Isolated Choreic Manifestations Indicative of Anti-Amphiphysin Antibody-Related Encephalitis in Breast Cancer

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Introduction

Over the past two decades, subacute abnormal movements have been increasingly associated with autoimmune or paraneoplastic encephalitis.[1] Only a few cases, however, have been reported in association with anti-amphiphysin autoantibodies,[2-5] and to our knowledge there is only one reported case of choreic movements in an anti-amphiphysin patient.[6] Similarly, we report here the case of a woman presenting with brachio-facial choreic movements with anti-amphiphysin autoantibody-related encephalitis in the context of breast cancer. This patient made a remarkable recovery following mastectomy, chemotherapy, and treatment with tetrabenazine.

Case Report

An 82-year-old woman with a history of well-controlled type 2 diabetes mellitus presented with a 6-month history of abnormal involuntary movements of her left upper limb. She initially described movements as paroxysmal episodes of ascending electric shock originating in the left hand with ipsilateral arm involvement, these movements progressively worsened until they eventually became permanent while remaining localized in the left upper limb and oro-buccal region. Despite the absence of epileptic activity on electroencephalogram (EEG), the patient was treated with levetiracetam 1500 mg/day with no observable effect. At this point, she was referred to our hospital.

During the first evaluation in our hospital (conducted by F.O.M.), she had permanent focal movements of the left fingers with oro-buccal involvement (Video 1a). These were involuntary, non-rhythmic, and partially controllable choreoathetosic and dystonic movements, affecting the left upper limb and upper lip. The frequency of these movements increased with stress and under specific emotional conditions and decreased when the patient adopted sustained postures, with a decrease in amplitude while at rest. No other neurological abnormalities and, in particular, no cognitive impairments were noted. Brain magnetic resonance imaging (MRI) (Fig. 1a) revealed mild atrophy in the amygdalohippocampal complex without other specific changes. Electromyography was normal. Routine laboratory tests (complete blood count, chemistry panel, liver and kidney function tests, vitamin B1, B6, and B12 assays) were unremarkable. Anti-neuronal and paraneoplastic antibodies (intracellular antibodies: ANNA1, ANNA2, PCA-1, CRMP5, anti-amphiphysin, anti-Ma2, anti-Ma1, anti-SOX1, anti-ZIC4, anti-Tr, anti-GAD; and antibodies targeting neuronal cell surface or synaptic proteins: anti-NMDA receptor, anti-LGI1, anti-Caspr2, anti-DPPX, anti-AMPA receptor, anti-GABA receptor) tests revealed positive anti-amphiphysin antibodies in two sera samples (Fig. 1b). Cerebrospinal fluid (CSF) analysis showed normal cell counts and proteins, but positive oligoclonal bands (3–10) and anti-amphiphysin antibodies. A full-body positron emission tomography (PET) scan and a thoraco-abdominal computed tomography (CT) scan were found to be normal.

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Video 1. (a) Patient aged 82 years. The patient presents chorea and athetosic movements. At the beginning of the video, the patient tries to control the movements, giving them a slower, writhing quality, more akin to athetosis. When she stops trying to control the movements, they become choreic and dystonic, affecting both the left hand and the face. (b) Patient aged 82 years, after treatment with tetrabenazine (75 mg/day). Tetrabenazine administration markedly improved the movements. (c) Patient aged 89 years. The patient presents only slight choreic movements in the left hand.
Video content can be viewed at https://onlinelibrary.wiley.com/doi/10.1002/mds.30140

Mammography revealed breast cancer without lymph node extension or spread into any other organ. Surgery was performed, followed by chemotherapy with docetaxel and a full course of cyclophosphamide (total dose of 4 g). Two courses of high-dose intravenous corticosteroids were administered. Another EEG was performed, but since there was no evidence of epileptic discharges, levetiracetam was tapered until it was stopped. Tetrabenazine (75 mg/day) was added, accompanied by a marked improvement in the abnormal movements (Video 1b).

At age 84 years, the patient's choreic movements were under good control with 50 mg/day tetrabenazine. They returned, however, when lower doses were administered (Video 1b). Anti-amphiphysin antibodies remained positive in blood and CSF. PET-CT scan, thoraco-abdominal, and pelvic CT scans remained normal and brain MRI was unchanged.

At the patient's latest evaluation at age 89 years, slight focal movements remained but they were very mild (Video 1c). There was no recurrence of the tumor and tetrabenazine was successfully reduced by 25 mg.

