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Case Report

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RHEUMATOID ARTHRITIS INDUCED BY AROMATASE INHIBITORS: A CASE REPORT

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ABSTRACT

The occurrence of rheumatoid arthritis triggered by aromatase inhibitors is rarely reported in the literature. We report the clinical case of a Moroccan patient who developed rheumatoid arthritis after treatment with aromatase inhibitors. This is a 57-year-old female patient, G0P0, menopause at age 51, with no notable personal history, having a family history of a sister followed for uterine cancer (declared cured). The patient had a left breast cancer in December 2021. It was a NST infiltrating breast carcinoma, SBR grade 1, classified as pT1bN0. She was treated by surgery with a left lumpectomy and homolateral axillary lymph node dissection (on 12/2021), then she received 25 sessions of radiotherapy (from 01/02/2022 to 03/03/2022), and then started taking a non-steroidal aromatase inhibitor "Letrozole GT" hormone therapy (on 05/03/2022); the patient received no chemotherapy. 20 days later, she presented with bilateral and symmetrical polyarthritis of the hands sparing the distal interphalangeal joints. Blood tests were ordered which revealed an accelerated sedimentation rate of 57 mm at the first hour and a negative C-reactive protein. Anti-cyclic citrulline peptide (Anti-CCP) antibodies were positive at 413 IU/ml and rheumatoid factor was positive at 102 IU/ml. Magnetic resonance imaging of both hands was performed (on May 24, 2022) and showed subchondral bone erosions associated with bone edema and grade 1 synovitis, suggesting a rheumatoid arthritis-type inflammatory origin without signs of activity. The patient met the American College of Rheumatology criteria for rheumatoid arthritis (ACR/EULAR 2010).

INTRODUCTION

Breast cancer is the most common cancer that affects women worldwide.[1]

Aromatase inhibitors are commonly used in the treatment of hormone-dependent breast cancer in postmenopausal women. The occurrence of joint pain during this therapy is frequently observed.

The occurrence of rheumatoid arthritis triggered by aromatase inhibitors is rarely reported in the literature. Even if we cannot exclude the fortuitous characteristic, some arguments from animal models can be advanced in favor of a potential triggering or revealing role of aromatase inhibitors in the occurrence of rheumatoid arthritis.[2]

We report the clinical case of a Moroccan patient who developed rheumatoid arthritis after treatment with aromatase inhibitors

CASE REPORT

This is a 57-year-old female patient, G0P0, menopause at age 51, with no notable personal history, having a family history of a sister followed for uterine cancer (declared cured). The patient had a left breast cancer in December 2021. It was a NST infiltrating breast carcinoma, SBR grade 1 measuring 0.9 cm with an estimated 5% intra-tumoral lymphocytic infiltrate, classified as pT1bN0.

Its immunohistochemical study showed estrogen receptor positivity on 100% of the nuclei (++ to +++) with progesterone receptor expression on 70% of the nuclei (+++) and Ki67 was positive on 10% of cells. FISH complementation did not show HER2 gene amplification. She was treated by surgery with a left lumpectomy and homolateral axillary lymph node dissection (on 12/2021), then she received 25 sessions of radiotherapy (from 01/02/2022 to 03/03/2022), and then started taking a non-steroidal aromatase inhibitor "Letrozole GT" hormone therapy (on 05/03/2022); the patient received no chemotherapy.

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The patient met the American College of Rheumatology criteria for rheumatoid arthritis (ACR/EULAR 2010).

DISCUSSION

Rheumatological manifestations occurring on anti-aromatase drugs are becoming better described and known. The pathophysiology of these disorders is an experimental field that allows us to analyze the links between the hormonal system, the pain system and the musculoskeletal system.

Few specific studies have been conducted to identify the risk factors for the occurrence of rheumatological complications with aromatase inhibitors. Age, race, mode of onset, age at menopause, type of aromatase inhibitor, and duration of treatment do not appear to be proven risk factors for the occurrence of aromatase inhibitor-related joint pain.[3] Data on weight have been published in a contradictory manner.[4]

Prior chemotherapy appears to put patients at greater risk of rheumatologic complications, with a shorter time of onset symptoms.[5] On the other hand, prior radiotherapy would not be a risk factor.[6] In our case, the patient did not undergo chemotherapy but developed rheumatoid arthritis within a short period of 20 days after hormone treatment.

The frequency of joint manifestations occurring under aromatase inhibitors has varied widely in the literature since the original description by Donnellan et al. in 2001.[7] Two very different types of data are available:

- In clinical trials to demonstrate the efficacy of aromatase inhibitors in adjuvant breast cancer, the prevalence of pain varies from 5.4% to 35.6%, mainly because there is no systematic search nor assessment of pain. Only musculoskeletal data collected as adverse events are available for the 3 marketed molecules. Under Letrozole, 5.6% arthritis, 21.3% arthralgia, and 11.8% myalgia are reported for respectively 3.5%, 16.6%, and 9.5% under placebo, with statistically significant differences for all these items.[8]

- In the few cross-sectional and prospective studies conducted on this issue, the prevalence of joint pain was higher: 47% of cases in one cross-sectional study[3] and between 30 and 45.4% in 3 prospective studies.[9,10] These joint pains started on average after 1.6 months of treatment, leading in 13 cases out of 100 to a discontinuation of treatment for joint complication.

CONCLUSION

We reported the clinical case of a patient who developed rheumatoid arthritis 20 days after treatment with aromatase inhibitors. Therefore, when osteoarticular pain occurs under aromatase inhibitor therapy, a particularly thorough evaluation of the type of pain and the associated manifestations should be made. The first element is, of course, to rule out a progressive neoplastic pathology, possibly with metastases, or inflammatory rheumatic disease. In this context, the specialized opinion of an oncologist and a rheumatologist will be necessary.

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