A Curious Case of Ankylosing Spondylosis and Motor Neuron Disease: A Mere Coincidence or Correlation?

Abstract
Ankylosing spondylitis (AS) is a chronic (progressive) painful inflammatory rheumatic disease with genetic predisposition. Genetic susceptibility and common expression cause susceptibility to other inflammatory diseases such as psoriasis, ulcerative colitis, and Crohn’s disease. However, cases of motor neuron disease (MND) in patients of biologically treated patients of AS have been rarely reported. AS does not follow the same course in everyone; even among affected members of one family, the outcome varies. Here, we present a case of an unusual AS without expression of human leukocyte antigen-B27 genetic marker who subsequently develops amyotrophic lateral sclerosis the most common form of MND. This mere correlation of one noncurable disease with one potentially treatable chronic rheumatological condition adds our knowledge to existing literature.

Keywords: Amyotrophic lateral sclerosis, ankylosing spondylitis, human leukocyte antigens B27

Introduction
Ankylosing spondylitis (AS) is an inflammatory disorder of unknown etiology that primarily affects the axial skeleton though peripheral joints and extraarticular structures are frequently involved. It is more common in males and usually begins in the second and third decades. AS belongs to the spondyloarthritis (SpA) family of diseases, which share several clinical, genetic, and immunologic features.[1] AS is distinguished in this family by involvement with sacroiliac (SI) joint inflammation or fusion and with more prevalent spinal ankylosis.[2]

Amyotrophic lateral sclerosis (ALS) is the most common form of progressive motor neuron disease (MND). It is the prime example of neurodegenerative disease and is arguably the most devastating of all neurodegenerative disorders. AS is associated with extraarticular manifestations; the most common extraarticular manifestations are represented by uveitis, bowel disease, lung, heart, skin, bone, and kidney involvement. Many epidemiological studies have found higher incidences of extraarticular manifestations to be a consequence of uncontrolled systemic inflammation.[3]

The goals of treatment of AS and axial SpA are to reduce symptoms, maintain spinal flexibility, and reduce functional limitations and complications. The mainstays of treatment have been nonsteroidal anti-inflammatory drugs and exercise, with the additional use of slow-acting antirheumatic drugs in patients with peripheral arthritis. Treatments with biological agents such as tumor necrosis factor α (TNF-α) inhibitors have revolutionized treatment of AS but not without serious side effects. Cases have been reported where ALS has been developed in TNF-α inhibitor treated patient of AS.[4] Here, we have experienced ALS in a known case of AS who had no history of any biological treatment.

Case Report
Eight years ago, a 31-year-old male patient presented with symptoms of dull back pain, insidious in onset, felt in the lower lumbar and gluteal region, accompanied by morning stiffness which initially improved with activity. Within a few months, the problems became persistent and bilateral. With the passage of time, he experienced neck pain and stiffness with restricted mobility. He was diagnosed with having AS based on available criteria. Then, after 8 years, at the age of 39 years, he experienced...
weakness of all four limbs which started gradually and was progressive for the past 1 year. It started with the right upper limb followed by involvement of the right lower limb. Both left upper and lower limb were also involved sequentially within a few months with progressive wasting and atrophy of muscles incapacitating him to perform his daily works. There was also a history of slurring of speech and occasional choking along with flickering movement of the muscle. Bladder and bowel functions were normal. The patient is nondiabetic but hypertensive. There was no history of chronic obstructive airway disease, tuberculous, or trauma. There was no history of fever, abdominal pain, convulsion, skin changes, diminished vision, ptosis, redness of the eye, or any episode of bloody diarrhea. He denied any substance or illicit drugs abuse. Family history was insignificant.

On clinical examination, general survey was unremarkable. Higher function and cranial nerve examinations were normal. The neck was stiff with restricted movements in all directions. Other signs of meningeal irritations were absent. The cranium was normal, but the spine was curved with concavity anteriorly. In motor system, there was gross atrophy of muscles of the shoulder and pelvic girdles and distal limb muscles without any sensory loss. There was gross atrophy of the tongue, and fasciculation was also seen. The tone was increased. Power was 3/5 in proximal group of muscles in all four limbs with severe weakness in distal muscles with bilateral claw hands [Figure 1].

Deep tendon reflexes in both the upper and lower limb were exaggerated bilaterally. Plantar reflex was extensor bilaterally. Glabellar tap and pout reflexes were present. Cerebellar signs were absent.

Movements were restricted in all directions in cervical, dorsal, and lumbar spines. Modified Schober test was positive. Small joints of hands were swollen without any signs of inflammation. There was clawing of fingers and toes. No extraarticular manifestation was present.

