Case Presentation

Dual Diagnosis: Rheumatoid Arthritis and Multiple Sclerosis

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Juvenile rheumatoid arthritis (JRA) is the most common rheumatologic disease in children. Moreover, multiple sclerosis (MS) is the most frequent demyelinating disease and has been associated with various chronic inflammatory diseases. However, its association with JRA has not been frequently described. Autoimmunity in both JRA and MS has been documented in the scientific literature, although there has been no definitive finding that patients with JRA are prone to the development of MS. An increasing frequency of MS resulting from an increased use of antitumor necrosis factor agents in the treatment of rheumatoid arthritis and other chronic inflammatory diseases has been reported recently. In this study, we report on the development of MS in a patient with JRA who did not have a history of antitumor necrosis factor use.

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INTRODUCTION

Juvenile rheumatoid arthritis (JRA) and multiple sclerosis (MS), which are both autoimmune disorders, can be associated with various autoimmune diseases, but the association of both diseases in the same patient has been reported very rarely. To the best of our knowledge, only 2 such cases have been published previously [1,2]. The likelihood of developing JRA and MS is influenced by largely unidentified genetic and environmental factors. The increasing frequency of MS as a result of increased use of antitumor necrosis factor (anti-TNF) agents used for the treatment of JRA and other chronic inflammatory diseases has been reported in recent publications. In this study, we report on the development of MS in a patient with JRA who did not have a history of anti-TNF use.

CASE REPORT

A 35-year-old woman presented to our neurology outpatient clinic with a report of weakness and numbness in her left leg. One year earlier, the patient had extensive numbness of the lower extremities of 2 weeks' duration. She was given vitamin B12 when it was observed at an outside clinic that she had a deficiency of this vitamin. The symptoms disappeared after she took the vitamin B12 supplement. Findings of a current neurologic examination revealed a motor power of 4/5 in the muscles of the left lower extremity, including the strength of the iliopsoas, quadriceps, hamstring, tibialis anterior, and gastrocnemius muscles. Extensive hypoesthesia was present in the left leg. The patient did not have Lhermitte's sign. Deep tendon reflexes were normo-active in both the upper and lower extremities. A pathologic reflex was not observed.

The patient's history was remarkable for the presence of JRA, which was diagnosed when she was 6 years old. She had no family history of MS or JRA, but an aunt had been diagnosed with Behçet disease. The patient reported limited movements in the hip and wrists, and radiographs exhibited arthritic changes in the bilateral hand joints and especially in the right hip joint (Figure 1). The patient used methotrexate, 5-acetylsalicylic acid agents, and intermittent corticosteroids during disease flare-ups. She did not have regular follow-up visits because of her unwillingness to use medicine.

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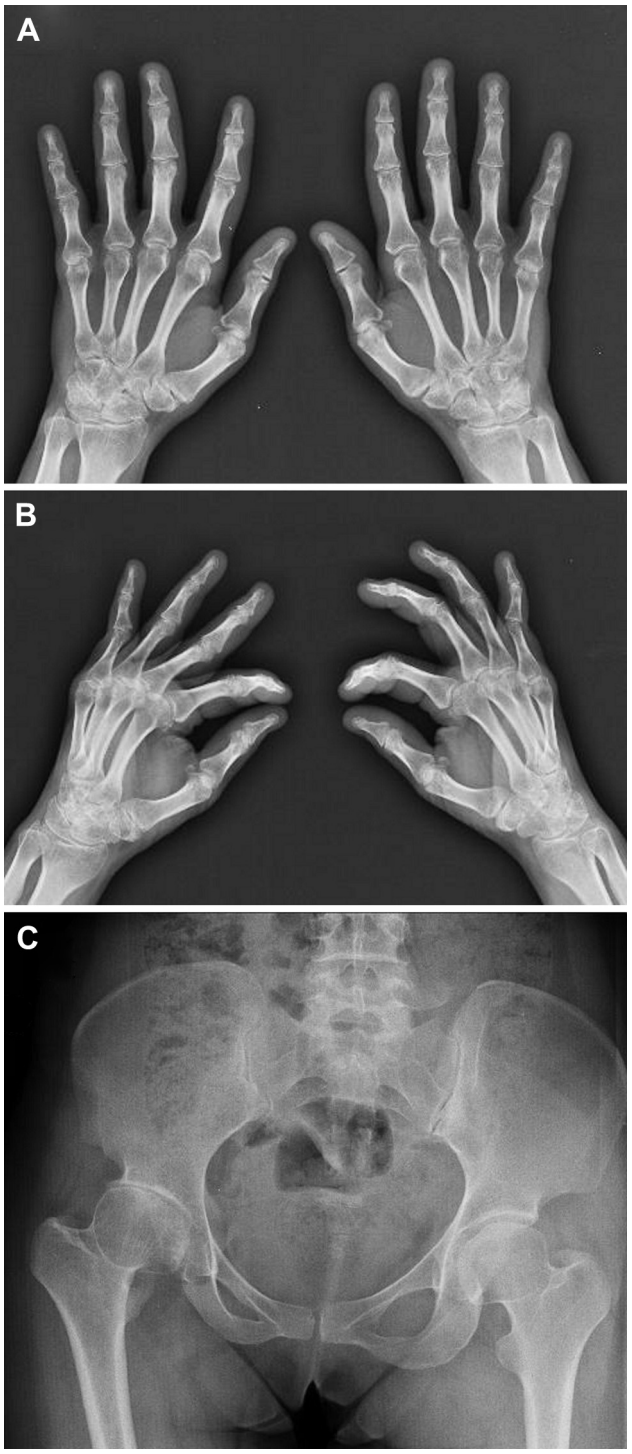

