

Purkinje Cell Antibody (PCA)-2 positive, Collapsin Response-Mediated Protein (CRMP)-5 negative paraneoplastic optic neuropathy

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Introduction

- Paraneoplastic optic neuropathy (PON) is a rare cause of vision loss that usually occurs in association with small cell lung cancer
- Most patients with this condition test positive for the Collapsin Response –Mediated Protein (CRMP)-5 antibody
- PON almost always coexists in the setting of multifocal neurological dysfunction including peripheral neuropathy, autonomic neuropathy, cerebellar ataxia (1)
- We present a case of PON associated with small cell lung cancer that was negative for CRMP-5 but positive for PCA-2, which has not previously been reported with PON

Case

- A 67 year old woman noticed a decline in vision in her right eye followed by her left eye 1 week later
- Around the same time she developed painful paresthesias in both her feet
- Her past medical history included coronary artery disease, COPD and a 40-pack year smoking history
- After an examination by an ophthalmologist revealed bilateral optic disc edema she was admitted to hospital for further workup by neurology and internal medicine

Case – cont'd

- Initial investigations revealed scattered white matter hyperintensities on FLAIR and T2 in the periventricular, deep and subcortical white matter:

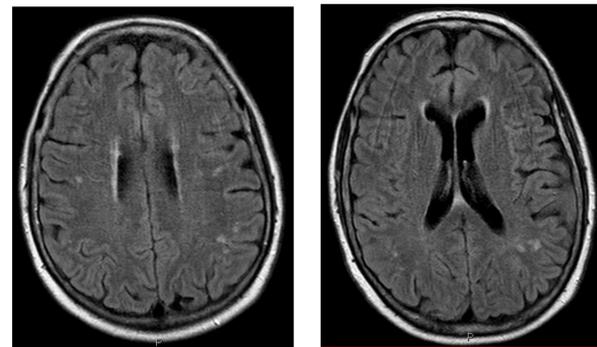


Figure 1. MRI of the brain revealing scattered white matter hyperintensities on T2/FLAIR

- Since a diagnosis of multiple sclerosis was entertained by her physicians, an MRI of the spine was ordered which incidentally revealed a large middle mediastinal mass and right hilar adenopathy
- A biopsy revealed small cell lung cancer (limited stage) and she began chemo (cisplatin/etoposide) and radiation to the chest
- A subsequent examination by a uveitis specialist revealed bilateral optic disc edema and vitritis. She was then referred to neuro-ophthalmology
- Her neuro-ophthalmological examination revealed:

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V 20/25
 20/25
P 5→2
 5→2
 No RAPD
 Normal ocular motility and alignment

Case – cont'd

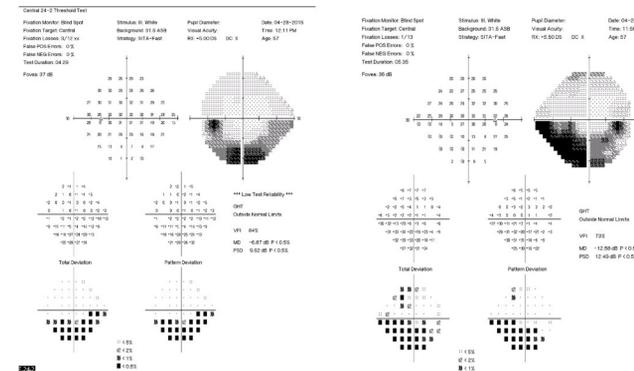


Figure 2. 24-2 Humphrey visual fields demonstrating inferior visual field defects

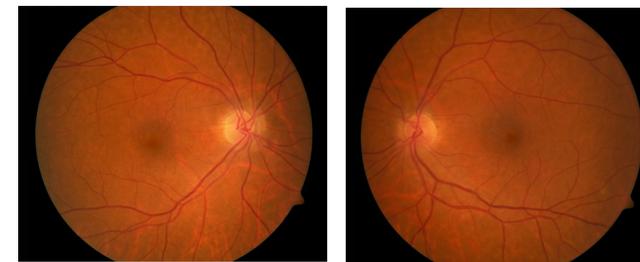


Figure 3. Fundus photos demonstrating subtle superior optic nerve pallor and resolved vitritis

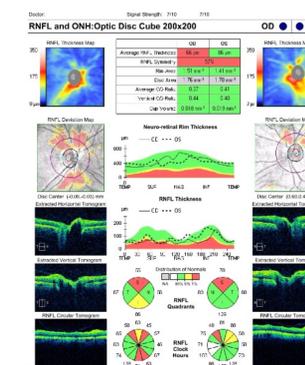


Figure 4. OCT of the RNFL demonstrated superior optic nerve atrophy corresponding to inferior visual field defects

- The clinical history and findings led to a diagnosis of PON and peripheral neuropathy and a paraneoplastic panel was ordered, which revealed:

PCA-2 positive 1:61440

CRMP-5 titers and western blot negative

Discussion

- Anti-PCA-2 is a paraneoplastic antibody which has been associated with different neurological presentations such as brainstem or limbic encephalitis, cerebellar ataxia, Lambert-Eaton, autonomic or motor neuropathy (2)
- CRMP-5 IgG frequently accompanies PCA-2 (44% are CRMP-5 IgG positive) (3)
- One explanation for the absence of CRMP-2 is that after treatment, CRMP-5 may have been suppressed
- Previous cases have demonstrated a dramatic decreased in CRMP-5 titers with carboplatin and etoposide (4)
- Antibodies other than CRMP-5 that have been associated with PON include:

Antibody	Other neurologic symptoms	Cancer	Reference
Anti-Hu	Lambert-Eaton	SCLC	Mason et al Brain 1997;120:1279
Anti-Tr	Cerebellar degen	Hodgkin's	Bernal et al Neuro 2003;60:230
Anti-Yo	Cerebellar degen	Gynecological	Peterson et al. Neuro 1992;42:1931
70 kDa protein	None	Pancreatic neuroendocrine	Slamovits et al. JNO 2013;33:21

Conclusions

- PCA-2 is an IgG paraneoplastic antibody that is associated with PON and small cell lung cancer

References:

- Rahimy et al. Surv Ophthalmol 2013;58:430.
- Vernino et al. Ann Neurol 2000;47:297.
- Pittock et al. Ann Neurol 2004;56:715
- Margolin et al. JNO 2008;28:17