The Cerebellum (2019) 18:976–982
https://doi.org/10.1007/s12311-019-01075-9

SHORT REPORTS

Stroke-Like Presentation of Paraneoplastic Cerebellar Degeneration: a Single-Center Experience and Review of the Literature

Alberto Vogrig[1,2,3,4] · Andrea Bernardini[5] · Gian Luigi Gigli[1,5,6] · Elisa Corazza[5] · Alessandro Marini[5] · Samantha Segatti[5] · Martina Fabris[7] · Jérôme Honnorat[2,3,4] · Mariarosaria Valente[1,5]

Published online: 29 August 2019
© Springer Science+Business Media, LLC, part of Springer Nature 2019

Abstract

Paraneoplastic cerebellar degeneration (PCD) is usually thought to have a subacute progression over several weeks. We report herein incidence and clinical features of hyperacute onset PCD, a vertebrobasilar stroke mimic. We performed a retrospective analysis of all suspected PCD cases referred to the Udine University Hospital between 2009 and 2017. Our center provides the only neuroimmunology laboratory for three provinces of the Friuli-Venezia Giulia region, Italy (983,190 people as of January 1, 2017). Inclusion criteria were (1) abrupt onset of neurological symptoms; (2) initial consideration of a vascular etiology; (3) final diagnosis of "definite PCD." We also carried out a systematic review of the literature in order to identify previous stroke-like PCD cases. Between 2009 and 2017, 24 patients received a final diagnosis of PCD. The age-standardized incidence rate of PCD was 0.22/100,000 person-years. Two cases (8.3%) had a stroke-like onset, with an incidence of 0.02/100,000 person-years. Additionally, 10 previously reported stroke-like PCD cases were identified. Among all cases ($n = 12$), 67% were female; median age was 51 years (range, 22–69). An associated cancer was discovered in all cases. Brain imaging was normal in most (75%) of the patients. Cerebrospinal fluid (CSF) analysis showed inflammatory alterations in 73% of the cases. Cancer treatment was more effective than immunotherapy in improving the neurological syndrome. Typical patients with hyperacute PCD are middle-aged women with normal brain imaging, inflammatory markers in CSF, and cancer. Surgery of the underlying cancer is probably the best treatment. PCD must be considered in the differential diagnosis of acute-onset ataxia and/or vertigo.

Keywords Paraneoplastic syndromes · Incidence · Epidemiology · Stroke · Differential diagnosis · Ataxia

Introduction

Acute dizziness, vertigo, and imbalance are common presenting symptoms in the emergency department, with vertebrobasilar stroke being the most common neurological etiology [1]. The preeminent role of stroke in the differential diagnosis of central acute vestibular syndrome risks to overshadow other less common nosological entities, as reflected

Alberto Vogrig and Andrea Bernardini contributed equally to this work.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s12311-019-01075-9) contains supplementary material, which is available to authorized users.

✉ Alberto Vogrig
alberto.vogrig@gmail.com

[1] Clinical Neurology Unit, Santa Maria della Misericordia University Hospital, Piazzale Santa Maria della Misericordia, 15, 33010 Udine, Italy

[2] French Reference Center on Paraneoplastic Neurological Syndrome and Autoimmune Encephalitis, Hospital for Neurology and Neurosurgery Pierre Wertheimer, Lyon University Hospital, Lyon, France

[3] SynatAc Team, NeuroMyoGene Institute, INSERM U1217/CNRS UMR5310, Lyon, France

[4] University Claude Bernard Lyon 1, University of Lyon, Lyon, France

[5] Neurology Unit, Department of Medicine (DAME), University of Udine Medical School, Udine, Italy

[6] Department of Mathematics, Informatics and Physics (DMIF), University of Udine, Udine, Italy

[7] Institute of Clinical Pathology, Department of Laboratory Medicine, Santa Maria della Misericordia University Hospital, Udine, Italy

by the growing rate of stroke mimics treated with intravenous thrombolysis (IVT) [2]. IVT is an effective treatment for acute ischemic stroke but has several potential adverse effects, including internal bleeding, intracranial hemorrhage, and death. Cancer patients are more prone to develop neurological deterioration after treatment with IVT, probably due to higher risk of brain hemorrhage [3, 4]. Patients who are not eligible for IVT usually receive antiplatelet and/or anticoagulant therapy, and the bleeding risk is higher in those with an associated cancer [5].

