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Case Report

A Case study on a Spondyloarthritic patient: Unresponsive to steroidal treatments, disease modifying antirheumatic drugs and non-steroidal anti-inflammatory drugs

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Abstract

Spondyloarthritis is a disease that creates a serious burden to the medical sector. This condition is defined by inflammatory spinal stiffness that affects the cartilaginous spinal joints and the sacroiliac joints. An 18 years old male patient was hospitalized because of spondyloarthritis, though no known family history of spondyloarthritis and uveitis were manifested. Diagnoses of HLA-B27-positive spondyloarthritis with mostly peripheral involvement were proposed in laboratory testing. X-ray report of pelvis and both S.I. joint were normal, so it confirmed this patient is affected by non-radiographic spondyloarthritis. Anti-inflammatory medications and steroids had little impact on the complaints, which were quite severe. Non-steroidal anti-inflammatory drugs, corticosteroids, and DMARDs are the medicines of preference but cannot give a comprehensive treatment in traditional approaches.

Keywords: Spondyloarthritis, non-radiographic, NSAID, DMARD, HLA-B27.

INTRODUCTION

Spondyloarthopathy (also known as spondyloarthritis) is a bunch of autoimmune inflammatory malady which is involved with joints and spine. Environmental and genetic components play together essentially to promote SpA [1]. Major signs of SpA are joint pain and inflammation, fatigue, stiffness and joint swelling. Moreover, a type of autoimmune disease related with SpA- chronic Inflammatory Bowel Disease (IBD), severe inflammation and swelling of toe and finger joints, sacroiliac joints inflammation, peripheral arthritis, entheses inflammation and uveitis are also perceived [1-3].The specific cause of SpA is still not known. Nevertheless, some studies suggested that several genetic factors are responsible for SpA in some individuals and environmental components like infections which occur gut dysbiosis resulting spondyloarthritis has been observed in some individuals [1]. HLA-B27 is the most suspicious genetic factor that is responsible for SpA. HLA-B27 gene encodes human MHC class I molecules. Studies suggested that about 5% to 7% HLA-B27 positive individuals are likelihood to develop SpA and HLA-B27 positive cases are found about 95% individuals who already develop SpA though only 10% prevalence to be HLA-B27 positive has been found among general public [4, 5]. HLA-B27 is located in the chromosome 6 in human and made up of two polypeptide chains- alpha chain and β2 microglobulin [4]. In general, HLA-B27 attaches and display peptides from HIV, influenza and other viruses to the CD8+ T lymphocytes to activate cell mediated immune response [4]. Some investigations assumed that a group of peptides (sometimes called "arthritogenic peptides") which are responsible for promoting SpA may be displayed by HLA-B27 and resulting inflammation and pain of joints and spine [4, 6]. Large scale genetic studies reveal that a significant number of unique genetic interrelationships beyond HLA-B27 indicates the pathways of inflammatory cytokines are responsible for promoting the condition of SpA and understanding these pathways help to make a potential therapeutics against SpA [7-9]. Analysis on SNPs (Single Nucleotide Polymorphisms), cytokine related intracellular signaling factors and cytokine receptors revealed major inflammatory cytokine pathways, such as- TNF, IL-1, IL-6 and IL-17/IL-23 which are responsible for promoting SpA [7]. IL-17 is the cardinal inflammatory cytokine among other inflammatory cytokines for playing key role in the inflammation and development of SpA in human [7,10,11]. Several therapeutic agents are using to alleviate the severity of damage via SpA, such as- DMARDs (Disease-modifying anti-rheumatic drugs), NSAIDs (Nonsteroidal anti-inflammatory drugs), TNF inhibitors, IL inhibitors, Janus kinase inhibitors. In this case study, we want to show several types of medications that didn't work or minor effect on a spondyloarthritic patient.

CASE REPORT

An 18 years of age male patient suddenly felt severe pain in the groin area which continuously involved with other joints like knee joints, toe joints, carpal-metacarpal joints, sternum-costal cartilage joints, spine and hip joint. The patient felt inflexibility for about nine months due to stiffed knee joints along with spine and hip joint pain. Day by day, his stiffness and pain increased and exacerbated the situation that he could not be able to sit for more than 5 minutes interminably. The right shoulder joint became inflamed severely that he felt pain during the movement of right hand. He also grumbled that due to hip joint pain and stiffness, he even could not bend forward for about 1 year. He was diagnosed as spondyloarthritic patient 6 years back by his doctor. He was signed up in the indoor ward of hospital for 2.5 days to diagnose and for the ministrations.

