Anti-PCA/Tr antibody detection in a case of rapidly progressive cerebellar ataxia: potential added value of the in-house tissue-based assay testing

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OBJECTIVES

We report a case of anti-PCA/Tr (DNER) rapidly progressive cerebellar ataxia which highlights the advantages of the in-house tissue-based assay (TBA) testing in paraneoplastic neurologic syndromes (PNS).

CLINICAL PRESENTATION

A 19-year-old female presented with subacute onset of vertigo, oscillopsia, diplopia, and progressive ataxia. Initial brain/spine MRI scans were unremarkable (Fig. 1). Four months after symptom onset, she was admitted to our Institution with **moderate cerebellar ataxia (SARA score = 8.5),** dysmetria, diplopia, and torsional nystagmus; MRI showed mild cerebellar atrophy (Fig. 2).

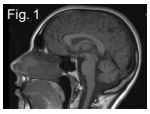
Fig. 1


Fig. 2

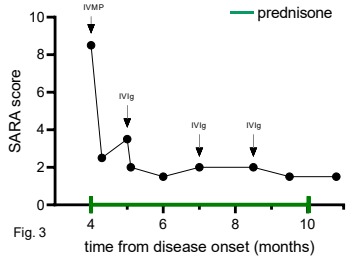

Fig. 3

TREATMENT AND NEUROLOGICAL OUTCOME

Immune-mediated ataxia was suspected, intravenous high-dose methylprednisolone (IVMP) was administered for 5 days, followed by a total of three cycles of intravenous immunoglobulin (IVIg, 2 g/kg over 5 days), due to fluctuations in neurological symptoms. At the end of the last IVIg cycle, the patient showed **substantial clinical improvement (SARA score = 1.5)**. At the last follow-up, after discontinuation of immunotherapy, the neurological condition remained clinically stable. Figure 3 reports the patient's clinical and therapeutic course assessed by SARA score.

AUTOANTIBODY TESTING

Pre-treatment **commercial indirect immunofluorescence tissue-based assay** (IIF-TBA, Euorimmun) on serum and CSF was **negative**. However, serum (1:200) testing by **in-house IIF-TBA** revealed characteristic Purkinje cell and molecular layer staining, suggestive of **anti-PCA-Tr/DNER antibodies** (Fig. 4), subsequently confirmed by immunoblot (Euroimmun), yielding a **PNS score[1] = 6** (probable PNS).

Figure 4. PC: Purkinje cells (arrow); ML: molecular layer; GL: granular layer; WM: white matter.

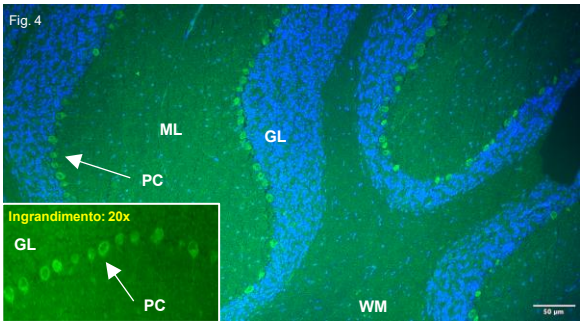

Fig. 4

ONCOLOGICAL WORK-UP

PCA-Tr/DNER antibodies are strongly associated with **Hodgkin Lymphoma** (HL; ~85%)[1]. FDG-PET/CT showed increased uptake in thoracic lymph nodes (Fig. 5). Initial lymph node (LN) biopsy was inconclusive (likely due to corticosteroid use). A subsequent mediastinal LN biopsy confirmed **HL, nodular sclerosis subtype (stage=IIIA)**. Chemotherapy was started with the ABVD regimen.

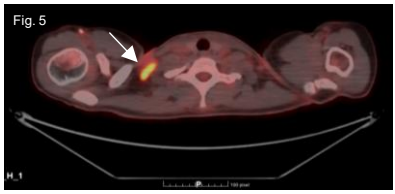
Fig. 5

DISCUSSION AND CONCLUSION

- **Second-line evaluation by in-house TBA identified anti-PCA/Tr/DNER antibodies** missed by the commercial assay, significantly impacting clinical management. This is in line with recent data showing that commercial IIF-TBAs are prone to false negatives compared to in-house techniques[2].
- Neural antibody testing is key for confirming autoimmune encephalitis and guiding cancer screening and treatment. **Negative antibody results at commercial assays should prompt referral to research labs for in-house antibody testing,** particularly in high pre-test probability settings.

References.

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2. Milano C, Businaro P, Papi C, Arlettaz L, Marmolejo L, Naranjo L, et al. Assessing commercial tissue-based assays for autoimmune neurologic disorders (I): Antibodies to intracellular antigens. Neurol Neuroimmunol Neuroinflamm. 2025 Jul;12(4):e200410. doi:10.1212/NXI.0000000000200410. Epub 2025 May 20. PMID: 40393022; PMCID: PMC12153943.