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The Three Nosogical Entities of Immune-Mediated Inflammatory Diseases (SEORA As Autoimmune Disease, Giant Cell Arteritis with Polymyalgia Rheumatica as Autoinflammatory Disease and Adenomyoma of Prostate as Inflammatory Disease of Undetermined Mechanism), The Multifactorial Osteoporosis and an Acute-Onset Disease Diagnosed in a Sexagenarian Man

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Abstract **Case Report**

***Introduction*:** Immune-Mediated Inflammatory Diseases (IMIDs) are characterized by three nosological entities and their nosological sub-entities: (i) autoimmune diseases (systemic autoimmune diseases, organ-specific autoimmune diseases), (ii) autoinflammatory diseases (monogenic autoinflammatory diseases, polygenic autoinflammatory diseases: "systemic" polygenic autoinflammatory diseases and "organ-specific" polygenic autoinflammatory diseases) and (iii) inflammatory diseases of undetermined mechanism (neoplasms, paraneoplastic syndromes and inflammatory diseases of iatrogenic origin). Here, to our knowledge, we report the first suspected case of interrelated type of diseases within the three nosogical entities of immune-mediated inflammatory diseases (seronegative for elderly onset rheumatoid arthritis (SEORA) as autoimmune disease, giant cell arteritis with polymyalgia rheumatica as autoinflammatory disease and adenomyoma of prostate as inflammatory disease of undetermined mechanism) associated with multifactorial osteoporosis and an acute-onset disease diagnosed in a sexagenarian man. ***Case Description*:** A 60-year-old man with no past medical history. At his first presentation in January 2019, he was diagnosed firstly SEORA with lung rheumatoid nodules and suspected subcutaneous rheumatoid nodules, secondly multifactorial osteoporosis related to smoking, alcohol and coffee consumption, denutrition and SEORA and thirdly adenomyoma of prostate. He was discharge with appropriate medication. He discontinued on his own initiative. After 5 months, he was hospitalized with pain and stiffness in the larger joints predominantly in the shoulder joint and hip joint then in the smaller joints. He reported additionally headache predominantly over the right temple, which was accompanied with blurred vision and jaw claudication. Physical findings included tenderness in the shoulder with limited abduction and in the hip; right temporal artery tenderness with weak pulse. The inflammatory workup showed that the erythrocyte sedimentation rate (ESR) was 140 mm at the first hour and the blood C-reactive protein level was 83.1 mg per. Electropheresis of protein noted albumin at 29, 61 g/l and alpha2 globuline 08 g/l and. Anti-body anti-nuclear was slightly positive with 1. 00 UE. Serum levels of rheumatoid factor (RF) and anti-citrullinated peptides antigens were in the normal ranges. Other immunogical tests were negative. Right temporal artery ultrasound showed some images calcifications. Temporal arterial biopsy results confirmed the diagnosis of giant-cell arteritis. Serum prostate-specific antigen (PSA) was 100 nanograms per deciliter. Abdominal computerized tomography showed a volumous prostate with 49 mm × 49 mm volume. Histological

examination concluded to adenomyoma of the prostate associated to the prostatitis. Multifactorial osteoporosis associated with SEORA with lung rheumatoid nodules and suspected subcutaneous rheumatoid nodules as autoimmune disease, giant cell arteritis with polymyalgia rheumatica as autoinflammatory disease and adenomyoma of prostate as inflammatory disease of undetermined mechanism was raised. Temporal arterial biopsy results confirmed the diagnosis of giant cell arteritis. Further, giant cell arteritis was retained on basis of ACR 1990 criteria. Polymyalgia rheumatica was retained according to EULAR/ACR 2012 Criteria. Acute *Escherichia coli* prostatitis was considered as an acute-onset disease on day five. ***Conclusion*:** This case has some interesting aspects; firstly, the first description of the interrelated type of diseases within IMIDs which is a SEORA with lung rheumatoid nodules and suspected subcutaneous rheumatoid nodules as autoimmune disease, Giant cell arteritis with polymyalgia rheumatica as autoinflammatory disease and adenomyoma of prostate as inflammatory disease of undetermined mechanism, secondly it should raise their pathogenic relationship, thirdly their association with osteoporosis should be more explored.
Keywords: SEORA, Osteoporosis, GCA, PMR, Adenocarcinoma of Prostate.