PATIENT'S CRUCIAL EXAMINATIONS

Anterior uveitis was first diagnosed 10 years back by an ophthalmologist which was treated by periocular corticosteroid injection because patient's anterior uveitis was not responding to topical corticosteroid like-Prednisolone Acetate 1%. Before the appearance of anterior uveitis, mild symptoms of joint pain was observed but that was avoided due to the lack of proper knowledge and diagnosis. From the first appearance of anterior uveitis, it comes twice or thrice in every year.

There is no known cases of spondyloarthritis were observed among patient's family members. While he was walking or sitting for 10 minutes or more, his pain became exacerbated. Even shifting position when resting, in winter season and in rainy season, and during full moon his pain also became exacerbated. Furthermore, some types of foods, like- Basella alba, Abelmoschus esculentus, Cocos nucifera, and Lathyrus sativus also showed negative impact on his spondyloarthritic condition. Long term resting in the dorsal posture throughout the night made pain more severe and at the time of dawn breathlessness had been observed.

X-ray report of pelvis AP and right hip oblique view showed no dislocation, well maintained joint spaces, and both S.I. joint were normal but tilting of pelvis was observed. Furthermore, lumbosacral spine B/V x-ray report showed normal vertebral alignment, no bony lesion in the lumbo sacral spines, both S.I. joint were normal, well maintained disc spaces but straightening of lumber lordosis was noted due to muscle spasm.

Due to elevated level of SGPT/ALT, doctor recommended ultrasonogram of HBS and Pancreas but no abnormality were observed in the liver, gall bladder, biliary tree, portal vein, pancreas, spleen and adrenals.

PREVIOUS TREATMENTS RECORD

For five months, the patient was monitored by the rheumatologist. Rheumatologist recommended HLA-B27 test six years ago. Hip joints MRI indicated seronegative spondyloarthropathy. HLA-B27 was found to be positive. For those five months of treatments, the patient had been prescribed several types of medications. Dosage administration of medications for daily intake has been shown on the (Table 1,2).

Moreover, Inj. Pamidronate+MP was injected through intravenously with saline to the patient and Cortisone was injected also to alleviate the pain and inflammation. But, the effect of Pamidronate and Cortisone did not last even for 24 hours with these medications no progress had been noticed [14]. However, the patient began to experience health complications such as edema, weight loss, and loss of appetite. Effects of

Table 1. Parameters that ensured the presence of Spondyloarthritis.

Examinations	Outcomes	Reference Values	Comment
Heart rate	65 bpm	60 bpm-100 bpm	Normal
Blood pressure	Systolic: 90 mmHg	Systolic: 120 mmHg	Low
	Diastolic: 50 mmHg	Diastolic: 80 mmHg	
Body temperature	(100-101)°F	<99°F	High
ESR (Westergren method)	87 mm in 1st hour	0 mm-10 mm in 1st hour	Very high
Platelets	700×10^9/L	$150\text{-}400\times10^9$/L	High
WBC	14×10^9/L	4×10^9/L-11×10^9/L	High
Hemoglobin	9.5 g/dL	13-17 g/dL	Low
SGPT/ALT	159 U/L	Up to 40 U/L	Very high
CRP test	192 mg/L	<6mg/L	Positive and very high
HLA-B27	---	---	Positive

Table 2. Dosage administration of medications for daily intake.

