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RELAPSING POLYCHONDritis: AN UNCOMMON CAUSE OF DEMENTIA

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Keywords

Relapsing polychondritis; dementia; encephalopathy; inflammatory meningoencephalitis

Relapsing polychondritis (RP) is a rare disorder characterized by recurrent and progressive inflammation of cartilaginous structures. [1] Nervous system involvement in RP has been described [1, 2, 3,4,5]. We describe two cases of RP with subacute dementia.

Case 1

A 51 year-old lawyer was diagnosed with RP when he presented with bilateral ear swelling. He was treated with 10mg of oral prednisone during this attack with a brief taper. He continued to have flare ups during the next several years treated with short duration of prednisone ranging from 10–40mg/day. Episodes of iritis and scleritis were treated with steroid eye drops. One year after the diagnosis of RP he started experiencing gradual onset coordination problems, difficulty presenting verbal arguments, distractibility and emotional lability. He developed insomnia and nocturnal myoclonic jerks.

Neuropsychological evaluation showed perseveration, prominent attention and concentration deficits. Brain MRI showed extensive periventricular and deep white matter high signal abnormalities. There was reduced metabolic activity in bilateral temporal cortex and parietal lobes on PET scan. Electroencephalogram was normal. Cerebrospinal fluid (CSF) contained 89 mg/dL of protein, 52 mg/dL glucose, 39 white blood cells (WBC) (65% lymphocytes) and 2 red blood cells. CSF Tau/Amyloid levels and ratio were considered consistent with Alzheimer's disease. CSF IgG index and synthesis rate were elevated. CSF14-3-3 protein, borrelia PCR, cryptococcal antigen, paraneoplastic titers, serum HIV serology, VDRL, heavy metal screen, p and c-ANCA, RPR were negative. HSV 1/2 IGG antibody was mildly elevated, IgM was negative. Serum WBC, sedimentation rate and C-reactive protein (CRP) were normal during the course of his progressive dementia. Cerebral angiogram was normal. Given lack of a diagnosis after non-invasive investigations, brain biopsy of right frontal cortex was performed 5 months after the onset of neurological symptoms. Biopsy showed findings consistent with non-specific inflammation without evidence of vasculitis. (Supplemental figure 1) A diagnosis of meningoencephalitis secondary to RP was made. Prednisone was increased up to 80 mg/day without clinical improvement. Cyclophosphamide was added at 150 mg/day 6 months after onset of neurological

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symptoms. He continued to decline, with increased confusion, speech latency, word-finding difficulty, and increased myoclonus. He died 5 months after brain biopsy. Autopsy confirmed diagnosis of non-specific meningoencephalitis involving the meninges, cortical and deep brain parenchyma. There was no evidence of vasculitis. Microglial nodules suggestive of viral encephalitis and protease-resistant prion protein were absent.

Case 2

A 68 year-old college instructor presented with myalgias, headache, fever, bilateral ear swelling and diagnosed with RP. He was started on low dosage of prednisone, which was discontinued due to side effects. Two months later he developed hoarse voice and vertigo, recurrence of ear swelling and was started on dapsone. Around the same time, he started exhibiting comprehension problems, emotional lability and visuospatial problems. During the course of his illness he had flare-ups of ear swelling. He also developed conjunctival involvement and a 30-pound weight loss. Over a course of 8 months, he gradually continued to decline cognitively to a degree where he was unable to do his day-to-day activities independently. He also had 2 discrete episodes of worsening confusion and language problems lasting several hours.

Neuropsychological testing showed impairment in verbal and visual memory, executive dysfunction, visuospatial impairment and mild anomia. CSF contained 49 mg/dl protein, 4 WBCs (44% lymphocytes), 124 RBCs and 39 mg/dL glucose. CSF fungal, viral and bacterial cultures, cryptococcal antigen, VDRL, angiotensin converting enzyme, stain and culture for acid fast bacilli were negative. Serum lyme titers, VDRL, paraneoplastic markers, anti ss-DNA, anti ds-DNA, anti-ENA, anti SSA, anti SSB antibodies, HIV, treponemal antibody, serological markers for Sjorgen's disease, SLE and Wegener's were negative. Sedimentation rates ranged from 9–15 mm/hr, and CRP was 0.2 mg/L. Brain MRI at the onset of his symptoms was normal. MRI at 5 months after symptom onset showed edema and high T2 signal in the right medial temporal lobe and a small area of enhancement in the left caudate with contrast administration. Repeat brain MRI 1 month later (6 months after onset of neurological symptoms) showed resolution of temporal lobe edema and caudate enhancement, increased T2 signal in both caudate heads and the right medial temporal lobe with atrophy. (Supplemental figure 2) Electroencephalogram showed bilateral low amplitude with beta frequency. He was diagnosed with CNS involvement of RP without brain biopsy and started on 80mg of prednisone 11 months after the onset of neurological symptoms with no further deterioration over a 12-month follow-up.

Both patients meet diagnostic criteria for RP. [1] Central nervous system (CNS) involvement has been attributed either to vasculitis or meningoencephalitis. [1,2,3] Only a few case reports describe histopathological findings in CNS involvement in RP. (Supplemental Table 1)

Dementia and limbic encephalitis have been reported. [3–5] Imaging findings of nonspecific white matter changes, preferential involvement of the medial temporal lobes and brain atrophy have been reported. [3–5] Cerebrospinal fluid may show inflammatory changes. [2–5]

The pathophysiology of CNS involvement in RP is not well understood. Diagnosis and treatment are not well established. Diagnosis may be delayed when patients present with CSN symptoms while on immunosuppressants for systemic disease and opportunistic infections are in the differential. To rule out steroid contraindications, a CSF examination to exclude bacterial, fungal, or TB meningitis and brain MRI to rule out ring enhancing lesions should be adequate. Empiric treatment for herpes encephalitis can be initiated early while awaiting PCR diagnosis. Brain biopsy and cerebral angiogram seem to provide minimal

diagnostic information in most cases. Steroids or cytotoxic agents have been used for treatment, while response to treatment is not consistent and relapses off of medications have been reported. [2,3] Greater awareness of the existence of a polychondritis-associated encephalitis may spare patients the morbidity of brain biopsy, and may also lead to prompt and aggressive immunosuppressant therapy, which may reduce morbidity and mortality.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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