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CASE REPORT

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A case of severe paraneoplastic itch resistant to antihistamines and responding to serotonin reuptake inhibitors

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Abstract

This article covers an interesting topic. Paraneoplastic pruritus is rare but can be severe. It can sometimes be resistant to usual treatments. In our case, it was resistant to antihistamines but was relieved by inhibitors of serotonin scrapping.

KEYWORDS

antihistamines, paraneoplastic itch, serotonin reuptake inhibitors

1 | INTRODUCTION

Paraneoplastic itch (PI) can accompany malignant diseases. It can be severe and affect the quality of life of patients. It can also be resistant to usual treatment. We report here a case of PI associated with breast cancer, which was resistant to antihistamine treatment but was relieved under serotonin reuptake inhibitors.

Paraneoplastic pruritus is rare. Its incidence depends on the associated malignant pathologies. It is a very annoying symptom for patients, which further degrades their quality of life. Its management is not well codified in the literature, and it can sometimes resist to usual therapies. Several molecules have proven to be effective in this situation. We report here the case of an intense paraneoplastic itch, resistant to antihistamines, and having responded to paroxetine, with a review of the literature.

2 | CASE REPORT

We report the case of a 70-year-old woman followed for left breast cancer with bone and pulmonary metastases. The patient was on palliative chemotherapy with EC (Epirubicin, Cyclophosphamide). After 9 days of the 3rd course of chemotherapy, the patient noted the appearance of a generalized itch which became more and more severe and caused her insomnia and a huge gene, without other associated signs. Physical examination revealed diffuse scratching lesions throughout the body, associated with seborrheic scaling of the back evoking the Leser-Trelat sign (Figure 1). Biological examinations were normal, and viral serologies were negative. The diagnosis of paraneoplastic itch (PI) was the most plausible, in the absence of other etiologies. Then, the patient was initially put on an antihistamine with prescription of emollient and moisturizing creams. However, no improvement in symptoms was noted, and the pruritus persisted stubbornly. In the absence of a response, treatment with selective serotonin reuptake inhibitor (SSRI) was used: paroxetine (started at a dose of 10 mg/day at night then increased to 20 mg/day). Thus, after 4 days, there was a marked regression of the pruritus. Currently, the patient is undergoing capecitabine-based chemotherapy (given the grade 4 hematotoxicity presented with the EC75 protocol), at the 8th course of treatment, with clinical and radiological stability of the disease. After a 6-month follow-up, the pruritus has almost completely disappeared, and the patient no longer takes paroxetine.

3 | DISCUSSION

Paraneoplastic itch (PI) is a rare disorder. At present, there is no clear definition of PI, neither in terms of applicability nor in terms of duration.

The SIG (special interest group) on "Paraneoplastic itch" defines it as follows: PI describes the sensation of itch as a

systemic (not local) reaction to the presence of a tumor or a hematological malignancy neither induced by the local presence of cancer cells nor by tumor therapy. It usually disappears with remission of the tumor and can return with its relapse.[1]

The true frequency of this symptom reminds unclear; epidemiological data in this field are limited.[2]

From previous studies, it is known that there are differences in the prevalence of itch depending on the type of cancer. In hematological malignancies, the prevalence of itch is higher than in nonhematologic malignancies.[3] Its prevalence is around 30% in non-Hodgkin lymphomas,[3,4] and around 15%-50% in Hodgkin lymphomas.[4]

Paraneoplastic itch may precede the diagnosis of the tumor. It may disappear when the tumor is completely treated and its reappearance can announce tumor recurrence.[5] Also, the intensity of pruritus can be correlated with the advanced stage of the disease.

Itch in malignancy may present on normally appearing skin or may be characterized by secondary scratch lesions like excoriations or prurigo nodules.[1]

Some paraneoplastic dermatoses may be associated with itch of varying intensity.[1,6]

In our case, PI was associated with the appearance of Leser-Trelat sign (eruptive seborrheic keratoses). The Leser-Trelat sign is described as a sudden increase in size and number of seborrheic keratoses in the setting of an underlying internal malignancy.[7] Generalized pruritus has been reported to occur in patients who display the Leser-Trelat sign.[8] This sign was more frequently described in the case of adenocarcinoma of digestive tract and hematological malignancies.[1,6]

