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Letter to the Editor

Isolated choroid plexus involvement in a case of granulomatosis with polyangiitis negative for antineutrophil cytoplasmic antibodies (ANCA)

Dear Editors,

granulomatosis with polyangiitis (GPA, formerly Wegener's) is a systemic necrotizing vasculitis that predominantly involves respiratory tract and kidneys [1,2]. GPA usually presents with nervous system involvement in the later course, mainly affecting the peripheral nervous system [3]. Vasculitis has been reported up to 6% of GPA cases with central nervous system (CNS) involvement [2,4]. Detection of either anti-proteinase 3 (PR3)-ANCA or myeloperoxidase (MPO)-ANCA can support the diagnosis, but in some cases ANCA are not detected [3]. Overall, 82–94% of patients with GPA are ANCA positive [5], leaving approximately 10% ANCA negative. A large-scale study has demonstrated that 83% of ANCA-negative GPA patients show severe CNS involvement, whereas only 10% of all the GPA patients have CNS involvement [6]. To diagnose GPA, histologic review via biopsy is one of the major criteria and imaging studies are helpful [3]. Characteristic histopathologic findings are necrotizing vasculitis that affects small- and medium-size vessels and extravascular granulomas.

We present a case of choroid plexus involvement in a patient with ANCA-negative GPA, whose diagnosis was confirmed on biopsy.

1. Case description

A 70-year-old woman with a past medical history of hypertension presented to our Clinic with memory loss, headache and hallucinations associated with fever, arthralgia and myalgia of 2 weeks' duration. On admission, neurological examination showed a bradykinetic, broad based, magnetic gait and halted speech with anomic latencies. A cognitive evaluation revealed a Mini-Mental State Examination (MMSE) score of 11/30. The patient underwent brain MRI that demonstrated extensive dilation of the temporal horns of the lateral ventricles, T2/FLAIR hyper intense signal in periventricular regions and hypertrophic choroid plexus strongly enhancing after gadolinium administration (Fig. 1 A–C). Neither hypertrophic pachymeningitis nor sinusitis were detected. MR angiography of extracranial and intracranial vessels was normal. Her routine blood tests were unremarkable, in particular no urinary sediment was detected. A detailed immunological screening, including antineutrophil cytoplasmic (both PR3 and MPO) and antinuclear antibodies, erythrocyte sedimentation rate, complement, immunoglobulins (including IgG4), anti-glomerular basement membrane antibodies, lymphocytic subpopulations and angiotensin converting enzyme resulted within normal limits. Quantiferon-TB Gold test gave a negative result. C-reactive protein was elevated (80 mg/L with reference < 6). A lumbar puncture demonstrated a normal cerebrospinal fluid (CSF) opening pressure with normal cells count and glucose but elevated protein (191 mg/dL with reference values 15–45). No atypical cells were detected. Blood and CSF cultures were negative. Viral testing (Hepatitis B, C virus, Immunodeficiency virus, Cytomegalovirus, Ebstein-Barr virus, Parvovirus B19) was also negative. Oligoclonal bands were seen on immunofixation.

A chest computed tomography (CT) as well as whole body positron emission tomography CT were negative. A choroid plexus biopsy was performed and showed fibro-inflammatory tissue with few scattered giant cells and basophilic granular material in the connective tissue, diagnostic for GPA (Fig. 1 G–I). Patient was treated with high-dose intravenous Methylprednisolone (1 g daily for 5 days) with a progressive clinical recovery. A cognitive evaluation demonstrated improvement of performance in MMSE (27/30). Thus, patient was treated with cyclophosphamide (15 mg/kg) and daily steroids (1 mg/kg). A one-month control brain MRI showed normal ventricular size but persistent enhancement of the choroid plexus (Fig. 1 D–F).

2. Discussion

The papillary fronds of the choroid plexus which protrude into the ventricle have an external epithelial lining that composes the structural basis of the blood-CSF barrier. The choroid plexus is continuous with the ependymal cell layer that lines the ventricles and it is characterized by a core of capillaries and loose connective tissue. For these reasons, choroid plexus is an important station both for immunological and infectious diseases. When the choroid plexus is involved, the main imaging features are of ventricular sequestration; usually the temporal horn is involved and the obstruction to free CSF flow results in a significant dilation of the temporal horn with CSF seepage in the surrounding tissue and mass effect [7].

