European Journal of Musculoskeletal Diseases
ISSN 2038-4106/2023

Case report

UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE WITH HYPERPLASIA OF YELLOW LIGAMENTS IN L4-L5 CAUSING SEGMENTAL SPINAL STENOSIS

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ABSTRACT

Undifferentiated connective tissue disease (UCTD) is a systemic autoimmune disease characterized by clinical and serological manifestations not fulfilling the criteria for defined connective tissue diseases. Up to 90% of the cases are young women. Usually, UCTD has a mild clinical course with a wide variety of signs and symptoms because it can involve any connective tissue in the body. 40% of patients with UCTD develop the stage of a well-defined systemic autoimmune disease during five years of follow-up, while 60% remain in an undifferentiated stage. The most used drugs in treating UCTD are nonsteroidal anti-inflammatory drugs, corticosteroids, calcium channel blockers, and antimalarial drugs. We report a rare case of a woman with UCTD in corticosteroid treatment, suffering from low back pain refractory to therapy, evidence a computed tomography (CT) of abnormal bone hyperplasia of the yellow ligament conditioning spinal stenosis.

KEYWORDS: *undifferentiated connective tissue disease; yellow ligaments; spinal stenosis; systemic autoimmune diseases*

INTRODUCTION

Undifferentiated connective tissue disease (UCTD) is a systemic autoimmune disease characterized by clinical and serological manifestations not fulfilling the criteria for defined connective tissue diseases (CTD) such as systemic lupus erythematosus, mixed connective tissue disease, Sjögren syndrome, systemic sclerosis, polymyositis, dermatomyositis, or rheumatoid arthritis (1, 2). Its diagnosis is considered exclusion (3). UCTD is defined if the following criteria are met:

Received: 23 July 2023
Accepted: 02 September 2023

ISSN: 2038-4106

signs and symptoms suggestive of a CTD, but not fulfilling criteria for a defined CTD, positive antinuclear antibodies on two separate measurement controls, and disease of duration of at least 3 years (4). The incidence is unknown due to the lack of a proper definition of this pathology, but it has been observed that 20-50% of patients presenting in a rheumatology department have a UCTD diagnosis (5).

From an epidemiological point of view, in more than 90% of cases, this pathology mainly affects women, particularly those between 32 and 44 years old (6, 7). There are two forms of UCTD called stable-UCTD and evolving-UCTD (4). The first case represents the forms that remain undifferentiated and are over 60% of the total, while the evolving forms represent about 40% of the UCTD evolve into defined systemic autoimmune disease during five years follow up (8, 9). Like all autoimmune diseases, the aetiology is unknown; what is known is that genetic factors and environmental triggers induce the triggering of these diseases (10). However, UCTD, like other known connective tissue disorders, is characterized by exaggerated immune system activity (11). The latter produces autoantibodies or activates antigen-specific T-lymphocytes that affect connective tissue at every site of the body (12).

Clinically, UCTD has a generally mild course; in most cases, it is characterized by the absence of severe organ damage or involvement, especially in the renal and neurological systems (3). The main symptoms are arthralgia, which can be present in more than 86% of patients; various skin lesions such as livedo, purpura, acrocyanosis, telangiectasias, urticaria (3, 7); Raynaud phenomenon (33%), sicca symptoms (30%), mucocutaneous symptoms included oral ulcers (23%); arthritis (22%) and thyroid disease (7%) (13-18). Constitutional symptoms, such as fever, malaise, and fatigue, are often the initial presentation of the disease (3). From a diagnostic point of view, serological markers are considered essential in the diagnostic criteria for UCTD (3). In particular, anti-Ro/SSA and anti-U1-RNP are considered markers detected in this disease (3, 5).

Regarding imaging studies, chest radiography and computed tomography (CT) can be helpful in studying cardiac and pulmonary involvement (19, 20). Additionally, ultrasonography of the salivary glands was a good test in differentiating between UCTD and other diseases such as Sjögren syndrome (21, 22). The main treatment of UCTD is pharmacological, and the most used drugs are nonsteroidal anti-inflammatory drugs, corticosteroids, calcium channel blockers and antimalarial drugs such as hydroxychloroquine (3, 23, 24). If the disease is not controlled with these drugs or the symptoms are severe, it is necessary to use immunosuppressive agents such as methotrexate and azathioprine (3, 7).

CASE PRESENTATION

A 75-year-old female patient with a medical history that revealed UCTD was receiving corticosteroid treatment for 15 years.

Since the age of 65, the woman had episodes of neck and low back pain investigated with a rachis x-ray showing diffuse spondyloarthritis manifestations; therefore, she was treated with nonsteroidal anti-inflammatory drugs to reduce the pain symptoms.

For about 60 days, she complained of acute left lumbosciatica with paresthesia and weakness of the left lower limb conditioning intermittent claudication. Furthermore, this symptomatology was not responsive to pain-relieving therapy.