Therefore, the early identification of patients with cancer that present with an acute vestibular syndrome unrelated to a vascular etiology is of utmost importance, since stroke therapies are likely to provide more risks than benefits in this subgroup of patients.

Paraneoplastic cerebellar degeneration (PCD) is a neurological syndrome characterized by cerebellar ataxia due to tumor-induced autoimmunity against cerebellar antigens.

Onset is usually gradual over weeks to months, although acute forms have been rarely described [6].

In this study, we report incidence and clinical features of hyperacute onset PCD, a vertebrobasilar stroke mimic. We also conducted a review of the literature to identify previous reports of PCD in adults with a stroke-like onset.

Methods

Our institution, the Udine University Hospital, provides the only medical laboratory assessing the presence of neuronal antibodies (Abs) for 3 provinces of the Friuli-Venezia Giulia region, Northeastern Italy (Udine, Pordenone, and Gorizia, for a total of 983,190 inhabitants as of January 1, 2017). PCD cases were identified from multiple sources: hospital-based database of patients tested for the presence of neural Abs at our Institution and hospital discharge diagnoses of all the Neurology Departments in the abovementioned provinces. We retrospectively reviewed the medical records of all patients who were referred between January 1, 2009, and December 31, 2017, for suspected paraneoplastic syndrome (PNS) and who received a definite diagnosis of PCD according to available diagnostic criteria [7]. All patients underwent a comprehensive laboratory examination for suspected PNS, including both line-blot analysis (Euroimmun AG, Luebeck, Germany) on recombinant proteins for the presence of onconeuronal Abs (anti-Hu, Yo, CV2/CRMP5, Ri, Ma2, and amphiphysin) and transfected cell-based assays (Euroimmun AG, Luebeck, Germany) for Abs directed towards neural surface antigens (NMDAR, LGI1, CASPR2, $GABA_BR$, AMPA1R, AMPA2R). Immunofluorescence on rat brain section was performed in indeterminate cases at the French Reference Center of Paraneoplastic Neurological Syndrome, Lyon, France.

The inclusion criteria for the present study were as follows:

1) Abrupt onset of the neurological symptoms;
2) Initial consideration of a vascular etiology;
3) Final diagnosis of "definite PCD" (PCD in a patient with or without well-characterized Abs and cancer that develops within 5 years).

Patients residing outside the study area were excluded. The present study was approved by the Institutional Review Board of the University of Udine Medical School.

Review of the Literature

A comprehensive search was performed on May 2019 without language restrictions on PubMed, Web Of Science and Scopus with the string (acute) AND ((ataxia AND paraneoplastic) OR ("paraneoplastic cerebellar degeneration")). All abstracts were screened in order to select adult cases of PCD with a stroke-like onset; full texts of pertinent articles were checked in order to exclude nonrelevant papers. The same procedure was performed on the references of relevant articles.

Statistical Analyses

Average annual incidence rate was estimated per 100,000 and calculated as the number of new diagnoses of PCD divided by the number of person-years at risk in the resident population. Data on the resident population were obtained from the Italian National Institute of Statistics (ISTAT).

Crude incidence rates were standardized to the European standard population (European Commission, 2013) by direct method. Mid-p exact 95% confidence intervals (95% CI) were calculated for incidence rates.