An accurate diagnosis of the disease underlying the involvement of choroid plexus is difficult due to the rarity and the deep location of the lesion. Differential diagnosis of choroid plexitis includes GPA, sarcoidosis, primary CNS angiitis, IgG4-related disease, CNS lymphoma and tuberculosis.

GPA is a necrotizing granulomatous inflammation usually involving the upper and lower respiratory tract, kidney and necrotizing vasculitis affecting predominantly small to medium vessels (e.g., capillaries, venules, arterioles, arteries, and veins). To our knowledge, this is the first report of a choroid plexitis GPA-related whose diagnosis was obtained on brain biopsy. Pathology of the choroid plexus showed the presence of necrotizing vasculitis of the small vessels, with leucocytoclasia, few giant cells and granulomata in the vessel walls and absence of immune deposits at immunofluorescence. According to Chapel Hill Consensus Conference, recently revised in 2012, limited expressions of GPA can occur without identifiable evidence of systemic vasculitis and the diagnosis can be achieved when the patients exhibit clinical and pathologic changes identical to those seen in GPA respiratory tract involvement [8].

Our literature review of cases of intracranial involvement in GPA yielded two reports of patients who had choroid plexus involvement.

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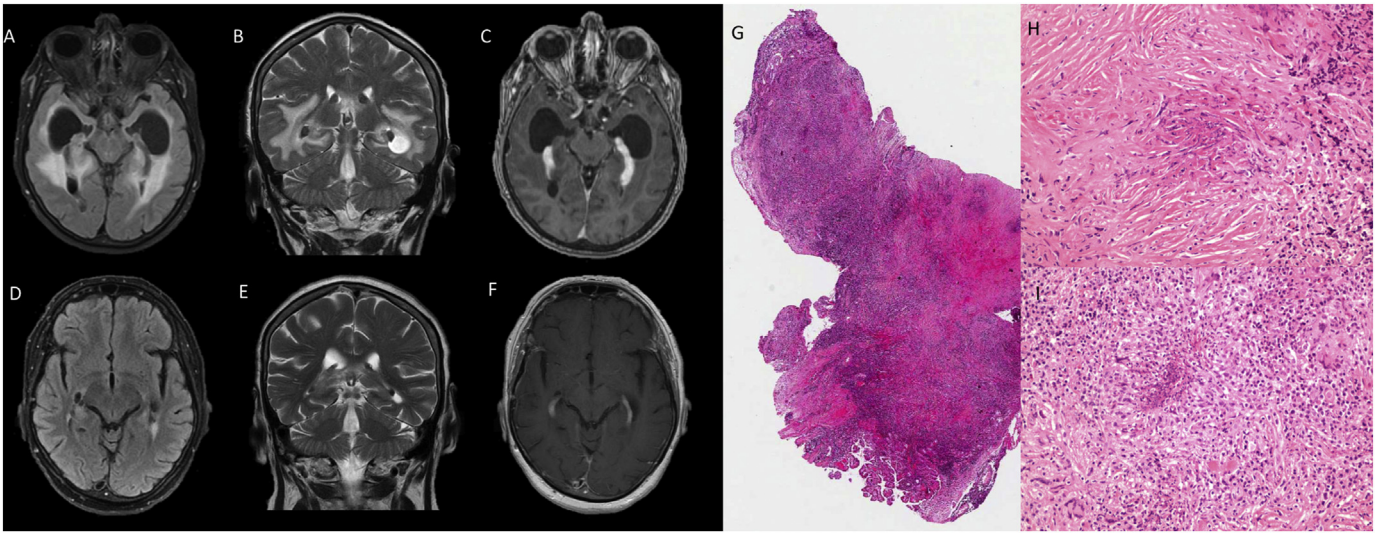