INTRODUCTION

Immune-Mediated Inflammatory Diseases (IMIDs) are characterized by three nosological entities and their nosological sub-entities: (i) autoimmune diseases (systemic autoimmune diseases, organ-specific autoimmune diseases), (ii) autoinflammatory diseases (monogenic autoinflammatory diseases, polygenic autoinflammatory diseases: "systemic" polygenic autoinflammatory diseases and "organ-specific" polygenic autoinflammatory diseases) and (iii) inflammatory diseases of undetermined mechanism (neoplasms, paraneoplastic syndromes and inflammatory diseases of iatrogenic origin) [1].

Some autoimune diseases are known to be interrelated type of diseases such mixed connective tissue diseases, multiple autoimmune syndrome and also some autoimmune and autoinflammatory diseases as giant cell arteritis, polymyalgia rheumatica, and SEORA [2-4].

Here, to our knowledge, we report the first suspected case of interrelated type of diseases within the three nosogical entities of immune-mediated inflammatory diseases (seronegative for elderly onset rheumatoid arthritis (SEORA) as autoimmune disease, giant cell arteritis with polymyalgia rheumatica as autoinflammatory disease and adenomyoma of prostate as inflammatory disease of undetermined mechanism) associated with multifactorial osteoporosis and an acute-onset disease diagnosed in a sexagenarian man.

CASE DESCRIPTION

A 60-year-old man, alcoholic, smoker with 20 pack-years, coffee consumer, he had no personal or family history of diabetes mellitus, renal or cardiovascular diseases. At his first presentation in January 2019, he was diagnosed firstly seronegative for elderly onset rheumatoid arthritis (SEORA) with lung rheumatoid nodules and suspected subcutaneous rheumatoid nodules, secondly multifactorial osteoporosis related to smoking, alcohol and coffee consumption, denutrition and SEORA and thirdly adenomyoma of prostate. He was discharge with appropriate medication. He discontinued on his own initiative. After 5 months, he was hospitalized with pain and stiffness in the larger joints predominantly in the shoulder joint and hip joint then in the smaller joints. He reported additionally headache predominantly over the right temple, which was accompanied with blurred vision and jaw claudication.

Physical findings included body mass index at 12, 12 kilogram per square meter; a tenderness of majority of joints more remarkable in the shoulder with limited abduction and in the hip and diffuse bone pain on palpation, and a diffuse amyotrophy with positive Tabouret sign in osteo-articular examination; mobile and painless subcutaneous nodules on the elbows and trunk in dermatological examination; right temporal artery tenderness with cord like temporal artery on palpation with weak pulse in cardiovascular examination; and an augmentation of prostate volume at the digital rectal examination.

The blood count showed a hemoglobin level of 8.7 g per deciliter, the mean corpuscular volume was 92.5 femtoliter, and the mean corpuscular hemoglobin concentration was 32 picograms. The inflammatory workup showed that the erythrocyte sedimentation rate (ESR) was 140 mm at the first hour (normal range, 0 to 29 millimeter) and the blood C-reactive protein level was 83.1 mg per liter (normal value, < to 6 mg per liter). Electrophoresis of protein noted albumin at 29, 61 g/l and alpha2 globulin 08 g/l and. Filtration glomerular rate (FGR) was 90, 36 ml/min. Anti-body anti-nuclear was slightly positive with 1. 00UE. Serum levels of rheumatoid factor (RF) and anti-citrullinated peptides antigens (ACPA) were in the normal ranges. Other immunogical tests were negative. Uric acid was normal. Tumor markers were normal. Right temporal artery ultrasound showed some images calcifications. Temporal arterial biopsy results confirmed the diagnosis of giant-cell arteritis. Serum prostate-specific antigen (PSA) was at 100 nanograms per deciliter. Abdominal computerized tomography showed a volumous prostate with 49 mm × 49 mm volume. Histological examination

concluded to adenomyoma of the prostate associated to the prostatitis.