Figure 1. Radiographs of the hands (A, B) show irregularity and sclerosis of the articular surface at the bilateral intercarpal line. A radiograph of the pelvis (C) shows a flattened bilateral femoral head and a narrowed right hip joint. In addition, minimal narrowing of the left sacroiliac joint and increased sclerotic changes in the sacrum and iliac bone are noted.

Magnetic resonance imaging showed that the patient had intracerebral plaques, a finding consistent with MS (Figure 2). A lumbar puncture revealed oligoclonal bands in the cerebrospinal fluid (CSF). The index for immunoglobulin G in the CSF was found to be 0.53 (2.50 mg/dL). The test for antinuclear antibodies was negative. The findings of a complete blood cell count and biochemistry were within normal limits. Findings from the assessment of bilateral visual-evoked potentials were normal. The patient was diagnosed with MS according to the McDonald criteria. She was prescribed 1000 mg of methylprednisolone for 5 days. The severity of the weakness and numbness in the left lower extremity dramatically decreased by the end of the fifth day of treatment. Interferon-beta-1a was prescribed for maintenance treatment. One month after beginning treatment, the motor power of all affected muscles had been recovered, and the numbness was gone. The patient had no recurrent symptoms during the next 12 months.

DISCUSSION

MS is a common autoimmune inflammatory demyelinating disease of the central nervous system (CNS). The incidence of MS increases in the third and fourth decades of life, and it affects female patients twice as often as male patients. MS is characterized clinically by the involvement of different parts of the CNS, which can cause different symptoms.

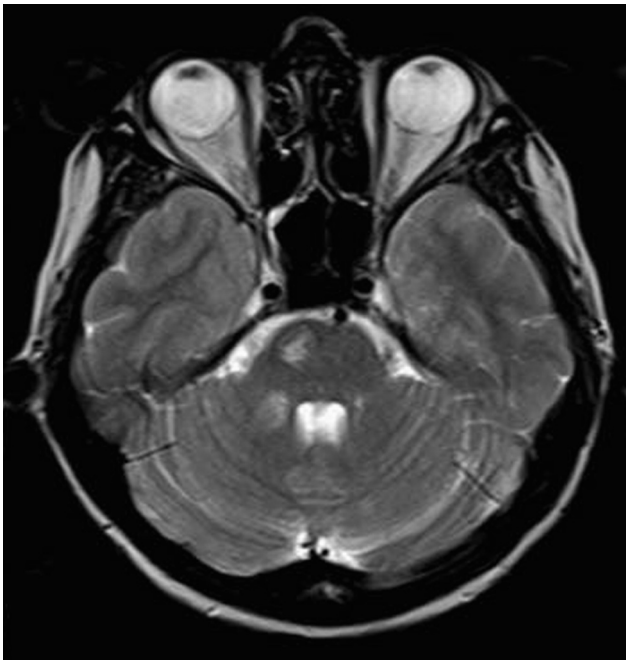

Figure 2. T2-weighted magnetic resonance imaging reveals hyperintense lesions at the right side of the pons and cerebellar peduncle.

