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CASE REPORT

Breast cancer: an atypical and challenging presentation

Cancro da mama: uma apresentação atípica e desafiante

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Abstract

Introduction: *Paraneoplastic syndromes are rare manifestations of oncological diseases, posing a diagnostic challenge.* **Case report:** *We report the case of a young female patient hospitalized with a neurological condition clinically compatible with stiff-person syndrome (SPS), presenting with an inability to walk independently at admission. During hospitalization, a diagnostic workup revealed an invasive carcinoma of no special type (NST), luminal B, with clinical staging cT1c N1 Mx, in the left breast. The diagnosis of paraneoplastic SPS with positive anti-amphiphysin antibodies was established. The patient underwent neoadjuvant chemotherapy with anthracyclines and taxanes, followed by left subcutaneous mastectomy and axillary lymph node dissection. Histology revealed residual invasive disease (NST): ypT1c N1a. Of the proposed adjuvant treatment, she has completed radiotherapy and continues with hormonal therapy and bisphosphonates.* **Conclusion:** *With the oncological treatment, the neurological symptoms improved progressively and significantly, allowing discontinuation of symptomatic treatment. Nine months post-surgery, she is pain-free, spasm-free, and has regained full autonomy.*

Keywords: *Breast cancer. Paraneoplastic syndrome. Stiff-person syndrome.*

Resumo

Introduçao: *As síndromes paraneoplásicas são manifestações raras de doenças oncológicas, que tornam o diagnóstico um desafio.* **Relato de caso:** *Reporta-se o caso de uma doente jovem internada com um quadro neurológico, clinicamente compatível com síndrome-da-pessoa-rígida (SPR), com incapaciadade de marcha autónoma à admissão. Após investigação diagnóstica em internamento, foi diagnosticado um carcinoma invasor de tipo não especial (NST), luminal B, com estadiamento clínico cT1c N1 Mx da mama esquerda. Estabeleceu-se o diagnóstico de SPR paraneoplásica, positiva para anti-anfifisina. A doente foi submetida a quimioterapia neoadjuvante com antraciclinas-taxanos, seguida de mastectomia subcutânea esquerda e esvaziamento ganglionar.* **Concluçao:** *A histologia da peça cirúrgica revelou doença residual invasiva (NST): ypT1c N1a. Do tratamento adjuvante proposto, já concluiu a radioterapia, mantendo a terapia hormonal e bifosfonatos. Com o tratamento oncológico, os sintomas neurológicos melhoraram progressiva e significativamente, permitindo a suspensão do tratamento sintomático. Nove meses pós-cirurgia, encontra-se sem dor ou espasmos e com autonomia restabelecida.*

Palavras chave: *Cancro da mama. Síndrome paraneoplásico. Síndrome-da-pessoa-rígida.*

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Date of reception: 05-02-2025
Date of acceptance: 01-04-2025
DOI: 10.24875/RPO.M25000010

Available online: 16-06-2025
Rev. Port. Oncol. 2025;8(2):75-77
www.rponcologia.com

Introduction

Paraneoplastic syndromes are rare and complex clinical manifestations caused by tumor aberrant production of hormones, cytokines, or autoantibodies, often targeting the nervous system. Among these, paraneoplastic neurological syndromes (PNS) present a unique diagnostic and therapeutic challenge, often preceding the identification of an underlying malignancy. Early recognition of PNS is critical as it can prompt timely investigation and treatment of the associated tumor, potentially improving both neurological and oncological outcomes[1-3].

Stiff-person syndrome (SPS) is a rare autoimmune disorder characterized by progressive muscle rigidity, painful spasms, and impaired mobility. It can occur idiopathically or as a paraneoplastic syndrome, associated with autoantibodies targeting synaptic proteins, such as anti-glutamic acid decarboxylase and anti-amphiphysin, the latter being more common in the paraneoplastic form[4-6].

Breast cancer is the most common malignancy in women worldwide, encompassing a complex biological and clinical spectrum. While it is primarily associated with older age, a significant subset of cases arises in younger women, under 50 years of age, who fall outside the universal mammographic screening programs in Portugal. In this population, breast cancer often presents delayed diagnosis, more aggressive tumor biology, and distinct psychosocial concerns[7,8].

With this article, we share the case of a young woman diagnosed with paraneoplastic SPS secondary to invasive breast carcinoma of no special type (NST). The case highlights the diagnostic complexity of PNS, the therapeutic potential of the cancer treatments, and the importance of a multidisciplinary approach in achieving both tumor control and neurological recovery.

