



REVISTA BRASILEIRA DE REUMATOLOGIA

www.reumatologia.com.br



Case report

Adult Still's disease associated with ovarian cancer - case report

Lilian Schade^{a,*}, Scheila Fritsch^a, Arthur Conelian Gentili^b, Lucia de Noronha^b,
Valderílio Feijó Azevedo^a, Eduardo dos Santos Paiva^a

^aService of Rheumatology, Hospital das Clínicas, Universidade Federal do Paraná, Paraná, PR, Brazil

^bService of Pathological Anatomy, Hospital das Clínicas, Universidade Federal do Paraná, Paraná, PR, Brazil

ARTICLE INFO

Article history:

Received on September 15, 2011

Accepted on May 14, 2013

Keywords:

Late-onset Still's disease

Ovarian neoplasms

Paraneoplastic syndromes

Palavras-chave:

Doença de Still de início tardio

Neoplasias ovarianas

Síndromes paraneoplásicas

ABSTRACT

We report a case of adult-onset Still's disease in a female patient with fever, myalgia, vanishing rash and bilateral inguinal lymphadenopathy, diagnosed after extensive workup to exclude other rheumatic, infectious and neoplastic diseases. The patient initially responded to corticosteroid therapy, but progressed to increased lymph nodes size that when biopsied, revealed serous ovarian adenocarcinoma. To our knowledge, this is the first report of ovarian neoplasm associated with adult-onset Still's disease.

© 2013 Elsevier Editora Ltda. All rights reserved.

Doença de Still do Adulto associada à neoplasia de ovário - relato de caso

RESUMO

Relatamos um caso de diagnóstico de Doença de Still do Adulto (DSA) em paciente feminina com febre, mialgia, rash cutâneo fugaz e linfonodomegalia inguinal bilateral, após extensa investigação para exclusão de outras doenças reumatológicas, infecciosas e neoplásicas. A paciente inicialmente apresentou resposta ao tratamento com prednisona, porém evoluiu com aumento de volume de linfonodos inguinais, cuja biópsia revelou adenocarcinoma seroso de ovário. De acordo com nosso conhecimento, esse é o primeiro relato de neoplasia ovariana associada ao diagnóstico de DSA.

© 2013 Elsevier Editora Ltda. Todos os direitos reservados.

Case report

Female patient, 37 years, reported to have suffered in the past two months from fever, myalgia, fleeting rash, and bilateral inguinal lymphadenopathy (2-3 cm). She had a history of hypothyroidism treated with levothyroxine and resection of endocervical polyp (anatomopathological analysis compatible with polyp, without further specification). In the investi-

gation, she had mild normocytic and normochromic anemia without evidence of hemolysis; 13,240 leukocytes; 1,390 lymphocytes; 483,000 platelets; normal CPK; ESR = 67 mm in 1 h, C-reactive protein = 7.74 (reference value [RV] < 0.5), ferritin = 353 ng/mL (RV = 4.63 to 204), ANF 1:320; nuclear dense fine speckled (DFS) pattern; positive anti-Ro; negative anti-Sm; anti-RNP and anti-DNA; normal C3 and C4; two negative blood cultures, one negative urine culture; negative serology for human immunodeficiency virus (HIV), cytomegalovirus,

* Corresponding author.

E-mail: lilianschade@yahoo.com.br (L. Schade).

Epstein Barr virus, toxoplasmosis, leptospirosis and hepatitis; and negative VDRL.

The echocardiogram showed a small pericardial effusion without vegetations. Tomography of the chest and abdomen, upper endoscopy, and thyroid ultrasound presented normal results. Increased uterine volume was observed at pelvic tomography and transvaginal ultrasound (probable uterine myoma). Hand X-rays showed no erosions. The diagnosis of Adult Still's disease (ASD) was made, and the patient was started on prednisone 0.5 mg/kg/day. The patient presented clinical improvement. Attempts to reduce the dose of corticosteroids were not successful due to the reappearance of fever, even though the patient was receiving methotrexate 15 mg/week. During evolution, the patient showed increased volume of the bilateral inguinal lymphadenopathy (approximately 9 cm), which became painful, hardened, and adhered. The dose of prednisone was increased again to 0.5 mg/kg/day and associated to a non-steroidal anti-inflammatory drug (NSAID), unsuccessfully.

A biopsy of the right inguinal lymph node was performed, and the histological and immunohistochemical report was compatible with serous ovarian adenocarcinoma (Figs. 1 and 2). A new pelvic ultrasound was performed, which showed enlarged left ovary (46×34 mm) with characteristics suggestive of neoplastic infiltration. It was decided to start chemotherapy with carboplatin and paclitaxel. The patient underwent six cycles and showed good response, as shown by a reduction in CA 125 from 7,312 to 34 and decrease in volume of the inguinal lymph nodes. A cytoreductive surgery is planned.

