CURRENT APPROACHES AND PROBLEMS IN ANKYLOSING SPONDILYTIS: IMMUNOLOGICAL PERSPECTIVES

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ABSTRACT
Ankylosing spondylitis (common form of spondyloarthropathy), chronic inflammatory disease disorder and affecting mostly on sacroiliac joints and axial skeleton. This disease is considered under the category of autoimmune disease. The cause of this seronegative disease is still unknown, but this disease normally tends to run in families and suggesting that genetics play an important role. Normally, this disease is reported more in men as compared to women, at a ratio of 2: 1. In this review article, we mentioned about ankylosing spondylitis and showed its correlation with nutrition and understanding their immunobiologically prospective along with complications and diagnosis of this disease.

KEYWORDS: ankylosing spondylitis; inflammatory; immunological; nutrition.

INTRODUCTION
Ankylosing Spondylitis is a chronic inflammatory disease of unknown aetiology which mainly affects spine. It is more commonly seen in second decade of life and affects mostly male. This seronegative disease may be associated with ulcerative colitis, aortic insufficiency and iritis. Clinical features includes insidious onset of low back pain and stiffness, poor chest expansion and exaggerated dorsal kyphosis.1-4 The chest expansion is decreased due to involvement of costochondral joints. Bilateral sacroiliac joint are affected initially and later are ankylosed, the disease gradually progresses to the whole spine and other major joints of the body like hip, knee, shoulder and temporo-mandibular joints.5-6 There is formation of syndesmophytes which are thin dense spicules that bridges the vertebrae along with ossification of outer fibers of annulus fibrosus. Spine of patient of ankylosing spondylitis (Fig.1) appears like bamboo on X-ray due to formation of these syndesmophytes (fusion of vertebrae; Fig.2). Spinal mobility is decreased considerably at this stage with gait deviation. The progression of spinal fusion leads to fixation of cervical and thoracic spine with postural dysfunctions and consequently compensatory deformity of hip and knee joints.1,8

Fig. 1: Comparison between normal spine and ankylosing spondylitis.

Physiotherapeutic of this disease at every stage. Aims of management are dependent on the stage of disease and its main objective is to increase the functional mobility of patients so that they can perform activities of daily living normally.6-9 Postural education has a vital role to play in these patients to carry on daily tasks without pain and discomfort. At advanced stage of this disease to correct ankylosed hip joint and fixed flexion deformity of the spine surgical intervention may be needed.7-10

The physiotherapist plays an important part in regular assessment and evaluation.
Correlation of Ankylosing Spondylitis with Nutrition
Ankylosing spondylitis is one of the example of autoimmune disease and number of nutrients may mimic an antigen like properties and showed some correlation. As per the literature, there is a strong genetic association with the onset of Ankylosing Spondylitis. In this regard, patients follow strictly healthy diet to reduce or control the burden of this disease. The major foods include omega-3 fatty acid (soya bean, walnuts, fish); fruits and vegetables (provide vitamins along with minerals for improving bone strength); fibre diet (e.g. whole wheat, brown rice etc.) that are beneficial in terms of decline in inflammation rate for those patients who are suffering from ankylosing spondylitis. In contrast, we avoid some of foods, only for those persons who are suffering from this disease. The major foods are caffeine, soda/aerated drinks, junk foods etc. Generally, these foods should be totally avoided because it tends to increase the inflammation rate. In other words, effective type of pharmacological therapy always is required i.e. anti-inflammatory diet containing adjuvant can help to reduce the burden of various inflammatory processes. So, this anti-inflammatory diet containing adjuvant is totally consistent with normal balanced diet and prevents malnutrition.

In 1973, extensive research on ankylosing spondylitis and claimed that more than 95 % of patients had HLA-B27 and also reported one of the pathogen i.e. Klebsiella lives in the intestine. As per the literature, if person consumed high quantities of starch so there is also showed some enhancement of Klebsiella in the bowels flora. In other words, starch is directly proportional to Klebsiella; if amount of this bacteria is more than the normal amount in the intestine, our body produce more antibodies causing an inflammatory response.

Immunological Prospectives
One of the immune-mediated inflammatory joint diseases i.e. ankylosing spondylitis showed some potential effect and targeted specific organ. This disease is directly targeted to axial joints and is generally correlated with tumour necrosis factor (TNF). Since number of therapies are available but anti-TNF therapy is proved to be more effective and is associated with class I HLA alleles. Generally, TNF blockers target this specific type of protein and helped us in order to reduce its pain, stiffness and tender or swollen joints. These are administered by injecting the medication under the skin or through an intravenous line e.g. Etanercept (Embrel); Infliximab (Remicade); reactivate latent tuberculosis and may cause certain neurological problems etc.