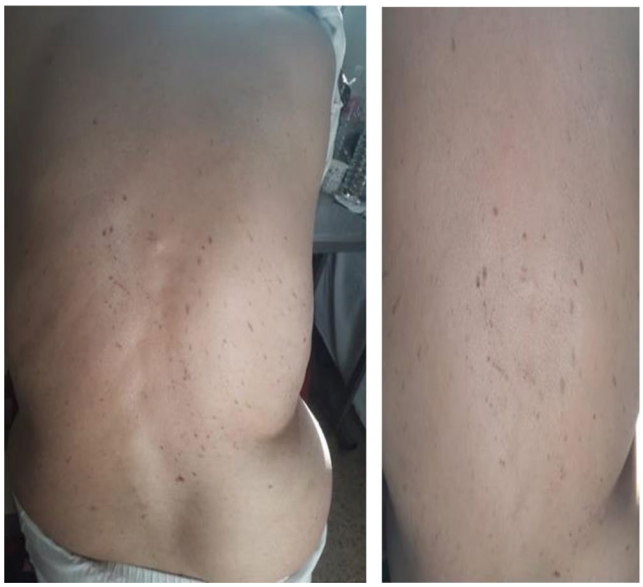

FIGURE 1 Diffuse scratching lesions associated with seborrheic scaling of the back evoking the Leser-Trelat sign

The mechanisms of PI are still ambiguous. Recently, interleukin-31 (IL-31) and a Th2-cytokine were found to be highly associated with itch in lymphoma and highly expressed in malignant T cells.[9]

Paraneoplastic itch can be severe, induce insomnia and depression, and affect the quality of life of patients; thus, the interest of treating it as quickly as possible. The treatment of PI comprises the treatment of the underlying origin which is the malignancy itself. Multiple treatments have been tested and shown to be effective to treat PI; however, the therapeutic strategy remains uncertain to relieve this symptom.

H1 antihistamines are frequently ineffective in PI but they may act as a sedative when hydroxizine (25-75 mg at night) is used at night time.[10,11] In our case too, this treatment was ineffective.

Some SSRI such as paroxetine (5-20 mg/day) and fluvoxamine (25-100 mg/day) had proven their effectiveness in the treatment of pruritus.[12,13] A randomized clinical trial demonstrated a 50% reduction in paraneoplastic itch severity when patients were administered 20 mg of paroxetine daily for 7 days.[13] In our case too, the use of paroxetine treatment was effective and calmed the pruritus in our patient. Another SSRI, sertraline may be used in a dose of 25-50 mg/day.

The SSRI needs to be started at low dose (eg, Paroxetine at 5 mg oral/day) and should be increased to 20 mg within 3-5 days because severe nausea and vomiting may occur.[13]

The antipruritic effect can be observed within 2-3 days.[13] In our patient too, the effect was observed from the 4th day with significant attenuation of pruritus.

Tetracyclic antidepressants such as mirtazapine 15 mg (up to 45 mg/day) were also described to have antipruritic effects in several case reports.[14,15]

Opioid receptor antagonists like the μ-opioid receptor antagonists such as naloxone or nalmefene may also show considerable relief of itch.[16]

Aprepitant is a NK-1 (neurokinin) receptor antagonist, used for the treatment of severe post-chemotherapy nausea and vomiting. It has also been used for itch in T-cell lymphoma, solid tumors, and itch related to biological cancer treatment [17-19] in an oral dose of 80-125 mg/day. It has also been reported to be an effective antipruritic agent in cases of Sezary syndrome with severe itch.[17]

Other nonpharmacological treatments have been tested. Some authors suggest that ultraviolet B light therapy acts on pruritus by reducing the number of mast cells and nerve endings free in the skin.[20,21]

4 | CONCLUSION

Paraneoplastic pruritus remains a fairly rare entity. Its exact prevalence is still unclear, and its pathophysiological mechanism remains ambiguous. Numerous therapies have shown

efficacy for the treatment of PI but the optimal treatment remains undefined. More researches are needed to determine the best strategy for this annoying symptom that often affects patients' quality of life.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

IW: contributed to acquisition of data, analysis and interpretation of data, drafting of the manuscript, and critical revision of the manuscript for important intellectual content. JF: contributed to analysis and interpretation of data, drafting of the manuscript, and critical revision of the manuscript for important intellectual content. SK: contributed to analysis and interpretation of data, drafting of the manuscript, and critical revision of the manuscript for important intellectual content. WBK: contributed to drafting of the manuscript and critical revision of the manuscript for important intellectual content. AK: contributed to drafting of the manuscript and critical revision of the manuscript for important intellectual content.

ETHICAL APPROVAL

This study is exempt from ethical approval in this institution.

CONSENT

Consent has been obtained from the patient.

DATA AVAILABILITY STATEMENT

Data openly available in a public repository that issues datasets with DOIs.

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