

Acute myeloradiculitis in a breast cancer patient. A need for a good differential diagnosis

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Abstract

Background: Acute myeloradiculitis is a severe disease with several causes. Elsberg syndrome is a cause of lumbosacral radiculitis with myelitis related to a recent herpes simplex virus infection that occurs most often in immunocompromised patients.

Case report: We present the case of a 45-year-old woman with newly diagnosed triple-negative breast carcinoma treated with neoadjuvant chemotherapy who, during the course of chemotherapy, developed rapid-onset cauda equina syndrome with initial suspicion of tumor progression. The patient had presented genital herpes in treatment with Acyclovir a week prior to the onset of neurological symptoms.

Conclusion: Cauda equina syndrome could have multiple causes. Differential diagnosis is crucial in an oncologic patient. Both the patient's prognosis and the treatment administered will depend on an adequate diagnosis.

Keywords

Elsberg syndrome; Leptomeningeal carcinomatosis; VHS-2; Breast cancer; Immunocompromised.

Background

Acute myeloradiculitis is characterized by a set of neurological alterations of sudden onset secondary to damage on the spinal cord. It can present with pain, urinary retention, constipation, paresthesia and muscle weakness, which can cause devastating consequences. There are various causes such as trauma, infections, autoimmune or oncological diseases... some of which may be reversible and others will have a fatal outcome, hence the importance of an adequate differential diagnosis.

Triple Negative Breast Cancer (TNBC) (hormone receptor negative and HER2 negative) [1] accounts for approximately 10-15% of breast cancer diagnoses and is associated with poorer long-term survival than other breast cancer tumor subtypes [2]. It is characterized by affecting a younger population, being more prevalent in the black race and with a greater association with germinal alterations in BRCA. This subtype presents certain histological features of greater aggressiveness such as grade III, lymphovascular invasion, perineural invasion, high proliferation index.

In local stages (from I to III) cure rates are between 60-90% (depending on the clinical stage) while in metastatic stage survival is only 12-18 months despite advances in oncological treatments. This tumor variant has a greater affinity for the Central Nervous System (CNS) than other histological subtypes, and the appearance of brain metastases or meningeal carcinomatosis is not uncommon throughout the disease [3].

Chemotherapy is the mainstay of treatment in the initial phase of this pathology, either in neoadjuvant or adjuvant settings. Approvals have recently been obtained for combinations of chemotherapy and immunotherapy in this stage of the disease. Combinations with immunotherapy and polychemotherapy used in these patients frequently produce neutropenia, which leads to a situation of transient immunosuppression, which favors the appearance of viral, bacterial or fungal infections with atypical presentations on some occasions.

Viral infections, particularly that attributable to Herpes Simplex Virus (HSV) is being seen with increased frequency in the oncologic patients [4].

Involvement of the central nervous system by HSV family varies greatly in frequency and severity. The HSV-1 virus causes most herpetic encephalitis, while HSV-2 causes encephalitis very infrequently. Exceptional cases of myelitis have been described, due to ascending spread of HSV-2 through the CNS [5].

Elsberg syndrome (ES) was first described by Charles Elsberg at the beginning of the 20th century and comprises a myeloradiculitis frequently associated with an infection by a virus of the herpes family [6].

Case Report

A 45-year-old woman with no personal or family history of interest, in screening with annual mammography for fibrocystic mastopathy, was diagnosed with a triple negative multifocal left breast carcinoma (focus of 24 mm and focus of 7 mm), corresponding clinically and radiologically to a cT2N0M0, stage II. A complete extension study was performed (including an MRI of the cervical-dorso-lumbar spine) which ruled out the presence of metastasis. The patient began chemotherapy with neoadjuvant intention, with carboplatin, paclitaxel, doxorubicin, and cyclophosphamide, with several episodes of afebrile neutropenia during the course of the treatment that resolved without the need of supportive treatment.

Five days after finishing chemotherapy, she presented intense anal pain, with an ulcerated vaginal lesion, being diagnosed with genital HSV infection (HSV-2) and started treatment with Acyclovir with clinical improvement. Two weeks after the HSV primary infection, she presented weakness in both lower ex-

tremities with neuropathic-type pain in the soles of her feet. Assessed by the medical oncology department and suspecting neuropathy secondary to taxanes, she started gabapentin.