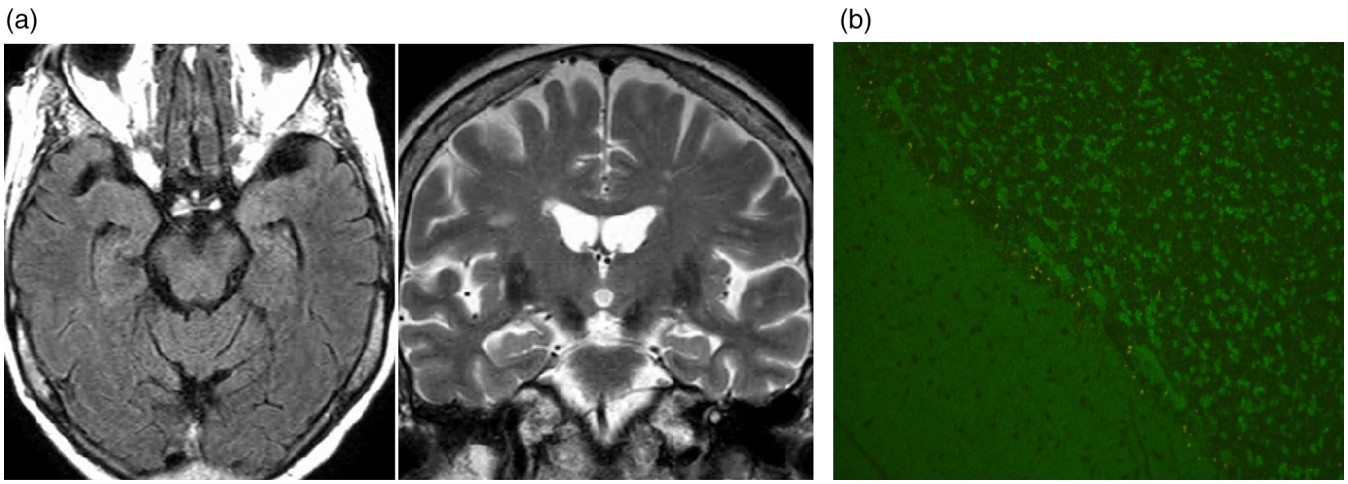

FIG. 1. Brain magnetic resonance imaging (MRI) and immunofluorescence of the antibody. (a) Brain MRI revealed bilateral T2/FLAIR (fluid-attenuated inversion recovery) hyposignal in the amygdalohippocampal complex and mild cortical atrophy without other specific changes. (b) Image of anti-amphiphysin antibody. Representative image of anti-amphiphysin antibody binding in patient's sera obtained by indirect immunofluorescence staining on cerebellum slice from monkey (original magnification ×40). [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 1 *Cases of isolated paraneoplastic hemichorea reported in the literature.*

Case reference	Age at onset (years)/ gender	Antibodies	Brain MRI	Associated tumor	Movement disorders associated with hemichorea	Other neurological manifestations	Treatment/chorea/ response/evolution
13	72/F	LGI1	Normal	Renal cell carcinoma	None	Dysdiadochokinesis and gait disturbance.	Partial nephrectomy with total regression of chorea
14	75/M	Hu/ANNA1	Temporobasal and temporomesial bilateral hyperintensity	Colon cancer 4 months after	None	Cognitive disorder	No therapy. Death in 6 months
15	69/M	CV2/CRMP-5	Normal	Lung cancer	Dystonia, hyperkinetic dysarthria	Vision loss	IVMP/improved. Death in 2 months
16	75/F	CASPR2	Normal	Lung cancer	None	None	Symptomatic treatment only with acceptable control
17	77/M	LGI1	Normal	None	None	Anterograde amnesia and executive dysfunction	Resolved with hyponatremia correction

Abbreviations: F, female; IVMP, intravenous methylprednisolone; M, male; MRI, magnetic resonance imaging.

This dosage was maintained because the movements would reappear when tetrabenazine was administered.

Discussion

Anti-amphiphysin antibody-related encephalitis is rare and manifests variable clinical presentations such as stiff person syndrome, sensory ganglionopathy, myelopathy, and cerebellar ataxia.[3,5,7,8] Our patient did not experience any other common neurological symptoms classically described in anti-amphiphysin antibody-related encephalitis patients such as limbic encephalitis, limb weakness/numbness, ataxia, sleep disorders, or dysautonomia.[9] On the contrary, she presented isolated choreic movements, which have rarely been described previously in anti-amphiphysin antibody-related encephalitis. Due to the atypical phenomenology and clearly unilateral localization of her abnormal movements, we considered the possibility of a paroxystic etiology prompting us to consider continuous focal epilepsy, as is casually observed in anti-amphiphysin antibody-related encephalitis.[2] But since no EEG abnormalities and no response to antiepileptic drugs were observed this was ruled out, although the patient's symptoms demonstrably responded to tetrabenazine.

Movement disorders, as a clinical presentation of paraneoplastic neurological syndromes, are rarely seen.[10] However, they may be the prominent and common feature in several autoantibody-associated neurological diseases or paraneoplastic neurological syndromes. Paraneoplastic chorea, in particular, typically starts subacutely, progresses rapidly, and involves the four limbs as well as the trunk, head, and neck. They are very rarely confined to only one hemibody (see Table 1). Moreover, it is an extremely rare occurrence of anti-amphiphysin antibody-related encephalitis.[11,12] Thus, this case highlights the importance of considering paraneoplastic origin of an atypical chorea and, notwithstanding the challenges of diagnosing patients with this condition, recognizing and treating the underlying cause is crucial. ■

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S.D.: 3A, 3B
M.R.: 1D, 2C
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Data Availability Statement

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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