Fig. 1. Brain MRI demonstrated extent dilation of the temporal horns in the lateral ventricles, T2/FLAIR hyper intense signal in periventricular regions (A, B) and strongly enhanced gadolinium hypertrophic choroid plexus (C). A one-month control brain MRI showed normal ventricular dilatation (D, E) but persistent strongly enhanced gadolinium hypertrophic choroid plexus (F). A panoramic view of the biopsy (haematoxylin and eosin stain): choroidal plexus papillary structures are still recognizable on the right, while most of the tissue is composed by a dense fibrous stroma with a prominent inflammatory infiltrate. Foci of bluish necrotic areas are evident in the left upper portion of the biopsy (G). Palisading microgranuloma consisting of a cartwheel-shaped arrangement of histiocytes surrounding a central eosinophilic focus with necrotic debries; the surrounding inflammatory infiltrate contains a few scattered giant cells (H). Focal necrosis of collagen (so called "pathergic necrosis"): the fibrous bands are dense and eosinophilic and intermixed with basophilic granular material (I).

However, these patients had systemic involvement and ANCA were detected on blood examination [9,10]. Nevertheless, despite the high sensitivity of PR3-ANCA/cANCA in active generalized GPA (nearly 100%), some patients with active generalized GPA remain consistently ANCA negative and have serious CNS involvement as the clinical hallmark [6].

Although this finding needs confirmation in larger series, it opens up a window on the possibility that choroid plexus abnormalities may indicate an isolated CNS involvement in GPA. To conclude, brain biopsy should be considered in those patients whose clinical and radiological findings are suggestive but not decisive, because appropriate therapy could dramatically change the course of the disease.

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Contributions

Monica Margoni has part in the clinical management of the patient, in designing, writing and revising the manuscript critically.

Mattia Barbareschi has part in the anatomo-pathological diagnosis and writing the manuscript critically.

Umberto Rozzanigo has part in the radiological management of the patient.

Franco Chioffi has part in the surgical management of the patient.

Giuseppe Paolazzi has part in the clinical management of the patient.

Sabrina Marangoni has part in the clinical management of the patient, in designing and revising the manuscript critically.

Conflicts of interest/disclosures

The authors declare that they have no financial or other conflicts of interest in relation to this research.

Consent

This is a descriptive, observational study in which the identity of the patient is completely protected; therefore, no informed consent is required.

References

[1] G.S. Hoffman, G.S. Kerr, R.Y. Leavitt, et al., Wegener granulomatosis: an analysis of 158 patients, Ann. Intern. Med. 116 (1992) 488–498.
[2] H. Nishino, F.A. Rubino, R.A. Deremee, J.W. Swanson, J.E. Parisi, Neurological involvement in Wegener's granulomatosis: an analysis of 324 consecutive patients at the Mayo Clinic, Ann. Neurol. 33 (1993) 4–9.
[3] E. Lee, J. Park, S.H. Hong Choi, Seronegative granulomatosis with polyangiitis presenting with multiple cranial nerve palsies, Neuropathology 38 (2) (2018) 192–197.
[4] J.U. Holle, W.L. Gross, Neurological involvement in Wegener's granulomatosis, Curr. Opin. Rheumatol. 23 (2011) 7–11.
[5] R.J. Falk, J.C. Jennette, ANCA small-vessel vasculitis, J. Am. Soc. Nephrol. 8 (1997) 314–122.
[6] E. Reinhold-Keller, K. de Groot, K. Holl-Ulrich, et al., Severe CNS manifestations as the clinical hallmark in generalized Wegener's granulomatosis consistently negative for anti- neutrophil cytoplasmic antibodies (ANCA). A report of 3 cases and a review of the literature, Clin. Exp. Rheumatol. 19 (5) (2001) 541–549.
[7] R.M. Neeini, J.H. Yoo, J.V. Hunter, Spectrum of choroid plexus lesions in children, Am. J. Radiol. 192 (2009) 32–40.
[8] J.C. Jennette, 2012 revised international Chapel Hill consensus conference nomenclature of vasculitides, Arthritis Rheum. 65 (1) (2013) 1–11.
[9] S. Sierra, N. Luquin, Choroid plexitis as a unique neurological manifestation in granulomatosis with polyangitiis (Wegener's disease), J. Rheumatol. 41 (2014) 6.
[10] C.N. Pisoni, S. Ibanez, M. Guevara, D. Castro, S. Romero Vidomlansky, Granulomatosis with polyangiitis: recurrence presenting as ependimoplexitis, Clin. Exp. Rheumatol. 32 (Suppl. 82) (2014) S70–S72.

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