At his first presentation, histological examination of subcutaneous or percutaneous biopsy of nodules was not performed. A diffuse demineralization, joint space loss and diffuse soft-tissue swelling were noted on x-rays of the left knee (figure 1). Thoracic computerized tomography demonstrated three thick-walled cavitory lung nodules (two in left lung fields, 17×12 mm and 10×08 mm and one in right lung fields, 12×09 mm). X-Ray of the full-leg and hip showed a diffused osteodensation. In the bone mineral density, total hip T-score was - 3, 6 and total femoral T-score was - 3, 1. Calcium and 25-hydroxyvitamin D dosages were without abnormalities.

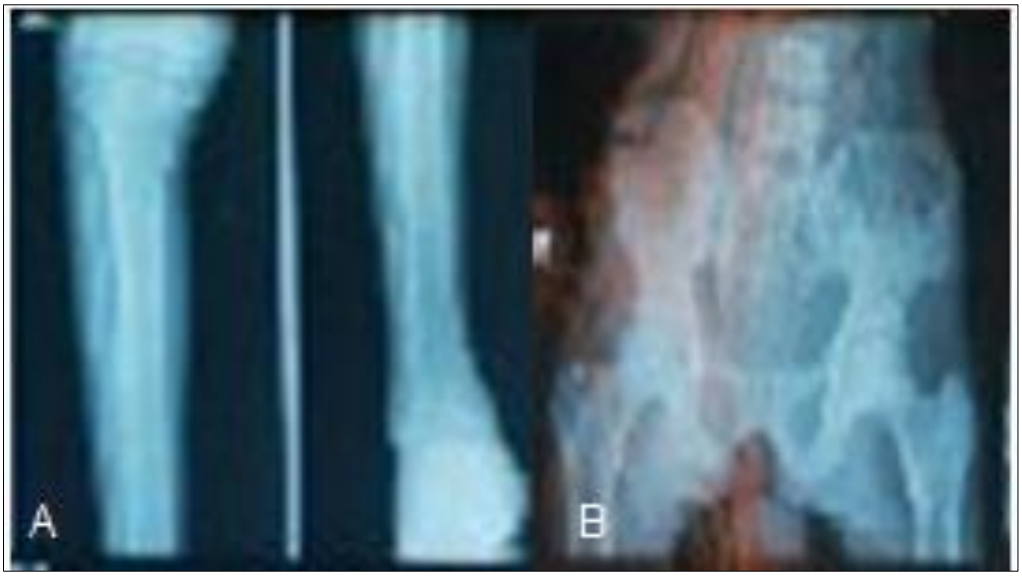

Figure 1: A diffuse demineralization, joint space loss and diffuse soft-tissue swelling were noted on x-rays of the left knee (A) and of the pelvis (B)

Multifactorial osteoporosis associated with SEORA with lung rheumatoid nodules and suspected subcutaneous rheumatoid nodules as autoimmune disease, giant cell arteritis with polymyalgia rheumatica as autoinflammatory disease and adenomyoma of prostate as inflammatory disease of undetermined mechanism was considered.

With EORA, tobacco use, alcohol and coffee consumption, denutrition, and sedentarity, we had been discussed multifactorial osteoporosis at his first presentation. Temporal arterial biopsy results confirmed the diagnosis of giant cell arteritis. Further, giant cell arteritis was retained on basis of ACR 1990 criteria (table 1) [5]. In addition, Giant-cell arteritis was known to be associated to osteoporosis. With a rapid clinical response obtained by corticoid treatment, pain in the shoulder and in the hip; elevated erythrocyte sedimentation rate in the first hour, a 60-year-old and histological confirmation of giant cell arteritis, polymyalgia rheumatica was retained according to EULAR/ACR 2012 Criteria (table 2) [6].

Table 1: Criteria of American Colleges of Rheumatology 1990 criteria for classification of Giant Cell Arteritis (GCA) found in our patient

Criterion	Our Patient
Age at disease onset ≥ 50 years	60-year-old man
New headache	Headache predominantly over the right temple
Temporal artery abnormality	Right temporal artery tenderness with weak pulse
Elevated erythrocyte sedimentation rate	ESR 140 mm at first hour
Abnormal artery biopsy	Temporal arterial biopsy results confirmed the diagnosis of GCA
Finaly, Our patient presented the five criteria, thus we retained the diagnosis of GCA	

Table 2: Criteria of 2012 classification criteria for polymyalgia rheumatica (PMR) found in our patient