Results

Epidemiology

Between 2009 and 2017, 24 patients received a final diagnosis of PCD in the study area. The age-standardized incidence rate of PCD was 0.22/100,000 person-years (95% CI, 0.13–0.31). Twenty-two cases had a classic subacute onset (91.7%), while 2 patients (8.3%) had a stroke-like onset. Hyperacute PCD showed an incidence of 0.02/100,000 person-years (95% CI, − 0.01–0.05). The 2 cases identified with stroke-like onset presented with sudden-onset down-beat nystagmus (case 1) and abrupt limb ataxia (case 2). Details on epidemiological data and clinical presentation of the PCD cases with stroke-like onset are available in the Supplementary Material.

Review of the Literature

Our literature search yielded 189 articles published between 1974 and 2019, among which we retrieved 10 additional cases of hyperacute PCD [8–17]. By combining our cases with those previously described, we were able to define the clinical phenotype of hyperacute PCD. All patients are presented in Table 1. Among all cases ($n = 12$), 67% were female; median age was 51 years (range, 22–69). All patients exhibited a sudden onset of neurological symptoms. Concomitant vascular risk factors were present in 67% of them. Brain imaging was normal in most (75%) of the patients and none had radiological evidence of an acute stroke. An associated cancer was discovered in all cases (breast in 2, ovarian in 2, small cell lung cancer in 3, other type of cancer in 5). Cerebrospinal fluid (CSF) results were available for 11 patients and abnormal in 8 (73%) with the most common abnormality being pleocytosis (6/11), followed by increased protein content (4/11) and presence of CSF-exclusive oligoclonal bands (3/11). Results of antibody testing was available for 10 patients: 6 showed Ab-positivity (3 Yo, 1 Hu, 1 Tr, 1 VGKC without further specifications). All patients received a final diagnosis of definite PNS according to the international guidelines. Eight patients (67%) received an immunotherapy (corticosteroids in 7 cases, plasmapheresis in 4, intravenous immunoglobulin in 4). Improvement was usually minor/mild after immunotherapy. Surgery of the underlying tumor with or without concomitant chemotherapy was adopted in 5 cases (42%): a major, albeit transitory, improvement or complete recovery was noticed in 4/5 cases.

Discussion

In this study, we provide incidence and clinical features of PCD, showing that a hyperacute onset is possible, and therefore, this syndrome should be considered in the differential diagnosis of acute neurovascular syndromes. Indeed, the 2 newly reported cases of PCD share a similar presentation: an acute vestibular syndrome with localizing signs of central involvement, initially mimicking a stroke. The presence of relevant vascular risk factors (Table 1) further strengthened the clinical impression of a vascular etiology. After an appropriate workup, a diagnosis of definite PCD [7] was established in both cases. Similarly, all previous cases of acute stroke-like PCD met the criteria for a definite paraneoplastic syndrome. No clear demographic, clinical or laboratory feature differentiates between acute cases and classic subacute patients described in literature [18]. Accordingly, time of onset is not considered among diagnostic criteria [7], although a subacute progression is widely recognized as usual [6]. An explanation for such variability in disease onset and progression despite the substantial demographic-laboratory homogeneity is currently lacking; individual predisposing factors are probably involved.

From an immunological prospective, it is difficult to explain how an immune-mediated process could present so acutely. Recent data, however, pointed out that a massive cerebellar inflammation and intense cytokine production take place in a murine model of PCD [19], and this inflammatory response is able to induce Purkinje cell death even at very early stages (substantial cell loss is detectable even after 6 days in a model of anti-Yo-associated PCD) [20]. The final effectors of this immune-response are $CD8^+$ T cells, coordinated by $CD4^+$ T cells, which can in turn increase the production of interferon-gamma (IFNγ) and tumor necrosis factor-alpha (TNF-α), leading to neuronal dysfunction and neuronal excitotoxicity due to an alteration in calcium homeostasis [19, 20]. This cascade of events is likely to be responsible for the subsequent neuronal apoptosis. To the contrary, the fact that neither immunoglobulin (Ig) binding nor complement deposition were detected in these models suggests that the humoral immune response does not play a major role in PCD [19]. Based on these data, our hypothesis is that there is an initial "functional" alteration of Purkinje cells that can be widespread and acute in relation to the intense cytokine production, and it may account for the "stroke-like" clinical presentation. Such early impairment is probably amenable to treatment. Later on, when diffuse Purkinje cell loss takes place, irreversible damage occurs and cerebellar atrophy ensues.