Clinical case

We present the case of a pre-menopausal woman in her forties with a medical history of benign breast disease, having undergone fibroadenoma excision a decade earlier. Her family history was significant for breast cancer in her mother (diagnosed in her thirties), maternal aunt (in her fifties), and maternal cousin (in her forties).

The patient was admitted to the Neurology department following a 3-month history of progressive rigidity, spasms, and pain in her axial muscles and legs. The spasms were spontaneous, intermittent and triggered by sudden movements, unexpected noise or emotional reactions, leading to frequent falls. Upon admission, she was very anxious and unable to walk independently. No urinary retention, gastrointestinal symptoms, or other autonomic alterations were observed.

During hospitalization, symptoms were controlled only with high doses of diazepam and baclofen. A diagnostic workup revealed serologic positivity for anti-amphiphysin antibodies, with no relevant findings on brain computed tomography (CT) or brain and spine magnetic resonance imaging. Thoraco-abdominopelvic CT identified three nodular lesions in the left breast, with the largest measuring 20 mm, and a suspicious ipsilateral axillary lymph node, confirmed by mammographic and ultrasound imaging.

Biopsies of the largest nodule and axillary lymph node revealed invasive carcinoma NST, grade 2. Immunohistochemistry showed estrogen and progesterone receptor expression in over 90% of cells, human epidermal growth factor receptor 2 expression negative (1+), Ki67 proliferation index of 40% (measured in a *hot spot*). Clinical staging was established as cT1c N1 Mx[9]. Therefore, a diagnosis of paraneoplastic SPS positive for anti-amphiphysin antibodies was established.

The patient underwent neoadjuvant chemotherapy with anthracyclines, cyclophosphamide, and taxanes, followed by left subcutaneous mastectomy, with immediate reconstruction, and axillary lymph node dissection. Although there was a clinical and radiological response to neoadjuvant treatment, histopathological analysis revealed residual invasive disease (NST), with a pathological staging of ypT1c N1a[9]. Following surgery, she completed adjuvant radiotherapy and is currently under hormone therapy, adjusted to her pre-menopausal hormonal status, and bisphosphonates[10-12]. Throughout this time the patient has also performed directed physical rehabilitation, as an adjuvant treatment for her recovery.

Due to her age and family history, genetic testing was performed, revealing no pathogenic variants or variants of unknown significance.

With the initiation of the oncological treatment and physical rehabilitation, the neurological symptoms progressively and significantly improved, allowing for the discontinuation of symptomatic therapy. Nine months after surgery, the patient is pain-free, spasm-free, and has regained full autonomy.

Discussion

Paraneoplastic syndromes are rare manifestations of oncologic diseases, posing significant diagnostic challenges. SPS is a rare neurological condition that requires careful investigation for the possibility of underlying malignancies when presenting in otherwise healthy adults. In this case, there was a discordance between the early-stage breast cancer diagnosis and the severity of the neurological symptoms at presentation, emphasizing the importance of recognizing PNS as a potential indicator of malignancy[1-6,13].

It is known that the evolution of the neurological symptoms is strongly dependent on the treatment of the underlying tumor, which can also help to prevent or reduce long-term complications[12]. Symptomatic management alone often provides only limited relief, as evidenced in this case, where significant improvement was observed only after antineoplastic therapy. The progressive recovery of the patient, leading to in the discontinuation of symptomatic therapy, highlights the importance of integrating oncological and neurological care.

This case also illustrates the diagnostic challenges of PNS as initial manifestations of malignancy, emphasizing the critical role of early tumor detection and multidisciplinary approach, involving oncologists, neurologists, and other health professionals, to optimize patient outcomes and enhance quality of life.

Conclusion

This case highlights the importance of considering paraneoplastic syndromes like stiff-person syndrome as early indicators of malignancy. Significant neurological improvement occurred only after oncological treatment, emphasizing that tumor control is key to symptom resolution. Early recognition, prompt cancer treatment, and a multidisciplinary approach are essential to optimize patient outcomes and restore quality of life.

Funding

No funding was received for this work.

Conflicts of interest

There are no conflicts of interest to declare.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The patient provided informed consent for the publication of clinical information. Care was taken to protect the patient's confidentiality; all identifying details were omitted or anonymized to ensure privacy.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript

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