Pathologically, MS is characterized by demyelination in multifocal areas, loss of oligodendrocytes, and astroglial scarring. Axonal injury was recently defined as a salient feature of this autoimmune disease [3]. Although MS has typical clinical features, the disease can progress at quite a different rate in different patients and has many atypical forms. The etiopathogenesis of MS is unknown, but the most widely accepted theory is that MS begins from autoreactive lymphocytes after a combination of genetic, hormonal, and environmental triggers [4].

JRA is the most common rheumatologic disease in children younger than 16 years. The etiology of JRA, like that of MS, is largely unknown, but genetic susceptibility, autoimmunity, infections, and environmental factors are thought to be important in the etiopathogenesis of JRA [5]. Cases of JRA with other autoimmune disorders, including Hashimoto thyroiditis, insulin-dependent diabetes mellitus, autoimmune oophoritis, and vitiligo have been reported [5]. Some researchers have pointed out an increased prevalence of other autoimmune disorders among relatives of patients with JRA [6].

The concurrence of JRA and MS has not been described frequently. Only 2 case reports have previously been published [1,2]. Moreover, no conclusive research has shown that patients with JRA are prone to the development of MS. In one study, researchers reported that MS developed in 1 of 332 patients who were given TNF-α blocker [7]. Our patient, who did not have regular follow-up visits, did not have a history of TNF-α blocker use. The coincidence of a neurologic disease and inflammatory arthritis may increase disability, psychological disturbances, and changes in quality of life [8]. Some studies have revealed that arthritis of the nonparalyzed side occurs more often than that of the paralyzed side in patients with hemiplegia [9]. Although this mechanism has not yet been thoroughly explained, control of the inflammatory process may occur via the CNS. According to some authors, it is conceivable that MS may reduce the incidence of arthritis by regulating the release of inflammatory mediators [8].

A number of studies have focused on the association of MS and RA. In one study, it was reported that 5 of 155 patients with RA were diagnosed with MS [10]. In contrast, in one study, the prevalence of RA was not found to be increased in 5296 patients with MS [11]. In a recent study, 14 patients with a codiagnosis of MS and RA were evaluated, and investigators found that in 3 cases, the diagnosis of RA was determined before the diagnosis of MS; in contrast, in 11 cases, RA was diagnosed after MS [8]. A patient diagnosed with JRA at the age of 6 years was diagnosed with MS in the follow-up in this study, as in our case.

A possible mechanism of the co-occurrence of the 2 diseases has not yet been clearly explained. One hypothesis is that high disease activity and/or high TNF-α levels in patients with RA could promote neurologic lesions. Neurologic events could also be brought about during TNF-α blocker treatment by latent neurologic disease unmasked by treatment or by pre-existing neurologic disease [8,12].

The description of neurologic events in patients with RA who are taking TNF-α blockers has led to some speculation regarding the causal relationship between neurologic signs and anti-TNF therapy [8]. In a report by Mohan et al [13], patients with progressive MS had high levels of TNF-α in their CSF, and thus increased TNF-α levels in the CNS were suggested to be correlated with disease severity. In contrast, the administration of anti-TNF-α in patients with MS has not been successful and has tended to increase MS attacks [8,12]. It has also been reported in recent years that increased use of anti-TNF-α in patients with RA is closely related to an increased prevalence of MS [8].

Autoimmunity in MS is well demonstrated, and it is reasonable to consider the possibility that patients with MS are prone to the development of other autoimmune diseases. The relationship between RA and MS is supported by reports on demyelinating events seen in the disease course of patients with RA who receive TNF-α antagonists [12,13]. Anti-TNF medication was not used by the patient in our case, but one relative of the patient had been diagnosed with Behçet disease. We can consider the possibility that the greater burden of autoimmunity in the relatives of the patient may be responsible for the development of MS in our case. New autoimmune diseases may develop when there is a personal or family history of a first autoimmune disease.

CONCLUSION

The development of ambiguous neurologic symptoms consistent with MS in patients with JRA—whether or not they are receiving anti-TNF-α blockers—should lead us to consider the possibility of MS development in this clinical context and lead clinicians to consider a diagnosis of MS.

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