On a therapeutic note, our cases as well as previous reports (Table 1) seem to confirm immune therapy as the main medical treatment. Nevertheless, a substantial proportion of cases show an unsatisfactory response. Tumor removal had a relevant clinical effect in the majority of surgically treated cases, as already demonstrated in autoimmune encephalitis [21]. Apart from medical or surgical treatment, physical therapy appears to play a significant role in the treatment of PCD, as seen in case 2 and in previous cases [22].

To the best of our knowledge, this is the first report on the incidence of hyperacute-onset PCD. Differential diagnosis with posterior circulation stroke can be challenging. We provide in Table 2 a list of clinical, neuroimaging, and laboratory features that should be considered in the process of differentiating between the two conditions [23–27].

In conclusion, PCD can present with a hyperacute onset mimicking stroke in about 8% of the cases. A high index of suspicion is necessary for early diagnosis and consequent cancer treatment, essential for a positive impact on outcome. On the other side, a more extensive availability of diffusion-weighted imaging brain magnetic resonance imaging would permit to reduce the number of cases inappropriately treated with IVT.

Table 1 Main characteristics of reported cases of paraneoplastic cerebellar degeneration with stroke-like onset

Case	Age	Sex	Signs and symptoms	Brain imaging[a]	CSF analysis	Antibodies	Vascular risk factors	Oncologic history/risk factors	Treatment and response	Primary neoplasm	Diagnostic probability (Graus et al. 2004)
1. Present series	44	F	Dizziness Nausea and vomiting Gait ataxia Downbeat nystagmus	Normal	Protein 71.6 mg/dl 58 lymphocytes/μl	Yo	History of atrial tachycardia Paroxysmal AF in ED	Family history of breast cancer (mother)	IV steroids: no response PE and IVIg: partial and transient improvement Clonazepam: mild improvement of head tremor Surgery: no improvement	Breast carcinoma ER−, PR−, HER2+	Definite
2. Present series	64	F	Gait imbalance Objective vertigo Nausea and vomiting Left limb dysmetria	Multiple focal supra- and infra-tentorial white matter T2 hyper-intensities; no diffusion restriction	Protein 41 mg/dl 2 lymphocytes/μl	None	Hypertension Diabetes Dyslipidemia Former smoker	Bilateral breast cancer 4 years before Former smoker	IV steroids: improvement	Small cell lung cancer	Definite
Anderson et al. 1988 (case 1)	49	F	Trunk and limb ataxia Vertigo Dysarthria Opsoclonus Myoclonus	CT: mild cerebral and cerebellar atrophy	Protein 47 mg/dl 70 leukocytes/μl (90% lymphocytes)	N/A	N/A	Small cell lung cancer 5 months before	PE and steroids: no response	Small cell lung cancer	Definite
Pradat et al. 1995	69	M	Gait instability Dysarthria Trunk and limb ataxia	Normal	Protein 110 mg/dl 93 leukocytes/μl (95% lymphocytes) Oligoclonal bands	Hu	Smoking	Smoking	None	Poorly differentiated carcinoma	Definite
Bhatia et al. 2003	47	M	Gait imbalance Trunk and limb ataxia Nystagmus Dysarthria	Normal	No pleocytosis Normal protein Oligoclonal bands	N/A	Diabetes Hypertension Smoking	Smoking	Surgery and ChT: marked improvement	Small cell lung cancer	Definite
Ypma et al. 2006	34	M	Gait and limb ataxia Dysarthria Diplopia Nausea Vertigo Headache	Normal	Protein 73 mg/dl 462 lymphocytes/μl	Tr	Smoking	Smoking	PE and ChT: stabilization	Hodgkin lymphoma	Definite
Bonakis et al. 2007	56	F	Broad-based gait Trunk and limb ataxia Diplopia on right gaze Deficit in smooth pursuit eye movements Downbeat nystagmus	Normal	Protein 43 mg/dl 32 lymphocytes/μl Oligoclonal bands	Yo	None	Ovarian carcinoma 6 years before	IVIg: no response IV steroids: slight improvement	Ovarian carcinoma	Definite
Hauspy et al. 2007	52	F	Postural instability Left ear pain Subsequent development of trunk ataxia, opsoclonus, myoclonus, dysarthria and dysphagia	Normal	Normal	None	None	Vaginal melanoma 3 months before	Surgery: marked improvement (Recurrence and death after 5 months)	Vaginal melanoma	Definite
Ammar et al. 2008	64	F	Broad-based gait Limb ataxia Dizziness	Normal	Protein 71 mg/dl 0 leukocytes/μl	None	Coronary artery disease	None	Surgery: almost complete remission	Clear cell renal cell carcinoma	Definite