Introduction

ASD is a rare systemic inflammation of unknown etiology, related to hyperactivation of Th1 lymphocytes. It is characterized by fever, fleeting rash, and arthritis. Other manifestations that are often found are lymphadenopathy, splenomegaly, myalgia, sore throat, and neutrophilic leukocytosis.¹ The diag-

nosis is clinical and requires exclusion of infectious diseases, cancer, and other autoimmune diseases; there are no specific histological or laboratory findings. The inflammatory activity is high, and antinuclear and rheumatoid factors are often negative.¹ A high level of serum ferritin can be useful for the diagnosis and act as a marker of disease activity.¹⁻³

Different diagnostic criteria have been proposed, but none have been accepted.^{1,3} The clinical course can be divided into self-limited or monophasic, intermittent or polycyclic systemic, and chronic articular.^{1,2} Treatment consists of NSAIDs, corticosteroids, and steroid-sparing drugs, such as methotrexate.^{1,4,5}

Discussion

Among the several differential diagnoses of ASD, neoplasms are among the main possibilities to be ruled out. Several neoplasms mimicking ASD have been described. Lymphoma is one of the main differential diagnoses, as lymphadenopathy and splenomegaly are common manifestations of ASD and histological findings may be similar.^{6,7} ASD has also been described in the course of myeloid leukemia,⁸ as paraneoplastic syndrome in breast cancer,⁹⁻¹¹ and in association with esophageal cancer,¹² papillary thyroid carcinoma,¹³ and hepatic angiosarcoma.¹⁴ The differentiation between concomitant diagnoses and paraneoplastic syndrome is not simple. The response to corticosteroid therapy or specific neoplastic treatment response may help in the differentiation, but the variable clinical course of ASD, as well as the therapeutic prognosis of neoplasia, may complicate this interpretation.

This study reported a case of ASD diagnosis in a patient with symptoms suggestive of the disease, after extensive investigation to exclude other rheumatologic, infectious, and neoplastic diseases. The patient initially responded to treatment with 0.5 mg/kg/day of prednisone, but developed increase in inguinal lymph nodes, whose biopsy showed the presence of serous ovarian adenocarcinoma. To the authors'

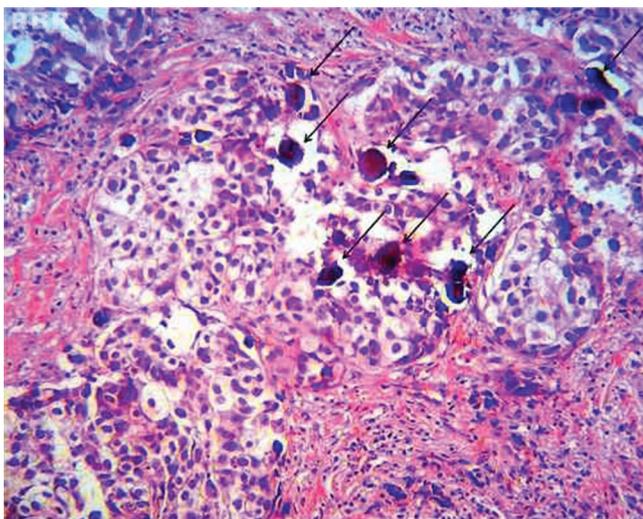


Fig. 1 – Lymph node biopsy, H&E, 100×. Fibroconnective tissue infiltrated by poorly differentiated carcinoma with psammomatous bodies (arrows).

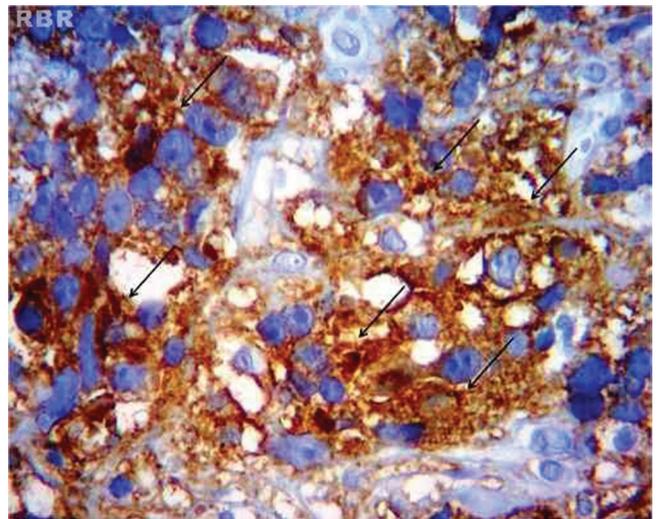


Fig. 2 – Lymph node biopsy, immunohistochemistry for CA 125, 400×. Tumor cells showing membranous and cytoplasmic positivity (arrows).

knowledge, this is the first report of ovarian cancer associated with the diagnosis of ASD.

