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Case Report

CASE REPORT

Paraneoplastic opsoclonus–myoclonus syndrome as a rare presentation of breast cancer

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Abstract

Opsoclonus–myoclonus paraneoplastic syndrome is a medical condition that includes opsoclonus along with diffuse or focal body myoclonus and truncal titubation with or without ataxia and other cerebellar signs. This rare neurological syndrome is poorly understood and can result in long-term cognitive, behavioral and motor sequelae. We report a case of a 49-year-old woman with anti-Ri antibody opsoclonus–myoclonus syndrome and an invasive ductal carcinoma with axillary nodes involvement. Following the diagnosis of opsoclonus–myoclonus syndrome, a multimodal immunotherapy treatment, with partial remission of the neurological symptoms. The patient underwent lumpectomy and axillary node dissection and the surgical pathology confirmed the diagnosis of breast cancer stage IIA. This was followed by chemotherapy, radiotherapy and hormone therapy with tamoxifen. At the 6 months follow-up there was a partial improvement, anti-Ri antibody was subsequently reported as negative and there was no evidence of disease recurrence.

INTRODUCTION

Breast cancer is the most common cancer in women in Europe which has been increasing with mammographic screening and continues to grow as population ages. The risk of breast cancer is age-dependent, with a quarter of breast cancers occurring before age 50, and <5% before age 35 [1]. The other most important risk factors include: genetic predisposition, exposure to estrogens, ionizing radiation, low parity, obesity and alcohol consumption [2].

In countries with screening programs, breast cancer is often detected before clinical symptoms are apparent, but occasionally the occurrence of paraneoplastic syndrome precedes the identification of the tumor. Paraneoplastic neurologic syndromes are rare immune mediated syndromes defined by the presence of neurological symptoms associated with the diagnosis of cancer within 4 years from the onset of the non-metastatic neurological manifestations and implies the exclusion of other neurological disorders [3]. The precise immunological mechanism is not well understood, however, specific autoantibodies, such as anti-Ri, anti-Yo and anti-Hu may be detected in the serum and cerebrospinal fluid of affected patients. In spite of the diagnosis of a paraneoplastic syndrome continues to be challenging, requiring an elevated degree of suspicion, due the heterogeneity in timing, symptomatology and the underlying cancer is only found in 20–40% of

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cases. Breast cancer related neurologic paraneoplastic syndromes includes sensory and motor-type neuropathies, paraneoplasic cerebellar degeneration, opsoclonus–myoclonus syndrome (OMS), stiff person syndrome, encephalomyelitis and paraneoplastic retinopathy [4, 5].

OMS associated with breast cancer is infrequent and is characterized by spontaneous, arrhythmic, conjugate saccades of eyes in all directions of gaze without a saccadic interval (opsoclonus) and brief, shock-like, involuntary movements caused by muscular contractions or inhibitions (myoclonus). Additional clinical features such as ataxia, tremors, dysarthria and psychiatric symptoms are usually observed. The most frequent tumor associated with OMS is small cell lung cancer, but other tumors, along with breast cancer, have been reported including ovarian teratoma and other gynecologic cancers, gastric adenocarcinoma, malignant melanoma and bladder cancer [5–7].

CASE REPORT

A 49-year-old woman with a past medical history of depressive disorder and bilateral breast reduction mammoplasty was admitted to anal sphincteroplasty for the treatment of fecal incontinence as a labor complication. During the post-operative period she presented a subacute onset of opsoclonus, mioclonus, ataxia, sleep disturbance and irritability. Neurologic examination revealed spontaneous, involuntary, arrhythmic and conjugate rapid eye movements; facial, axial and appendicular myoclonus and gait ataxia. Her motor strength and deep tendon reflexes were normal. Sensation was intact in all modalities.

For etiological clarification, a full workup was conducted with blood tests, including tumor markers and serology for human immunodeficiency virus, cytomegalovirus and Epstein Barr virus; brain magnetic resonance imaging (MRI), CT scan of the chest, abdomen and pelvis, thyroid and breast ultrasound and all revealed normal. Her cerebrospinal fluid (CSF) showed normal cell counts and protein values, and negative cytology and viral markers. For further investigation of the clinical hypothesis of idiopathic opsoclonus–myoclonus syndrome, the patient was transferred to Neurology Department. Electroencephalogram was negative for epileptiform activity. The CSF was tested for presence of onconeural antibodies and anti-Ri was positive. A positron emission tomography was performed and revealed a small solid nodular lesion in the left breast and homolateral axillary adenopathy. Breast screen with mammography and ultrasound, followed by MRI showed a nodular opacity under the left nipple and axillary adenopathy. MRI guided core biopsy of the breast lesion revealed an invasive ductal carcinoma (IDC) luminal A type. The left axillary node biopsy confirmed lymph node metastasis. Meanwhile, patient received immunotherapy with a combination of corticosteroids and rituximab. Symptomatic medication as clonazepam, levetiracetam, thiamine was prescribed. An intensive rehabilitation program was initiated in Neurology Department and comprised both physical and occupational therapy.