Investigations of routine blood were not remarkable apart from high erythrocyte sedimentation rate of 72 mm. Liver function and lipid profiles were normal. C-reactive protein was positive. Rheumatoid factor and anti-cyclic citrullinated peptide both were negative. Urine and stool analysis were normal. Both antithyroglobulin and anti-microsomal antibodies along with thyroid profiles were in normal range. Analysis of human leukocyte antigen-B27 (HLA-B27) was negative. Electrocadiography showed normal sinus rhythm. Echocardiogram was normal. Electromyography and nerve conduction velocity study of all four limbs revealed chronic diffuse alternating hemiplegia of childhood disease with secondary motor axonopathy. Dual-energy X-ray absorptiometry scan of hip and left forearm showed osteopenia (T score is 1.3 and 1.2, respectively) and lumbosacral spine was normal (T score 0.3).

Chest X-ray showed increased reticular markings. X-ray of the cervical and dorsolumbar spine revealed gross ligamentous calcification of both anterior and intraspinal ligaments along with the loss of cervical and lumbar lordosis [Figure 2]. Shoulder and bilateral knee joint X-rays were both normal. Hip X-ray showed left hip arthritis. Juxtaarticular osteopenia was seen in X-ray hand and wrist. X-ray of SI joint revealed mild sclerosis bilaterally. Magnetic resonance imaging of the spine revealed ankylosis of lower thoracolumbar vertebra with calcified intervertebral discs. Discs were fused in all direction with height reduction. No evidence of cord compression and significant compromise of neural foramina were present. Based on the clinical presentations, examinations, and radiological features, this patient was diagnosed with a case of seronegative spondyloarthropathy, i.e., AS and amyotrophic lateral sclerosis.

He was put on methotrexate 10 mg once a week with folic acid and calcium supplementation. He was already
on levothyroxine 50 µg once a day plus antihypertensive in the form of amlodipine and losartan combination. At his last turn up in outpatient, bath ankylosing spondylitis disease activity index score remains the same.

Discussion

The patient was presented features of inflammatory back pain with additional features of AS including typical posture and sacroiliitis. However, HLA-B27 was negative in this patient. HLAs are cell surface proteins, helps the body to fight illness by presenting peptides derived from foreign proteins or from the body’s own proteins, to T lymphocytes and other cells of the immune system.[5] Usefulness of HLA-B27 typing as an aid to diagnosis of AS has been discussed in depth by Khan.[6] A group has reported 93%–94% HLA-B27 positivity rate among AS patients seen in Delhi (Northern India).[7] As a result, it has been a standard exercise in clinical practice to carefully exclude the mimics of AS if the patient proves negative for HLA-B27 gene. The list of causes of back pain is long. Briefly, however, if clinically a patient has “spondylogenic” and “inflammatory” features, the possibilities are narrowed down to AS, infections (tuberculosis, etc.), and some of the rare metabolic conditions (e.g., ochronosis). These conditions were excluded by clinical methods and investigations discussed above.

The diagnosis of AS before the occurrence of irreversible damage is difficult. This delay is most likely due to the low awareness among non-rheumatologists of AS or SpA and the fact that radiological proof of sacroiliitis is a late feature of the disease.[8] AS can almost always be readily diagnosed on the basis of history, physical examination, and X-ray findings. A knowledge of the presence of HLA-B27 can sometimes be valuable as an aid to the diagnosis, although the prevalence of HLA-B27 and the strength of its association with AS vary markedly in different ethnic and racial groups.[8]

In the absence of any other diagnostic possibility, this patient was treated as AS. However, during the ensuing follow-up, he was fortuitously found to have MND that was confirmed by clinical examination and various investigations. Once MND was detected, the main diagnostic focus shifted to whether the patient had two separate diseases occurring together by coincidence or whether there was a link between them. An association of MND and AS has been very sparsely reported in the literature.

Prognosis is related to disease severity. Some cases may have times of active inflammation followed by remission while others never have times of remission and have acute inflammation and pain, leading to significant disability. As the disease progresses, it can cause the vertebral and the lumbosacral joint to ossify, resulting in the fusion of the spine as noticed in our patient. Our patient has no extraarticular manifestation of AS.

MND, or ALS, is a neurodegenerative disorder of unknown etiology. Several cases have been reported where mimickers of MND have been diagnosed or even cured with available treatment.[9] Every attempt should be made to exclude potential treatable mimickers of MND. TNF-α inhibitor treatment has been implicated as a potential etiology of ALS in preexisting rheumatological conditions in few reports.[4] However, here, we find the development of ALS in a known case of AS who had no history of any biological treatment.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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