Criterion	Our Patient
Required criteria	
Age 50 years or older	60-year-old man
Bilateral shoulder aching	Pain in the larger joints predominantly in the shoulder joint and hip joint
Abnormal CRP and/or ESR	ESR 140 mm at first hour and CRP 83. 1 mg/l
Criteria without ultasound	
Morning stiffness duration >45 min (2 points)	Morning stiffness lasting at least one hour in the larger joints predominantly in the shoulder joint and hip joint (2 points)
Hip pain or limited range of motion (1 point)	Tenderness in the shoulder with limited abduction and in the hip (1 points)
Absence of RF or ACPA (2 points)	Serum levels of rheumatoid factor (RF) and anti-citrullinated peptides antigens (ACPA) were in the normal ranges (2 points)
Absence of other joint involvement (1 point)	Pain and stiffness in the smaller joints (0 points)
Finaly, We found five points in our patient, thus we retained the diagnosis of PMR.	

The treatment with prednisone at a dose of 1 mg per kilogram of body weight a day with 1-year tapering course associated with adjuvant treatments, methotrexate 7.5 mg a week associated with folic acid 5 mg with 15 mg a week, and analgesic drugs with rapid regression of some symptoms such as a right side temple tenderness and pain in the joints. Antithrombotic drug was administered for thromboprohylaxis. Renutrition prescriptions and anti-osteoporotic treatment were maintained.

At the day five, the patient complained fever. The physical examination revealed a temperature of 38.1°C, a heart rate of 94 beats per minute, a respiratory rate of 28 cycles per minute. Pulmonary examination noted bilateral crakling rales and genito-urinary examination revealed a dark and cloudy urine, and an augmentation of prostate volume at the digital rectal examination. A diagnosis of an acute-onset disease as acute prostatitis and pneumonia were raised. Cytobacteriological examination of sputum was negative. Bacterial urinary test isolated *Escherichia coli* was sensitive to colistin, and ciprofloxacin. Ciproflaxin was prescribed. At the day ten, the patient was discharged against medical advice and then he died a week later.

DISCUSSION

This case reports a case of giant cell arteritis with polymyalgia rheumatica (auto-inflammatory disease) with 6-month history of diagnosed multifactorial osteoporosis associated with SEORA with lung rheumatoid nodules and suspected subcutaneous rheumatoid nodules (autoimmune disease) and adenomyoma of prostate (inflammatory disease of undetermined mechanism) revealed by pain and stiffness in the larger joints predominantly in the shoulder joint and hip joint then in the smaller joints; headache predominantly over the right temple; blurred vision; and jaw claudication. In addition, there were an acute-onset disease occurred in day five which is an acute *Escherichia coli* prostatitis.

To our knowledge, it is the first reported suspected interrelated type of disease within IMIDs.

Patient Presented Giant Cell Arteritis with Polymyalgia Rheumatica

Giant Cell Arteritis

Giant cell arteritis is a systemic inflammatory vasculitis of unknown etiology that occurs in older persons and can result in a wide variety of systemic, neurologic, and ophthalmologic complications. Giant cell arteritis is a granulomatous necrotizing arteritis with a predilection for large and medium sized arteries. It is considered to be uncommon in the black race with very few reports from Africa [7]. The present case is reported in Malian sexagenarian man. The gold standard diagnostic modality for GCA is temporal artery biopsy and the histopathologic findings shows transmural inflammator infiltrates with numerous multinucleated giant cells, the vascular lumen get narrowed by concentric intimal hyperplasia [8]. Temporal arterial biopsy results in our patient confirmed the diagnosis of giant-cell arteritis.

Polymyalgia Rheumatic

Polymyalgia rheumatica is a common inflammatory rheumatic disease of older individuals and a common indication for long-term corticosteroid therapy. There is no diagnostic laboratory test, inflammatory markers are not specific, and clinicians

often turn to the corticosteroid response as a 'test of treatment' to establish the diagnosis [6-9]. To diagnose the polymyalgia rheumatica, the EULAR/ACR 2012 for polymyalgia rheumatica classification Criteria is the most commonly used [6]. We found five point in our patient (table 2).

