

Incidental papillary thyroid cancer diagnosis in patient with adult-onset Still's disease-like manifestations

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SUMMARY

Adult onset Still's disease (AOSD) is a systemic inflammatory disease characterized primarily by a triad consisting of daily fever, arthritis and maculopapular exanthema. The pathogenesis and etiology of AOSD are unknown and the diagnosis, which can be very challenging, is often made by exclusion. Here, we report a case of a 61-year-old woman with a history of mild psoriatic arthritis, fever, arthritis and maculopapular exanthema. Her initial laboratory tests showed neutrophilic leukocytosis, hypertransaminasemia, and markedly elevated levels of the erythrocyte sedimentation rate and C-reactive protein. With a presumptive diagnosis of AOSD, based on Yamaguchi criteria, the patient started an extensive diagnostic work-up to exclude other potential differential diagnoses. With fluorodeoxyglucose (FDG) positron-emission tomography, a thyroid nodule with moderate FDG uptakes was detected. The fine needle aspiration biopsy led to diagnosis of papillary thyroid cancer. The history of psoriatic arthritis, the patient's age, and atypical features of the skin rash described as not concomitant with fever flares, suggested a diagnosis of paraneoplastic AOSD-like manifestations.

Key words: Adult onset Still's disease; Paraneoplastic; Malignancy.

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■ INTRODUCTION

Adult onset Still's disease (AOSD) is a systemic inflammatory disease characterized by evanescent salmon pink rash, sore throat, liver dysfunction, lymphadenopathy, hepatosplenomegaly, arthritis, and leukocytosis (1-3).

Since AOSD is a complex syndrome without pathognomonic clinical or laboratory signs, its diagnosis is made by exclusion through diagnostic work-up, which comprises extensive laboratory and imaging evaluation to rule out malignancies, infectious, or autoimmune conditions. There are case reports suggesting the presence of an AOSD-like syndrome in the course of leukemia, lymphoma, breast cancer, esophageal cancer, lung cancer, and thyroid cancer. Nevertheless, it is controversial whether this association is the result of a paraneoplastic syndrome or a coincidence of overlooked diagnosis of an occult malignancy (4).

■ CASE REPORT

In February 2017, a 61-year-old woman presented to our outpatient clinic with a syndrome lasting 2 weeks, characterized by sore throat, daily fever, polyarthritis involving large and small joints, and non-itchy maculopapular exanthema. The patient also reported a history of primary biliary cholangitis with persistently normal transaminases and a mild psoriatic arthritis with mono-oligoarticular pattern, treated with cycles of non-steroidal anti-inflammatory drugs and intra-articular steroid injections. The laboratory tests recommended by her family physician revealed neutrophilic leukocytosis (12,000/uL, with 88% neutrophils), marked elevation of the erythrocyte sedimentation rate (103 mm/h) and C-reactive protein (102 mg/L), normal lactate dehydrogenase (LDH) levels, mild hypertransaminasemia (AST 65 U/L and ALT 128 U/L, normal value less than 40), hyperferritinemia (412 ng/mL, normal val-

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ue 13-150) and negative serology for Epstein-Barr virus, cytomegalovirus, hepatitis B-C. Lung and cardiac examinations were unremarkable; abdomen was not tender to touch and hypochondriac organs were not palpable; no peripheral lymph nodes were palpable. The skin rash was characterized by maculopapular lesions localized on the trunk and the proximal part of lower limbs, which were described as not concomitant with fever flares (Figure 1). Medium dose oral corticosteroid was started for presumptive diagnosis of AOSD, based on Yamaguchi criteria (5), and consequently the empiric antibiotics therapy prescribed by her family physician was stopped. At the same time, an intensive diagnostic work up including chest radiograph, echocardiography and abdominal ultrasound was performed in order to rule out infections and malignancies.

The ultrasound examination of the abdomen revealed an irregular contoured hypoechogenic hepatic lesion. To further investigate the hepatic lesion, a whole-body computed tomography (CT) was performed. Abdominal CT showed an iso-hypodense solid lesion with elevated contrast enhancement in the arterial phase localized in the left lobe of the liver, consistent with focal nodular hyperplasia.