Ankylosing spondylitis is considered to be one of the autoimmune disease that involves its combination of environmental along with genetic factors. As per the literature, highly heritable disease and more than 90% of developing disease risk has been determined genetically. In future for this disease, we need to identify those genes which is directly associated with the disease and showed its role in pathogenesis. Now a day, pathogenesis is still unclear but innate as well as adaptive type of immune responses could have a role in disease development. Number of research papers were published related to ankylosing spondylitis and claimed the presence of different types of T cell subsets in different body fluids. As per the literature, there is enhancement in CD4 count which is observed in those persons which is suffering from ankylosing spondylitis; indirectly, it also enhanced Th1 cytokines as well. In other words, release of Th1 cytokines i.e. IFN-gamma and TNF alpha are more as compared to Th2 type of cytokines and is responsible for causing autoimmune disease. In view of this, ankylosing spondylitis accounted as acute as well as chronic type of spinal inflammation initiating or originated from sacroiliac joints and is accompanied with enthesisitis, presenting as chronic inflammation at the sites of ligamentous and tendinous insertions into bone. In addition, HLA (human leukocyte antigen) -B27 is directly associated with ankylosing spondylitis but its pathogenesis is still not well defined. Only observations were made on the basis of Th1 cytokines, there is decline in Th1 profile i.e. TNF alpha and IFN-gamma and it is detected in HLA-B27 (folding of heavy chain) patients.

Actually, HLA-B27 stands as one of the earliest and most robust as well as important genetic marker associated with disease. In normal circumstances, HLA-B27 cell surface consisting of heavy chain and is associated with beta2 microglobulin along with peptide. Ultimately, this complex is assembled in endoplasmic reticulum but if there is misfolded heavy chain is reported then it will remove from endoplasmic reticulum. In contrast, if there is deficiency or shortage of peptide or beta2 microglobulin so there is enhancement in misfolded heavy chains. Finally, increased in the expression of the protein (BiP) and generate a required number of unfolded protein response in endoplasmic reticulum, leading to activation of nuclear factor-kB. Number of studies were conducted related to HLA-B27 and claimed that slow folding is...
reported in HLA-B27 but if there is exposure of viral infection so misfolding of proteins will occur. In other words, viral infection is directly associated with misfolding of proteins. Normally, cells possess and reported HLA-B27, if there is association with ankylosing spondylitis which exhibit higher rate of beta2 microglobulin dissociation from surface HLA-B27 complex. From these points, it is clear that release of beta2 microglobulin from a subpopulation of cell surface–expressed HLA-B27 molecules leads to b2m deposition within the synovium and to the initiation of chronic inflammation. In addition, HLA-B27 may also decrease or suppress the costimulatory molecules population of antigen presenting cells (dendritic cells, macrophages).[31–36] Similarly, other genes are also reported i.e. HLA-B60, important contributor to Ankylosing spondylitis susceptibility and may act as an independent factor in B27-positive and B27-negative Ankylosing spondylitis patients. There was a report that HLA-DR1 is associated with Ankylosing spondylitis. In comparison with other HLA alleles, HLA-B27 appears to be slower because of specific amino acid residues in the B pocket.[31–36]

HLA means leukocytes (white blood cells) are responsible for protection against various foreign substances. The prevalence rate of HLA-B27 is totally varied especially between ethnic and also observed in worldwide population but not considered a common haplotype. Only Caucasians (8%), North Africans (4%), Chinese (2-9%), and Japanese (0.1-0.5%) people possess HLA-B27 and is associated with ankylosing spondylitis, an inflammatory disease where some of the vertebrae spine will be fuse together, inhibiting mobility.[31–36] An estimated 88% of people with ankylosing spondylitis are HLA-B27 positive, yet only small fraction of HLA-B27-positive people will develop ankylosing spondylitis. Other interconnected autoimmune diseases with HLA-B27 haplotype which includes Crohn’s disease; ulcerative colitis, psoriasis; reactive arthritis, and uveitis. The most common subtypes of HLA-B27 (i.e. B2704 and B2705) are normally link or associated with increased risk of ankylosing spondylitis, while other subtypes (like HLA B2706 and B2709) actually appear to be protective against the disease. In contrast, ankylosing spondylitis patients were identified as having elevated levels of serum IgA, suggesting the abnormal movement of microbes from the gut into the blood stream.[37]