Paraneoplastic syndromes associated with ovarian epithelial neoplasms described to date are nervous system (cerebellar degeneration, polyneuropathy), collagen (dermatomyositis), hematologic (hemolytic anemia, disseminated intravascular coagulation), and skin (acanthosis) disorders, as well as nephrotic syndrome.¹⁵ Autoimmunity is one of the proposed physiopathological mechanisms for paraneoplastic syndrome related to ovarian cancer, due to the evidence of circulating immune complexes, autoantibodies against cerebellar Purkinje cells, and therapeutic response to plasmapheresis in some cases.¹⁵

When evaluating the abovementioned case, regarding whether it was a paraneoplastic syndrome or a concomitant diagnosis of ovarian neoplasm and ASD, the excellent therapeutic response to corticosteroids of the fever, rash, and myalgia symptoms led to the initial conclusion of concurrent diagnoses. However, the fact that the patient had an inguinal lymphadenomegaly at the disease onset, although with inflammatory features, followed by an increase in volume in the presence of corticosteroids, contradicted the possibility of concurrent diagnoses and favored that of paraneoplastic syndrome, which the authors believe to be more likely.

It is necessary to perform a thorough investigation of differential diagnosis in suspected ASD, as well as to monitor the clinical course of patients regarding response to treatment and appearance of new findings that may raise suspicion of another diagnosis, including cancer.

Conflicts of interest

The authors declare no conflicts of interest.

REFERENCES

- Bagnari V, Colina M, Ciancio G, Govoni M, Trotta F. Adult-onset Still's disease. *Rheumatol Int*. 2010;30(7):855-62.
- Colina M, Zucchini W, Ciancio G, Orzincolo C, Trotta F, Govoni M. The evaluation of adult-onset Still's disease: a observational and comparative study in a cohort of 76 italian patientes. *Semin Arthritis Rheum*. 2011;Mar(4).
- Jiang L, Wang Z, Dai X, Jin X. Evaluation of clinical mensures and different criteria for diagnosis of adult-onset Still's disease in a chinese population. *J Rheumatol*. 2011;Feb(1).
- Kim HA, Sung JM, Suh CH. Therapeutic responses and prognosis in adult-onset Still's disease. 2011;Jan(29).
- Manger B, Rech J, Schett G. Use of methotrexate in adult-onset Still's disease. *Clin Exp Rheumatol*. 2010; 28(5 suppl 61): S168-71.
- Sono H, Matsuo K, Miyazato H, Sakuguchi M, Matsuda M, Hamada K et al. A case of adult-onset Still's disease complicated by non-Hodgkin's lymphoma. *Lupus*. 2009;9(6):468-70.
- Trotta F, Dovigo L, Scapoli G, Cavazzini L, Castoldi G. Immunoblastic malignant lymphoma in adult-onset Still's disease. *J Rheumatol*. 1993;20(10): 1788-92.
- Nakagawa Y, Furusyo N, Taniai H, Henzan H, Tsuchihashi T, Hayashi J. Chronic myelogenous leukemia that occurred two years after the diagnosis of adult Still's disease. *Int Medicine*. 2005;44(9): 994-7.
- Neishi J, Tsukada Y, Maehara T, Ueki K, Maezawa A, Nojima Y. Adult Still's disease as a paraneoplastic manifestation of breast cancer. *Scand J Rheumatol*. 2000;29(5):328-30.
- Rogues AM, Vidal E, Boudinet F, Loustaud V, Arnaud M, Liozon F. Brest câncer with systemic manifestations mimicking Still's disease. *J Rheumatol*. 1993;20(10):1786-7.
- Komano Y, Kubota T, Wakabayashi S, Ochi S, Nonomura Y, Hagivama H et al. A case of paraneoplastic syndrome mimicking adult-onset Still's disease. *Mod Rheumatol*. 2004;14(5):410-3.
- Shibuya Y, Matuo K, Kawada T, Kosugi T, Gomi T. Adult-onset Still's disease associated esophageal câncer: a case report. *Rymachi*. 2003;43(3):577-82.
- Ahn Jk, Oh JM, Lee J, Kim SW, Cha HS, Koh EM. Adult-onset Still's disease diagnosed concomitantly with occult papillary thyroid câncer: paraneoplastic manifestation or coincidence? *Clin Rheumatol*. 2010;29(2):221-4.
- Mekinian A, Lambert M, Quevrel V, Launay D, Morell-Dubois S, Hachulla E, et al. Adult-onset Still's disease and hepatic angiosarcoma, a fortuitous association or a paraneoplastic syndrome: a case-report. *Rev Med Interne*. 2008;29(11):936-9.
- Shanbhogue AK, Shanbhogue DK, Prasad SR, Surabhi VR, Fasih N, Menias CO, et al. Clinical syndromes associated with ovarian neoplasm: a comprehensive review. *Radiographics*. 2010;30(4):903-19.