CT scan of neck displayed a calcified solid nodule in the left lobe of thyroid. In fluorodeoxyglucose (FDG) positron-emission tomography, thyroid nodule, seen on CT, showed moderate FDG uptakes, and no other abnormal FDG uptake was observed. The fine needle aspiration biopsy (FNAB) of the thyroid nodule led to diagnosis of papillary thyroid cancer (PTC).

On the basis of these findings, the patient was diagnosed with occult PTC and at the same time, she was concomitantly diagnosed with AOSD-like manifestations.

The medium dose corticosteroid therapy led to the resolution of fever, arthritis and exanthema in a week. After 14 days the patient achieved remission with the normalization of inflammatory markers. Consequently the dose of corticosteroid was tapered slowly over a period of three months, and a follow up (FU) visit was scheduled



Figure 1 - Skin rash characterized by maculopapular lesions localized on trunk and the proximal part of lower limbs.

at 3 months. Six weeks after complete remission of AOSD, thyroidectomy was performed and post-operative radioiodine therapy was planned.

At a follow up visit after 6 months, clinical and laboratory parameters confirmed complete remission.

■ DISCUSSION

Rheumatic syndromes can accompany, anticipate or follow an underlying malignancy. In some cases, therefore, they may be due to a paraneoplastic disorder, but the pathogenesis has not been elucidated in most instances. Therefore, this association has been based on plausible temporal concurrence, clinical course, and response to cancer therapy (6). Decreasing paraneoplastic rheumatic syndrome (RS) symptoms in line with the primary tumor treatment can provide an idea about the pathogenesis. There are three proposed hypotheses:

- 1) paraneoplastic RS and malignancy are independently triggered by the same initiative factor (bacteria, virus, radiation, etc.);
- 2) paraneoplastic RS is caused by toxins produced by the tumor cells, which trigger inflammation;

3) paraneoplastic RS is mediated by a hypersensitivity reaction due either to tumoral expression of antigens shared by the cells targeted by the autoimmune disease or the release of intracellular antigens from apoptotic tumor cells (7).

A diagnosis of AOSD-like manifestations associated with malignancy is very uncommon and we have little knowledge about it. Of all cases with paraneoplastic AOSD published in the literature, half were diagnosed with a solid tumor, the other half with a hematopoietic malignancy.

Solid tumors originated from a wide variety of organs and tissue types with ductal breast cancer and non-small lung cancer being the most frequent histological entities. Furthermore, similarly to other forms of paraneoplastic arthritides, paraneoplastic AOSD is frequently associated with hematopoietic malignancies, especially malignant lymphomas (4).

PTC is the most common type of thyroid cancer and usually presents as asymptomatic nodule.

Cases of paraneoplastic syndromes are sparse in patients suffering from PTC, such as polymyalgia rheumatica, hypercalcemia, syndrome of inappropriate antidiuresis, dermatopolymyositis, paraneoplastic neutrophilia, and neurological syndromes (myoclonus, optic neuritis and Isaac's syndrome) (8-16).

To our best knowledge, two cases of concomitant diagnosis of AOSD and occult PTC have been reported in literature (17, 18). The authors concluded that it was a coincidental diagnosis of occult PTC and AOSD, rather than an AOSD-like paraneoplastic syndrome. Nevertheless, considering some reports of cases presenting a paraneoplastic syndrome of PTC, they did not completely rule out the paraneoplastic hypothesis.

In our case, the AOSD-like manifestations developed abruptly and were concomitant with the diagnosis of PTC, as a paraneoplastic syndrome of the thyroid cancer.

More recently, Hofheinz et al. (4) conducted a systematic literature review on AOSD associated with malignancy, identifying some red flags that should raise suspicion of

an underlying malignancy: advanced age, male sex, skin rash differing from the characteristic macular or maculopapular morphology and/or not parallel fever flares, high levels of LDH, atypical cells in the differential blood count. Therefore these clinical and laboratory features should prompt further diagnostic steps, such as whole-body CT, bone marrow, and lymph node biopsies. In our patient, the history of psoriatic arthritis, the patient's age, and atypical features of the skin rash with its appearance without fever were suited to a paraneoplastic hypothesis.

■ CONCLUSIONS

In a patient with AOSD symptoms, the exclusion of an underlying malignancy is mandatory and it can be very challenging. In our case, the disease course, the age, and the skin rash differing from the characteristic macular or maculopapular morphology and not parallel to fever flares, have led us to conclude for paraneoplastic AOSD-like manifestations.

Consent: written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Conflict of interest: None

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