Table 1 (continued)

Case	Age	Sex	Signs and symptoms	Brain imaging[a]	CSF analysis	Antibodies	Vascular risk factors	Oncologic history/risk factors	Treatment and response	Primary neoplasm	Diagnostic probability (Graus et al. 2004)
Park et al. 2014	22	F	Ataxia Vertigo Vomiting Oscillopsia Dysarthria	Normal	First: lymphocytic pleocytosis Second: protein 17 mg/dl 6 leukocytes/μl (93% lymphocytes)	None	Diabetes Deep venous thrombo-sis	Family history of breast, colon, and bladder cancer	IV steroids, PE and IVIg: minimal improvement Surgery: complete remission	Mature ovarian teratoma	Definite
Pavolucci et al. 2017	67	M	Ataxia Vertigo Nausea and vomiting Dysarthria Nystagmus (Subsequent development of occasional diplopia, xerostomia, and fatigue consistent with LEMS)	Normal	Normal	VGCC	Passive smoking	Weight loss of 5 kg in 6 months Passive smoking	IV steroids: mild reduction of nausea IVIg (3 cycles): partial improvement of dysarthria and ataxia (3-4DAP: reduction of fatigue)	Merkel cell carcinoma	Definite
Enríquez-Marulanda et al., 2018	50	F	Vertigo Ataxia Occipital headache Projectile vomiting when standing or with Valsalva maneuver	Diffuse tonsillar edema with tonsillar descent and leptomeningeal enhancement	Not performed (Meningeal biopsy with diffuse lymphocytic infiltrate with slight CD4+ predominance)	Yo	None	None	Suboccipital decompressive craniectomy Methylprednisolone: progressive improvement	Breast ductal carcinoma ER+, PR−, HER2+++	Definite

AF, atrial fibrillation; *CSF*, cerebrospinal fluid; *CT*, computed tomography; *ED*, emergency department; *ER*, estrogen receptor; *HER2*, human epidermal growth factor receptor 2; *IV*, intravenous; *IVIg*, intravenous immune globulin; *LEMS*, Lambert-Eaton Myasthenic Syndrome *MRI*, magnetic resonance imaging; *PE*, plasma exchange; *PR*, progesterone receptor

[a] MRI unless stated otherwise

Table 2 Red flags and distinguishing features between posterior circulation stroke vs. hyperacute paraneoplastic cerebellar degeneration