As per the literature, Interleukin 17 (IL-17), proinflammatory cytokine which played an important role in the pathogenesis of autoimmune diseases (ankylosing spondylitis) and inflammatory diseases. This cytokine also mediate the release of other cytokines (i.e. IL-6 and IL-8) as well but this is still under the control of T helper 17 (Th17) cells.[38,39] One of the studies where scientists claimed that IL-23 is able to induce or express IL-17 production and is considered to be one of the crucial factor in the Th17 response. In other words, Th17 cells may involve in promoting the inflammatory process in ankylosing spondylitis and there is significantly enhancement in the level of Th17 cells have been reported in the peripheral blood of patients with ankylosing spondylitis, suggesting that they could have a role in inflammation.[38–41]

In ankylosing spondylitis, number of studies have been conducted to determine the levels of T regulatory cells in the peripheral blood of patients; however, low percentages of T regulatory cells have been reported in peripheral blood and synovial fluid of patients with ankylosing spondylitis, suggesting an imbalance between T regulatory cells and adaptive immune response.[38-41] Moreover, ankylosing spondylitis patients treated with anti-TNF therapy showed similar levels of T regulatory cells to those observed in healthy subjects. These data suggest a possible role of T regulatory in ankylosing spondylitis, and Th17/T regulatory imbalance has been proposed as playing a novel role in ankylosing spondylitis.[38-41]

Diagnosis of ankylosing spondylitis in patients

According to the literature, symptoms (especially chronic low back pain) will appear after long time and this is one of the indicators of ankylosing spondylitis. Blood tests should be performed to measure various inflammatory markers (i.e. erythrocyte sedimentation rate and C-reactive protein) in blood. On the other hand, genetic tests also performed in order to determine HLA-B27 gene and also determining through radiographic techniques.[38–41] This techniques especially radiographic (X-rays) and magnetic resonance imaging (MRI) are able to detect or determined sacroilitis inflammation in ankylosing spondylitis and is considered to be one of the best non-clinical indicator of disease.[38–41]

Cardinal symptoms of ankylosing spondylitis

Inflammatory low back pain is considered to be one of the cardinal symptom observed in these patients. Reduced flexibility due to stiffness of spine and hip joint also restrict mobility of patients.[2–7] Some of the complications as shown in Fig and some of them are-

- Osteoporosis (Calcium-poor bones; weak, fragile bones may fracture; half of all patients have osteoporosis).
- Increased risk of heart disease (aortitis, aortic valve disease, conduction problems, ischemic heart.

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disease and cardiomyopathy) is observed in ankylosing spondylitis.\cite{6}\cite{6} The incident rate of this disease which involves cardiac system has been reported around 10% to 30%. In general, there is involvement of conduction disorder or aortic insufficiency (5-10%) in ankylosing spondylitis patients. Apart from these, smoking; reduced physical activity and hypertension are also associated with worse outcomes in ankylosing spondylitis.\cite{6}\cite{6}
c) Smoking is associated with increased counts of macrophages and neutrophils in the lung parenchyma, and may worsen existing lung disease in ankylosing spondylitis patients.\cite{6}\cite{6}\cite{6}\cite{6}
d) Several pulmonary disorders have been observed in patients with ankylosing spondylitis, and this can be associated with significant morbidity and mortality.\cite{6}\cite{6}\cite{6}\cite{6}\cite{6}\cite{6} In general, the ability to work and function in daily life is related to pulmonary function, and patients with reduced function have more respiratory complaints. Further, pulmonary function level is associated with prognosis and morbidity, including fatal outcome from heart and lung disease.\cite{6}\cite{6}\cite{6}\cite{6}\cite{6}\cite{6}
e) Another risk factor i.e. bone involvement where inflammation of the spine settles down so calcium ions is ultimately laid down where ligaments are attached with bones that make up the spine. This reduces its mobility of the back and causes bone to grow from the sides of the vertebrae. Eventually the individual bones of our spine may link up (fuse) and called as ankylosis\cite{3}\cite{3}\cite{3}\cite{3} and observed on x-rays. Normally, ankylosing spondylitis typically starts from joints (between spine and pelvis) and spread from spine to neck and also affect other parts of our body i.e. tendons or eyes.
f) Rarer complications are also observed i.e. Amyloidosis (Caused through buildup protein i.e. amyloid in organs, amyloidosis can cause symptoms i.e. weight loss, water retention and tiredness). Secondly, Cauda equina syndrome (inflammation causes overgrowth of bone and leads to pressure and swelling at the end of the spinal cord).

In addition, other complications are also reported in ankylosing spondylitis e.g. eye complications; involvement of skin and lung; gastrointestinal problems etc.

CONCLUSION

This study provides some information about incidence and prevalence of this disease, related to immunological aspects along with complications of ankylosing spondylitis. People should be aware about course of this disease and its prognosis. This study mentions about disabling nature and difficulties in activities of daily living of patients suffering from this disease.

REFERENCES

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