The case was then referred to Oncological Multidisciplinary Group. Patient underwent a breast-conserving surgery, lumpectomy with left axillary node dissection and Grisotti mammoplasty; vertical symmetrization mastopexy was performed in the contralateral breast. The surgical pathology revealed IDC pT1cN1aM0—Stage IIA. This was followed by chemotherapy, radiotherapy and hormone therapy with tamoxifen. The neurological deficit progressed after the first cycle of chemotherapy and improved with intravenous immunoglobulin administration. At the 6 months follow-up there was a partial improvement, anti-Ri antibody was subsequently reported as negative and there was no evidence of disease recurrence.

DISCUSSION

Paraneoplastic neurological syndromes in which OMS is included are rare, occurring as a remote immune mediated effect of tumor. However, the differential diagnosis with other neurological manifestations related to metastasis, infection (HIV, Lyme disease, Enterovirus, West Nile virus, Epstein Barr virus, Cytomegalovirus), ischemia and metabolic disturbances is imperative. Therefore, it is required a thorough medical history to determine the risk factors, clinical complaints and physical examination [8].

The pathogenic mechanisms of OMS remain unclear, but it has been suggested that specific tumor types are associated with well-characterized antineural antibodies. Antibody anti-Ri has been described in association with breast cancer. The target antigens are the Nova proteins, Nova-1 and Nova-2 which are widely expressed in the central nervous system and play a role in the regulation of synaptic proteins [9]. Patients with neurologic manifestations that are unexplained by any other neurological disorder should be tested for antineural antibodies. These antibodies are only found in 60–70% of paraneoplasic syndrome patients with breast cancer so their absence does not exclude the diagnosis of this condition. Unknown antibodies may still be involved in the rest of the cases—these patients are assumed as idiopathic OMS [4].

Some adults with paraneoplastic OMS have resolution of neurological symptoms with surgical treatment of the underlying neoplasm. Immunotherapy treatment may lead to partial or complete recovery of OMS in some cases and can involve steroids, intravenous immunoglobulin and cyclophosphamide. Immunosuppressive therapy should not be delayed as the sooner the treatment, the better the outcome [4].

Recognition and diagnosis of paraneoplasic neurological syndromes is important as neurological symptoms almost invariably predate direct symptoms of the primary tumor, and treatment at early stages provides better chance of good outcome. Proper treatment is also important as most paraneoplastic syndromes causes severe disabilities.

Since adult paraneoplastic OMS is rare, there are only small case series and a few case reports associating it with breast cancer. With the publication of this case report, the authors hope to contribute to a better understanding of this neurological syndrome.

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CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Autier P, Boniol M, LaVecchia C, Vatten L, Gavin A, Héry C, et al. Disparities in breast cancer mortality trends between 30 European countries: retrospective trend analysis of WHO mortality database. *Br Med J* 2010;**341**:c3620.
2. McTiernan A. Behavioral risk factors in breast cancer: can risk be modified? *Oncologist* 2003;**8**:326–34.
3. Graus F, Delattre JY, Antoine JC, Dalmau J, Giometto B, Grisold W, et al. Recommended diagnostic criteria for

paraneoplastic neurological syndromes. *J Neurol Neurosurg Psychiatry* 2004;**75**:1135–40.
4. Fanous I, Dillon P. Paraneoplasic neurological complications of breast cancer. *Exp Hematol Oncol* 2016;**5**:29.
5. Weizman D, Leong W. Anti-Ri antibody opsoclonus-myoclonus syndrome and breast cancer: a case report and a review of the literature. *J Surg Oncol* 2004;**84**:143–5.
6. Gatti G, Simsek S, Kurne A, Zurrida S, Naninato P, Veronesi P, et al. Paraneoplastic neurological disorders in breast cancer. *Breast* 2003;**12**:203–7.
7. Klaas JP, Ahlskog JE, Pittock SJ, Matsumoto JY, Aksamit AJ, Bartleson JD, et al. Adult-onset opsoclonus-myoclonus syndrome. *Arch Neurol* 2012;**69**:1598–1607.
8. Titulaer MJ, Soffietti R, Dalmau J, Gilhus NE, Giometto B, Graus F, et al. Screening for tumors in paraneoplasic syndromes: report of an EFNS Task Force. *Eur J Neurol* 2011;**18**: 19–e3.
9. Dalmau J, Gultekin HS, Posner JB. Paraneoplastic neurological syndromes: pathogenesis and physiopathology. *Brain Pathol* 1999;**9**:275–84.