Feature	Posterior circulation stroke	Hyperacute PCD
Previous medical history	Vascular risk factors Red flag: cancer, especially pancreatic, colorectal, and lung tumors, increase the risk of stroke [23]	Recent (< 5 years) history of cancer (especially breast, ovary, and small cell lung cancer) Red flag: vascular risk factors (e.g., smoking) are commonly present also in PCD
Ataxia	Asymmetric onset is common, often associated with involvement of long tracts [24]	Pancerebellar syndrome is the rule, with ataxia affecting both trunk and limbs, although asymmetric onset has been reported previously [25, 26]
Early hyperacute MRI features	Lesion(s) involving the distribution of vascular territories, or multiple lesions in case of embolic strokes, demonstrating increased DWI signal and reduced ADC values	Typically normal A case with diffuse MRI signal abnormality in the cerebellar hemispheres early in the course of PCD has been reported [27]
CSF examination	Typically normal Inflammatory alterations may be present in a subset of patients (e.g., vasculitis syndromes)	CSF pleocytosis (white blood cell count of more than five cells per mm^3) is common Presence of oligoclonal bands Increased protein content often detected

ADC, apparent diffusion coefficient; *CSF*, cerebrospinal fluid; *DWI*, diffusion-weighted imaging; *MRI,* magnetic resonance imaging; *PCD*, paraneoplastic cerebellar degeneration

Author Contributions Drs. Vogrig and Bernardini designed and conceptualized the study, collected and interpreted the data, and wrote the manuscript. Drs. Corazza, Marini, Segatti, and Fabris collected and analyzed the data. Prof. Honnorat analyzed and interpreted the data and provided critical revision of the manuscript. Prof. Gigli and Prof. Valente interpreted the data, revised the manuscript, and supervised the study.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Standard This study followed the tenets of the Declaration of Helsinki and was performed according to the guidelines of the Institutional Review Board of University of Udine Medical School.

References

1. Choi J-Y, Lee S-H, Kim J-S. Central vertigo. Curr Opin Neurol. 2018;31:81–9.
2. Burton TM, Luby M, Nadareishvili Z, Benson RT, Lynch JK, Latour LL, et al. Effects of increasing IV tPA-treated stroke mimic rates at CT-based centers on clinical outcomes. Neurology. 2017;89:343–8.
3. Nam K-W, Kim CK, Kim TJ, An SJ, Oh K, Ko S-B, et al. Intravenous thrombolysis in acute ischemic stroke with active cancer. Biomed Res Int. 2017;2017:4635829.
4. Weeda ER, Bohm N. Association between comorbid cancer and outcomes among admissions for acute ischemic stroke receiving systemic thrombolysis. Int J Stroke. 2019;14:48–52.
5. Shireman TI, Howard PA, Kresowik TF, Ellerbeck EF. Combined anticoagulant-antiplatelet use and major bleeding events in elderly atrial fibrillation patients. Stroke. 2004;35:2362–7.
6. Mitoma H, Adhikari K, Aeschlimann D, Chattopadhyay P, Hadjivassiliou M, Hampe CS, et al. Consensus paper: neuroimmune mechanisms of cerebellar ataxias. Cerebellum. 2016;15:213–32.
7. Graus F. Recommended diagnostic criteria for paraneoplastic neurological syndromes. J Neurol Neurosurg Psychiatry. 2004;75:1135–40.
8. Anderson NE, Budde-Steffen C, Rosenblum MK, Graus F, Ford D, Synek BJ, et al. Opsoclonus, myoclonus, ataxia, and encephalopathy in adults with cancer: a distinct paraneoplastic syndrome. Medicine (Baltimore). 1988;67:100–9.
9. Pradat PF, Uchuya M, Fontaine B, Lubetzki C. Pure cerebellar syndrome associated with anti-Hu antibodies. Rev Neurol (Paris). 1995;151:341–3.
10. Bhatia R, Prabhakar S, Lal V, Khurana D, Das CP. Acute onset paraneoplastic cerebellar degeneration in a patient with small cell lung cancer. Neurol India. 2003;51:244–5.
11. Ypma PF, Wijermans PW, Koppen H. Paraneoplastic cerebellar degeneration preceding the diagnosis of Hodgkin's lymphoma. Neth J Med. 2006;64:5.
12. Bonakis A, Papageorgiou SG, Mandellos D, Galani E, Kalfakis N. Acute onset paraneoplastic cerebellar degeneration. J Neuro-Oncol. 2007;84:329–30.
13. Hauspy J, Nevin A, Harley I, Mason W, Quirt I, Ghazarian D, et al. Paraneoplastic syndrome in vaginal melanoma: a case report and review of the literature. Int J Gynecol Cancer. 2007;17:1159–63.
14. Ammar H, Brown SH, Malani A, Sheth HK, Sollars EG, Zhou SX, et al. A case of paraneoplastic cerebellar ataxia secondary to renal cell carcinoma. South Med J. 2008;101:556–7.
15. Park JE, Liang T-W. Reversible cerebellar ataxia due to ovarian teratoma. J Clin Neurosci. 2014;21:1467–9.
16. Pavolucci L, Giannini G, Giannoccaro MP, Foschini MP, Lang B, Avoni P, et al. Paraneoplastic cerebellar degeneration and Lambert-Eaton myasthenia in a patient with merkel cell carcinoma and voltage-gated calcium channel antibodies: short reports. Muscle Nerve. 2017;56:998–1000.
17. Enríquez-Marulanda A, Beltrán-Osorio LD, Escobar LA, Granados AM, Velásquez-Lasprilla F, Orozco JL. Anti-Yo-associated paraneoplastic cerebellar degeneration manifesting as acute cerebellitis with posterior cranial fossa hypertension. World Neurosurg. 2018;112:117–22.
18. Vernino S. Paraneoplastic cerebellar degeneration. Handb Clin Neurol. 2012;103:215–23.