Giant Cell Arteritis with Polymyalgia Rheumatic

Polymyalgia rheumatica and giant cell arteritis are related inflammatory disorders occurring in persons aged 50 years and older [10]. More than a fifth of the pure PMR patients had US findings consistent with subclinical giant cell arteritis [11]. In this present work, we report a case of giant cell arteritis with polymyalgia rheumatic.

Patient Presented 6-Month History of Diagnosed SEORA with Lung Rheumatoid Nodules and Suspected Subcutaneous Rheumatoid Nodules

Elderly-onset rheumatoid arthritis (EORA) is, by definition, a rheumatoid arthritis (RA) developing in persons >60 years of age. Recent studies have confirmed that RA is among the most common inflammatory disease in older age groups, with a 2% prevalence. When rheumatoid factor (RF) and anticitrullinated peptide/protein antibodies (ACPA) are absent, seronegative EORA (SEORA) is diagnosed [12-14]. Moreover, Pulmonary rheumatoid nodules are a rare complication of rheumatoid arthritis, and complications of rheumatoid nodules are scant in literature [15]. SEORA complicated by both lung rheumatoid nodules and suspected subcutaneous rheumatoid nodules was considered in our patient.

Patient Presented 6-Month History of Diagnosed Adenomyoma of Prostate

The benign prostate tumours are dominated by prostatic adenomyoma. They are the first uro-genital pathology worldwide. The average age of the patients is 75.5 years. The prostate specific antigen (PSA) is high among more than 80% [16]. Our patient presented an elevated serum prostate-specific antigen (PSA) at 100 nanograms per deciliter; a volumous prostate with 49 mm × 49 mm volume in abdominal computerized tomography; an adenomyoma of the prostate associated to the prostatitis on histological examination.

Patient Presented 6-Month History of Diagnosed Multifactorial Osteoporosis

Osteoporosis is a skeletal disorder characterized by compromised bone strength, which predisposes the individual to an increased risk of fractures of the hip, spine, and other skeletal sites [17]. Many risk factors are associated with osteoporotic fracture, including low peak bone mass, hormonal factors, the use of certain drugs (eg, glucocorticoids), cigarette smoking, low physical activity, low intake of calcium and vitamin D, race, small body size, and a personal or a family history of fracture [17]. These risk factors are associated with osteoporotic fracture in our patient include: GCA, EORA, tabacco use, alcohol and coffee consumption, denutrition, and sedentarity.

Patient Presented Acute-Onset Disease Occurred in Day Five Which is an Acute *Escherichia Coli* Prostatitis

Acute conditions are severe and sudden in onset [18]. Moreoever, Acute diseases refer to a medical condition that occurs suddenly and lasts for a shorter period of time [19]. The common cause of acute diseases is either an infection or a virus. Besides, an injury caused by an accident or a fall, or by the misuse of medications or drugs can also contribute to the occurrence of acute diseases [20]. Here, Our patient present, as an acute-onset disease, the bacterial infection.

Interrelated Type of Disease within IMIDs

The known interrelated type of disease such mixed connective tissue diseases and multiple autoimmune syndrome were well-described. In addition, giant cell arteritis, polymyalgia rheumatic, and SEORA are currently known to be interrelated type of diseases with simultaneously or consecutively onset [2]. Thus these are part of immune-mediated inflammatory diseases (IMIDs). We suspect the first case of interrelated type of disease within IMIDs, which is a SEORA with lung rheumatoid nodules and suspected subcutaneous rheumatoid nodules as autoimmune disease, Giant cell arteritis with polymyalgia rheumatica as autoinflammatory disease and adenomyoma of prostate as inflammatory disease of undetermined mechanism. Upon this epidemiological relationship, the pathogenic relation should be more explore. The diagnosis of a nosogical entity of IMIDs should lead to explore the two others nosological entities and osteoporosis condition should be assessed.

In perspectives, efforts must carry out on research about nosological constellation in IMIDs.

CONCLUSION

This case has some interesting aspects; firstly, the first description of the suspected interrelated type of diseases within IMIDs which is a SEORA with lung rheumatoid nodules and suspected subcutaneous rheumatoid nodules as autoimmune disease, Giant cell arteritis with polymyalgia rheumatica as autoinflammatory disease and adenomyoma of prostate as inflammatory disease of undetermined mechanism, secondly it should raise their pathogenic relationship, thirdly their association with osteoporosis should be more explored.

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