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Case Report

Adult onset still's disease in a 60 year old male patient with fever of unknown origin and chronic diarrhea

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مريض بداء ستيل عمره ستون عاما , يعاني من حمى مجهولة المنشأ و إسهال مزمن

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قسمي الباطنية والروماتيزم- كلية الطب- جامعة أم القرى- مكة المكرمة- المملكة العربية السعودية مستشفى الملك فيصل التخصصي - جدة

الملخص العربي

قمنا بكتابة وصفية لحالة لمريض سعودي يبلغ من العمر 60 عاماً مصاباً بداء ستيل. كان المريض يشكو من حمى مجهولة المنشأ, طفح جلدي, التهاب في الحلق, نقص في الوزن, التهاب في المفاصل و إسهال مزمن. الإسهال المزمن لم يذكر في البحوث الوصفية السابقة كأحد الأعراض السريرية لمرض ستيل.

كانت نتائج تحاليل الأمصال سالبة, اما مختبر التشريح فقد اتضح وجود التهاب جلدي وعائي و التهاب بسيط في القولون. ولقد تمت السيطرة على المرض بإعطاء المريض علاج الكوتيزون و الميثوتريكسات.

ABSTRACT

Abstract

We report a case of Adult onset Still's disease (AOSD) in a 60 year old Saudi male patient. He presented with fever of unknown origin, skin rash, sore throat, weight loss, arthritis and chronic diarrhea. Chronic diarrhea was not listed as one of the manifestations in several large case series of AOSD. Serological tests were negative. Pathological findings revealed cutaneous inflammatory vascular reaction and mild colitis. The disease has been successfully controlled with prednisone and methotrexate.

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Keywords*: *Stills disease, Fever of unknown origin, Chronic diarrhea.

INTRODUCTION

Adult onset Still's disease (AOSD) is a rare, systemic inflammatory disease of unknown etiology, characterized by daily high spiking fevers, evanescent rash and arthritis [1,2]. There are several gastrointestinal manifestations reported with AOSD. Chronic diarrhea was not listed as one of these manifestations in several large case series [3,7]. We report a case of AOSD in a 60 year old Saudi male patient with synchronous onset of gastrointestinal symptoms including chronic diarrhea.

CASE REPORT

A 60 year old Saudi male patient known to have diabetes mellitus and hypertension was referred to our hospital as a case of fever of unknown origin. He presented initially to his local health authorities with history of sore throat and recurrent upper respiratory tract symptoms. He sought medical advice and received a course of antibiotic therapy but without benefit. Detailed history at time of his presentation to our hospital revealed one month history of fever, sore throat, diarrhea, left knee joint pain and swelling and generalized fatigability. His body temperature was reported to reach 38 - 40 degrees Celsius on several occasions during the day. Diarrhea was watery and large in amount, three to four times daily and contained no mucus or blood. He had no prior history of diarrheal illnesses before. There was mild epigastric discomfort but no history of jaundice or hepatitis exposure. He had significant weight loss of around 20 kg during this period. He complained of migratory joints pains but persistent left knee pain and swelling that affected his activity level. He also described an intermittent, macular skin rash that occasionally may accompany his fevers. It was salmon-colored that may involve arms, trunk, face and knees. It only lasted a day or two maximum. The patient was exposed to raw camel milk ingestion and was treated in a peripheral hospital as a case of brucellosis with no improvement. He is a bus driver with no history of contact with sick patients including tuberculosis and no history of mosquito bites. His medications include gliclazide, lizinopril, simvastatin and aspirin.

Physical examination revealed the presence of tachycardia with heart rate at 112 beats per minute and temperature 36.8. The salmon-colored macular rash was present on several parts of his body during hospitalization; face trunk and extremities particularly during febrile attacks. His pharynx was mildly congested and erythematous. There was no abdominal tenderness and no organomegaly or lymphadenopathy. There was joint line tenderness in several metacarpophalangeal (MCP) and wrist joints bilaterally. His shoulder joints were both tender on active and passive range of motion. There was joint line tenderness in his left knee with significant amount of effusion. He had no signs of infective endocarditis. The rest of the examination was unremarkable.

Routine laboratory investigation showed the following: ESR 98 mm/hour, CRP 66.3 mg/litre, WBC 6.17/ UL (28000/UL in the report requested from the previous hospital with a 83% neutrophilic predominance), hemoglobin 12.6 g/dL, platelets 328000/UL, an extremely high ferritin level of 17234 ng/mL, serum albumin 2.7 g/dL, ALT 15 U/L, ALP 61 U/L, Brucella titer was negative, Cultures were negative for microorganisms, antinuclear antigen and rheumatic factor were all negative as well. Synovial fluid examination obtained from left knee showed turbid appearance with WBC count of 6600/mm3. It was predominantly neutrophils and negative for malignant cells and crystals. A pelvi-abdominal ultrasound and an abdominal CT scan shows hepatomegaly with fatty changes and no lymphadenopathy. A radiograph of the hands and knees were normal with mild osteoarthretic changes and joint effusion of both knees. Skin biopsy was taken and histopathology showed inflammatory vascular reaction. There was no major abnormalities detected with upper and lower gastrointestinal endoscopy. Histopathological examination revealed chronic gastritis and mild colitis.

