchyma but no evidence of vasculitis [5]. The patient from Storey et al. had autopsy findings which showed nonspecific inflammation of the meninges as well as grey and white matter but no vasculitis [7]. However cerebral and meningeal vasculitis has been reported in autopsied cases of RPC [11]. All types of vasculitis have been reported in association with RPC; polyarteritis nodosa, granulomatosis with polyangiitis, microscopic polyangiitis, Behcet's disease, Henoch-Schonlein purpura, Cogan's syndrome, thromboangiitis obliterans, cutaneous leukocytoclastic angiitis. In fact, many of the clinical features are shared between RPC and granulomatosis with polyangiitis such as saddle nose deformity, episcleritis and laryngotracheal involvement [13].

Cerebral vasculitis has been proposed many times as the mechanism of encephalitis, meningitis and meningoencephalitis in cases of RPC. There is currently not enough evidence to definitively confirm that hypothesis. The frequent co-existence of RPC and vasculitis as well as other systemic autoimmune diseases represents a predisposition to autoimmune disease. Therefore one must consider the possibility of an autoimmune etiology involving the CNS that targets the brain and meninges unrelated to vasculitis. However, in all cases referenced in this

paper where a battery of antibodies was sent, the serology was negative. Perhaps the antigen responsible for nervous system pathology in RPC is yet to be discovered.

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Cite this article

Litvinsky N, Wichter MD (2014) Nonparaneoplastic Limbic Encephalitis in a Patient with Relapsing Polychondritis. *J Neurol Transl Neurosci* 2(2): 1053.