Medicines	Mechanism of action
Indomet suppository 100 mg	Antipyretic and analgesic activities are found in Indomethacin.
	The pituitary gland and the adrenals have no impact on indomethacin.
Domperidone maleate 10 mg	Domperidone is a dopamine antagonist that works by blocking dopamine receptors in the Chemoreceptor Trigger Zone (CTZ) in the stomach.
	Its gastroprokinetic function derived from its ability to inhibit dopamine receptors, which affect gastrointestinal motility.
Tolperisone hydrochloride 50 mg	Tolperisone Hydrochloride is a muscle relaxant that operates from the central nervous system.
	It's mostly used to treat high muscular stiffness and stress, along with specific circulation abnormalities in the extremities.
Ketoprofen 100 mg	Ketoprofen exhibits both analgesic and antipyretic properties.
	In vitro and *in vivo*, it hinders prostaglandin biosynthesis and maintains lysosomal membranes.
	At high doses it hinders leukotriene production in vitro.
	In vivo, it possesses antibradykinin properties as well.
	Ketoprofen exhibits an antipyretic effect via reducing prostaglandin biosynthesis in the Central nervous system (most likely in the hypothalamus).
Baclofen 10 mg	Baclofen suppresses monosynaptic and polysynaptic impulses in the spinal cord by activating GABAB receptors, which hinders glutamate and aspartate production.
Prednisolone 10 mg	The function of the enzyme Phospholipase A2, that produces many inflammatory agents such as SRS-A, Prostaglandins, Leucotrienes, etc., is inhibited by prednisolone explicitly.
Sulfasalazine 500 mg	Sulfasalazine's mechanism of actions are ongoing evaluation but may be linked to animal and in vitro studies with anti-inflammatory and/or immunomodulation
Prednisolone 5 mg	The function of the enzyme Phospholipase A2, that produces many inflammatory agents such as SRS-A, Prostaglandins, Leucotrienes, etc., is inhibited by prednisolone explicitly.
Methotrexate 10 mg	Methotrexate hinders dihydrofolic acid reductase enzyme.
	DNA synthesis, repair, and cellular replication all are impeded by methotrexate.
Naproxen Sodium 375 mg	Naproxen hinders the prostaglandin biosynthesis.
	It possesses both antipyretic and analgesic characteristics.
Tramadol Hydrochloride 50 mg	Two types of neurotransmitters-serotonin and noradrenaline absorption are impeded by tramadol hydrochloride
	It regulates pain signals by stimulating analgesia-related descending serotonergic and noradrenergic pathways.
	Tramadol's analgesic properties are maintained through μ-opioid receptor activation and indirect regulation of central monoaminergic inhibitory pathways.

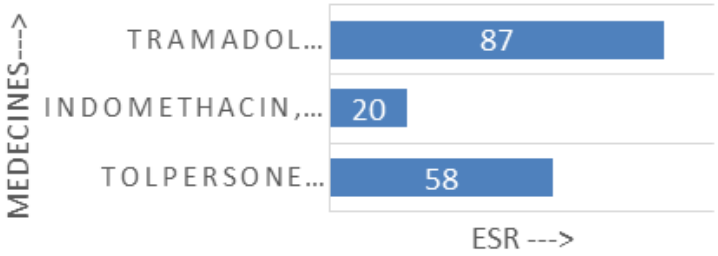

Fig.1. Several types of steroidal drugs, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and disease modifying antirheumatic drugs were used to treat the condition but higher level of ESR showed the unresponsiveness of those drugs.

steroidal drugs, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and disease modifying antirheumatic drugs on ESR are shown in (Figure 1).

DISCUSSION

Dactylitis occurring in around 30% of the patients with SpA was described more than 40 years ago back stiffness caused by inflammation in the spine and/or pelvic area [12, 13]. Inflammatory back discomfort often develops progressively before the age of 45, improves with exercise but not relaxation, and is accompanied by morning stiffness lasting at least 30 minutes. Ankylosis, or new bone development in the spine, can develop fusion of the leading parts of the spine in a permanent, immovable posture. A thought-provoking viewpoint in this study is that NSAIDs (Indomet, Ketoprofen, Naproxen Sodium), DMARD (Sulfasalazine), opiate analgesic (Tramadol Hydrochloride), antimetabolites (Methotrexate), corticosteroids (Prednisolone), skeletal muscle relaxant (Baclofen) did not show any efficacy to improve the condition of this patient.

CONCLUSION

Since spondyloarthritis mostly affects the adolescent generation, the younger community's life expectancy is jeopardized. The individual is worried and in emotional turmoil due to the constraints of the traditional medicare facility. The primary objective of SpA treatment is to minimize disease recurrence while also controlling joint degeneration and extra-articular symptoms. The care of the individual patient with his or her diverse complication is a critical issue for physicians, as a result, the therapeutic treatment of SpA must be diversified. Conventional treatments include NSAIDs and steroids in the primary stages and/or moderate types of the illness, as well as monotherapy or combination pharmacotherapy with DMARDs for flare regulation in recalcitrant distal joint dysfunction. The initial option of treatments for SpA are NSAIDs, oral and intra-articular low-dose corticosteroids and are likewise implemented in case of SpA. These treatments are still not investigated thoroughly and information on their validity in the improvement of illness results are not comprehensive. The most commonly utilized DMARDs in SpA individuals with distal chronic condition is delineated by Sulfasalazine; nevertheless, their usage might be justified by a lack of scholarly support. Nonetheless, more comprehensive randomized trials with extended follow-up durations are required to confirm current findings on this topic.

DECLARATION OF PATIENT CONSENT

This case study is written by the patient himself. First author of this manuscript is suffering from spondyloarthritis.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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