19. Yshii LM, Gebauer CM, Pignolet B, Mauré E, Quériault C, Pierau M, et al. CTLA4 blockade elicits paraneoplastic neurological disease in a mouse model. Brain. 2016;139:2923–34.
20. Panja D, Vedeler CA, Schubert M. Paraneoplastic cerebellar degeneration: Yo antibody alters mitochondrial calcium buffering capacity. Neuropathol Appl Neurobiol. 2019;45:141–56.
21. Vogrig A, Pauletto G, Belgrado E, Pegolo E, Di Loreto C, Rogemond V, et al. Effect of thymectomy on refractory autoimmune status epilepticus. J Neuroimmunol. 2018;317:90–4.
22. Kato N, Hashida G, Konaka K. Rehabilitation for a patient with anti-Yo antibody-positive paraneoplastic cerebellar degeneration caused by breast cancer: a case report and literature review. Medicine. 2017;96:e8468.
23. Navi BB, Reiner AS, Kamel H, Iadecola C, Elkind MS, Panageas KS, et al. Association between incident cancer and subsequent stroke. Ann Neurol. 2015;77:291–300.
24. Mehndiratta M, Pandey S, Nayak R, Alam A. Posterior circulation ischemic stroke-clinical characteristics, risk factors, and subtypes in a north Indian population: a prospective study. Neurohospitalist. 2012;2:46–50.
25. Peterson K, Rosenblum MK, Kotanides H, Posner JB. Paraneoplastic cerebellar degeneration. I. A clinical analysis of 55 anti-Yo antibody-positive patients. Neurology. 1992;42:1931–7.
26. Shams'ili S, Grefkens J, de Leeuw B, van den Bent M, Hooijkaas H, van der Holt B, et al. Paraneoplastic cerebellar degeneration associated with antineuronal antibodies: analysis of 50 patients. Brain. 2003;126:1409–18.
27. Gilmore CP, Elliott I, Auer D, Maddison P. Diffuse cerebellar MR imaging changes in anti-Yo positive paraneoplastic cerebellar degeneration. J Neurol. 2010;257:490–1.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.