The patient underwent lumbosacral computed tomography (CT) (Fig. 1) that showed marked hyperplasia of yellow ligaments at the fourth lumbar disc and

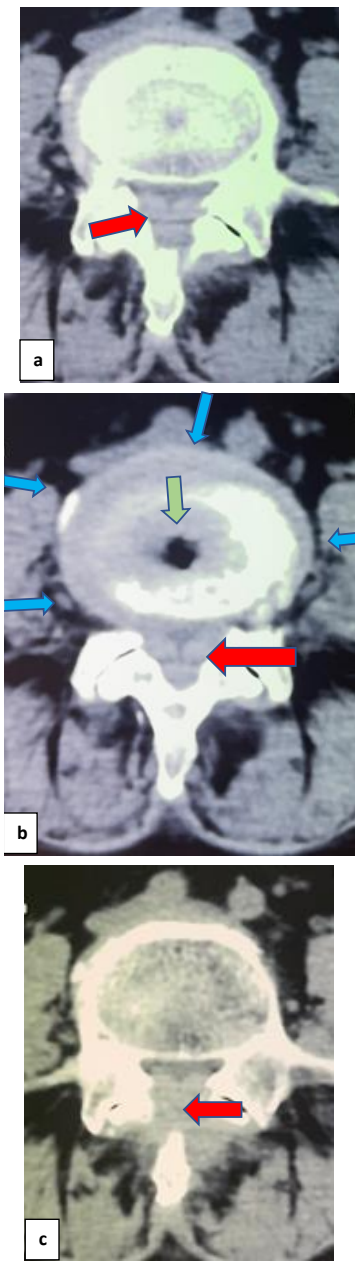

Fig. 1. ***a), b), c):*** *Marked hyperplasia of the yellow ligaments at L4-L5 (**red arrows**), which determines important segmental canal stenosis, where the dural sac appears compressed and displaced anteriorly against the posterior wall of L4 and L5. The disc between L4 and L5 appea rs modestly protruded circumferentially (**blue arrow**) with associated gaseous vacuolar degeneration of the nucleus pulposus (**green arrow**).*

fifth lumbar disc (L4-L5). This hyperplasia determines important segmental canal stenosis, where the dural sac appears compressed and displaced anteriorly against the posterior wall of L4 and L5. Moreover, the intervertebral disc between L4 and L5 appears modestly protruded circumferentially with associated gaseous vacuolar degeneration of the nucleus pulposus. Hyperplasia and subsequent ossification of the yellow ligaments is a rare event that can occur in cases of UCTD.

DISCUSSION

The case report shows a rare hyperplasia of the yellow ligaments that condition root canal stenosis associated with UCTD. As known, the yellow ligament is located inside the spinal canal that connects posterolaterally two laminae of adjacent vertebrae, and it is divided into two portions: capsular portion and interlaminar portion (25, 26). Histologically, connective tissue comprises 80% elastic fibres and 20% collagen fibre (27). It maintains the inherent stability of the spine, controlling intervertebral movement and maintaining a smooth surface of the posterior dural sac (26, 27).

The pathogenesis of the yellow ligament's thickening is unclear (28). Multifactorial agents such as age, mechanical stress, growth factors and systemic disease like connective tissue diseases are known to contribute to hyperplasia development up to ossification of yellow ligaments (28-30). The hypertrophied yellow ligament shows an increase in collagen fibres, calcification, ossification and chondrometaplasia (27); this is due to the production by the cells present in the yellow ligament of a high volume of type II collagen at the expense of elastic fibres (28-30). Subsequently, this collagen is converted to type-1, which can lead to endochondral ossification of the yellow ligament (28-30).

Thickening of the yellow ligaments causes spinal canal narrowing and mechanical compression of the nerve roots, cauda equina and spinal cord (31). This mechanical compression causes low back pain, sciatica, paresthesia, pain and muscle weakness, gait disturbance and bladder-bowel disturbance (26). These symptoms occur even in the absence of bulging *Annulus fibrosus* and herniated nucleus pulposus (26).

Diagnosis is based on the neurological findings, imaging examinations using X-ray, CT and magnetic resonance imaging (MRI) and electrophysiological examinations (32). Generally, the treatment of symptoms brings pain and numbness, and the pain in the lower extremities requires the use of nonsteroidal anti-inflammatory drugs, muscle relaxants and vitamin B12 (26). Physical therapy is recommended at an early stage.

However, dynamic physical therapy, such as massage and stretching of the spine by others, is contraindicated because it increases the risk of hypertrophic yellow ligament injury. Surgical treatment is recommended for patients with ineffective conservative treatment and with severe spastic gait, severe muscle weakness of the lower extremities, and bladder-bowel disturbance. Surgical decompression methods include open-door laminectomy, bulk laminectomy, fenestration, and hemilaminectomy (33-37).

CONCLUSIONS

Hyperplasia of the yellow ligaments and subsequent ossification are rare events of multifactorial aetiology due to advanced age, mechanical stress and systemic disease. Among the pathologies that could cause an alteration of the structural composition and, therefore, the yellow ligaments' functionality are connective tissue diseases, but insufficient data are currently available in the literature. Future studies will be needed to evaluate the relationship between connective tissue diseases such as UCTD and yellow ligament hypertrophy. Studies will then be necessary to make diagnoses with in-depth and targeted imaging techniques to evaluate the spinal column and the subsequent and appropriate medical or surgical therapy.

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