A case of Glial fibrillary acidotic protein (GFAP) meningoencephalitis with Rheumatoid Arthritis

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Abstract

The reported case is a 53-year-old woman with the history of long-standing rheumatoid arthritis who first presented with acute-onset dizziness and gait disturbance, periventricular linear and radial enhancement pattern on MRI and normal CSF analysis, successfully treated with an increase in the dose of oral steroids.

Introduction:

Autoimmune glial fibrillary acidic protein (GFAP) astrocytopathy is an inflammatory disease of the central nervous system (CNS). It can affect optic nerve, cerebral and cerebellar white matter, cortex, spinal cord and meninges producing a wide spectrum of clinical manifestations. Meningoencephalitis is the most common clinical presentation. Diagnosis is confirmed by the presence of CSF immunoglobulin-G (IgG) against GFAP, an intracellular astrocytic intermediate filament protein.(1)

Common clinical presentation includes encephalopathy, psychiatric disorders, tremor, ataxia, seizures, myelopathy, and meningitis. (2,3)

This disorder is equally common in both men and women.(4) Association with other autoimmune disorders like autoimmune thyroid disease, Type-1 diabetes mellitus, and rheumatoid arthritis is seen in about 20% of the cases. (3) Neoplasm is found in about 25% of cases, most common being ovarian teratoma. (3)

Brain imaging studies reveal a characteristic pattern of linear and radial perivascular enhancement in the cerebral white matter, originating from GFAP-enriched periventricular areas. Occasionally a similar pattern of radial enhancement is seen in the cerebellum. (3,5) CSF analysis invariably shows distinct inflammatory changes. (3) An extensive inflammation is seen around microvessels in pathological studies, which is in correlation with the radial inflammatory changes seen in brain MRI. (6) Here we report a case of GFAP associated meningo-encephalitis in a case of rheumatoid arthritis.

Case report:

A 53-year-old Iranian woman was visited in neurology clinic with a history of acute onset dizziness and gait disturbance for 1 week. There was no history of ear discharge, fullness, tinnitus or hearing loss. She gave

a history of long-standing rheumatoid arthritis and was on low dose maintenance corticosteroid therapy. Physical examination revealed normal higher mental functions, speech and cranial nerves. There was no nystagmus, and saccades and pursuit were normal. Head impulse test was normal. Gait examination showed wide base, ataxic gait with difficulty in doing tandem walk. No dysmetria was seen in upper limbs. Rest of the neurological exam was normal. Brain MRI showed periventricular linear and radial enhancement pattern. CSF analysis including protein, glucose, WBC, ADA, ACE, VDRL, and cytology were normal. She was treated with an increase in the dose of oral steroids and all her symptoms improved in few days.

After a year she once again presented with a subacute onset, moderate to severe holocephalic headache. There was no papilledema and her neurological examination was normal. This time again she responded to an increase in the dose of oral steroids. A year later, for the third time she presented with rapid cognitive decline and gait unsteadiness. This time she had gaze evoked nystagmus and ataxic wide base gait on physical exam. Brain MRI with contrast was repeated which showed bilateral diffuse, pachymeningeal and leptomeningeal enhancement (Figure 1). CSF examination was once again normal. Her work up for infective causes including tuberculosis was negative. According to her Brain MRI imaging with relapsing remitting course steroid responsive ataxia and aseptic meningitis, a clinical decision was made to send her serum for GFAP IgG antibodies, which came back as positive.

Discussion:

Autoimmune glial fibrillary acidic protein (GFAP) astrocytopathy, is a recently described clinical entity presenting with aseptic meningitis and a variety of neurological manifestations. It is a relatively new addition to an ever-increasing list of autoimmune cerebellar ataxia syndromes. it is defined by the presence of GFAP IgG in serum and CSF which shows a similar pattern of immuno-florescence like AQP4 antibody binding to pial and subpial astrocytes. (1)

Autoimmune glial fibrillary acidic protein (GFAP) astrocytopathy can appear with other autoimmune diseases, systemic infections or as a para-neoplastic disorder. (3,4,6) Many other antibodies including NMDAR-IgG, AQP4-IgG, antinuclear, anti -endothelial cell, anti -cardiolipin, anti -neutrophil cytoplasmic and anti -double -stranded DNA can be found in serum of patients with GFAP astrocytopathy.(7) 30–40% of patients may have symptoms of systemic infection before the onset of CNS manifestations. (3) Some patients develop the disorders after Herpes Simplex type 1 or Varicella zoster viral infections.(8,9) Our case also had a history of long-standing rheumatoid arthritis. In a previously published case series of 22 patients with GFAP associated syndrome, three subjects had coexisting rheumatoid arthritis. GFAP has also been identified as an auto-antigen in the synovial fluid of patients with RA. (10) Pachymeningitis in GFAP astrocytopathy has never been reported before but can rarely be seen in long standing rheumatoid arthritis.

Clinical symptoms in our case responded very well to oral steroids. Most of the cases show rapid clinical and radiological improvements upon starting corticosteroids with 20–50% of patients having relapsing course requiring more prolonged therapy. (3,7,8,11,12) Prognosis varies but is good with appropriate treatment in most of the cases. (2,13)

Conclusion:

This case highlights the co-occurrence of rheumatoid arthritis with GFAP associated astrocytopathy, and expands on the previously reported cases with similar association. This might also suggest a common immune pathogenesis.

Abbreviations:

GFAP: Autoimmune glial fibrillary acidic protein

CNS: central nervous system

CSF: cerebrospinal fluid

IgG: immunoglobulin-G

AQP4: aquaporin-4

NMDAR: N-methyl-D-aspartate receptor

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Figure Legends:

Figure 1: Sagittal and axial T1-weighted post gadolinium brain MRI showed bilateral diffuse, pachymeningeal and leptomeningeal enhancement.

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