After establishment of the diagnosis a course of prednisone 1mg/kg was initiated in addition to methotrexate 10 mg weekly. During clinic visits an obvious improvement of his symptoms was noticed, his CRP declined to 6.40 – 0.91 mg/L and ferritin level dropped steadily from 2055 to 1146 ug/L. His last clinical visit 9 months after initial presentation showed maintained clinical improvement with no symptoms on prednisone 15 mg daily and methotrexate 17.5 mg weekly. CRP and ferritin level were normalized.

DISCUSSION

AOSD usually presents with a variety of clinical symptoms, including quotidian fever, rash, arthritis, lymphadenopathy, and splenomegaly.[8] There are other symptoms mostly related to pharyngitis, hematologic, cardiopulmonary and hepatic involvement. Fever is the dominant symptom and infectious etiologies must always be ruled out. AOSD represents the most frequent etiology among connective tissue diseases causing fever of unknown origin.[5]

There are variable gastrointestinal manifestations of AOSD. Liver abnormalities, predominantly hepatomegaly and elevated liver enzymes are present in approximately 50-75% of patients.[6,9] Several observations of severe hepatitis have been reported [9-11] justifying strict monitoring of liver enzymes in these patients.[9, 12, 13] It is not believed that AOST can coexist with autoimmune hepatitis.[14,15] Use of non-steroidal anti-inflammatory drugs may be a significant cofactor [6, 9]. Splenomegaly has been reported in 52% of cases, while weight loss (>10%) in 76% of cases [6, 16]. Abdominal pain as a feature of AOSD was underreported, it

has been described in only 12% of cases worldwide,[17] but in one report it has been present in approximately 50% of patients and it can simulate a surgical abdomen in severe cases.[6, 17]

In the case described here there was hepatomegaly but normal liver enzymes and no splenomegaly. There was significant weight loss and chronic diarrhea. Chronic diarrhea has never been reported as one of the gastrointestinal features of AOSD. In addition, AOSD was not listed as a possible cause to consider in the diagnostic workup for patients with chronic diarrhea.[18] The associated mild colitis reported with this case may be related to AOSD or just a non-specific mild form of idiopathic colitis. All symptoms reported with this case including chronic diarrhea responded well to high dose steroid and methotrexate therapy.

AOSD affects young people and has a bimodal age distribution with two peaks-at 15-25 and 36-46 years of age.[19] It is generally considered a disorder of youth, but there are several reports of AOSD in the elderly.[20,22] Low-grade and atypical pattern of fever is sometimes seen in older patients,[23] otherwise no major differences in clinical manifestations have been observed. Good response to steroid therapy and use of low dose methotrexate has been observed in these reports consistent with our findings in the case presented.

Other features presented in this case are similar to common features reported with AOSD in the literature. Sore throat is known as a cardinal sign of AOSD and may be associated with odynophagia.[24] The most common joints involved in AOSD are the knees, wrists, ankles and elbows. [25] Our patient had arthritis affecting his left knee, wrists, several MCPs, shoulders and hip joints. The classical destructive form of arthritis that affects the carpal joints was not observed in the patient presented. It is reported that destructive arthritis of the hips occurs in 5% to 33% of patients.[6] Joint fluid aspirate often discloses marked leukocytosis with a neutrophilic predominance[26] consistent with the observation in the case presented. The reported rash for the case presented with maculopapular, salmon-pink eruption which appeared during febrile attacks was classical. Skin biopsy findings in the literature, as in the case presented, usually shows nonspecific and mild perivascular inflammation.[27] Hyperferritinemia in AOSD is not related to iron metabolism and is likely to be a consequence of cytokine secretion induced by the reticuloendothelial system or hepatic damage.[28,29] A fivefold increase in serum ferritin has 41% specificity and 80% sensitivity for the diagnosis of AOSD.[30] The levels correlate with disease activity as was demonstrated in our case. The constellation of clinical manifestations in the case presented has met the Yamaguchi's classification criteria for AOSD.[31] Several drugs have been used in the treatment of AOSD from multiple case reports and small scale retrospective studies. In general most patients will require corticosteroids treatment at some point in their disease course, with responses ranging from 76 to 95%.[1] Methotrexate was particularly found effective in patients with arthritis and joint destruction.[21,32] Drugs like azathioprine, cyclosporine, cyclophosphamide and biological therapies like infliximab, etanercept, anakinra have all been used in management of AOSD with favorable outcomes.[33]

We reported an elderly patient with classical manifestations of AOSD in addition to chronic diarrhea. We would like to remind clinicians to consider autoimmune diseases like AOSD in the diagnostic workup of patients with chronic diarrhea. In addition, AOSD should be considered in the differential diagnosis of elderly patients presenting with fever of unknown origin. AOSD in the elderly responded well initially to prednisone and methotrexate.

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