She was admitted a week later due to difficulty in initiating urination, constipation and weakness in the lower limbs, detecting allodynia in the pelvic and genital area and dysesthesia in the lower limbs, more striking at the distal level.

During admission, an oncological extension study with PET CT was performed, showing a complete radiological response of the tumor disease, which was confirmed with breast MRI. An MRI of the cervico-dorso-lumbar spine was performed, showing punctate enhancements on the posterior surface of the medullary cord at the D7, D8 and D9 levels, which do not rule out metastatic disease given the patient's history.



Figure 1: Transverse myelitis. T2- hyperintense spinal cord lesion (red arrows) in different levels.

Lumbar puncture detected 66 cell/mm^3 pleocytosis, with protein and glucose within normal limits. PCR was performed on the cerebrospinal fluid (CSF) for CMV, HSV, VZV, EV, HHV-6 and COVID-19, all negative, as well as cytology for malignancy. A study of a skin lesion in the genital area was performed, being positive for HSV-2.

Suspecting ES, the patient received treatment with acyclovir and corticosteroids with progressive improvement of the condition. 9 months after discharge, the patient has completed her oncological treatment by surgery of the primary tumor and is disease-free and neurologically asymptomatic with recovery of all sensory functions.

Discussion

The appearance of neurological symptoms in a patient diagnosed with TNBC suggests the possibility of disease progression. Cauda equina syndrome in a patient with a diagnosis of breast cancer makes it necessary to rule out the presence of meningeal carcinomatosis, which, although infrequent, has an acute and progressive presentation of neurological symptoms, as our patient had.

Clinical suspicion requires the performance of an MRI that can show enhancements in the nerve endings simulating myelitis. The certainty diagnosis would be given by the presence of tumor cells in the CSF. After a diagnosis of meningeal carcinomatosis with involvement only of the sacral area, the treatment of choice would be exclusively palliative and the patient's prognosis would be poor in a short period of time (3-6 months).

ES is characterized by the appearance of lumbosacral myelitis and radiculitis, generally associated with an infection by a virus of the herpes family, although some cases associated with SARS-Cov-2 have been described, increasing the spectrum of neurological alterations presented by COVID-19 [7].

The presence of genital HSV-2 infection in the week prior to the onset of symptoms led to consideration of other differential diagnoses. The radiological image was suggestive of myelitis without being able to differentiate between the different etiologies. HSV-2-associated myelitis appears more frequently in HSV-2 reactivations, but cases of ES have been described in primary infections, especially in immunocompromised patients.

The positivity of the polymerase chain reaction (PCR) of the CSF for HSV-2 provides a certain diagnosis, but a negative result does not exclude this diagnosis, especially in immunocompromised patients and the determination of antibodies in CSF adds little value in the acute moment of the symptomatology [8].

The appearance of a cauda equina syndrome associated with an herpes infection, a radiological image and a CSF analysis compatible with the disease establishes the diagnosis of ES. MRI should show contrast enhancement in the sacral nerve endings and signal hyperintensity in the conus medullaris (both signs of myelitis). The presence of pleocytosis and elevated CSF proteins is common in ES but is only present in less than 50% of cases.

If viral infection is confirmed, the treatment of choice is IV acyclovir [8]. Cases of HSV-2 infections have been described in immunocompromised patients causing myelitis with less radiological expression and less alteration at the CSF level but with a more severe clinical course [9,10].

ES accounts for approximately 5-15% of cauda equina syndromes. 27% of them present a partial recovery, 10% do not recover, 7% will present relapses, 3% present complete recovery and 3% have a fatal outcome. Relapses frequently occur in the first year after the episode, so it seems appropriate to follow these patients thoroughly this first year to detect possible reactivations.

Conclusion

The appearance of sudden-onset neurological symptoms in patients with early-stage breast cancer requires an adequate differential diagnosis and histological confirmation in cases of suspected tumor progression, since the appearance of neurological symptoms associated with infections is not uncommon, with a prognosis and treatment very different from that of the underlying disease.

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