Isolated MPO/pANCA Pachymeningitis

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Introduction/Case Presentation

65yo M w/ PMHx remote prostate cancer s/p resection, 60 pack year former smoking, on no medications presented with subacute headaches, gait instability.

- 01/2018: Healthy
- 02/2018: Bifrontal constant headaches with MR finding meningeal enhancement. Hospitalized x2 with unremarkable studies, discharged after Valtrex still with headache
- 03/2018: Progressive gait instability from normal to walker in 1 month, weight loss of 10-15lbs
- March 14, 2018: Hospitalized at UVMC

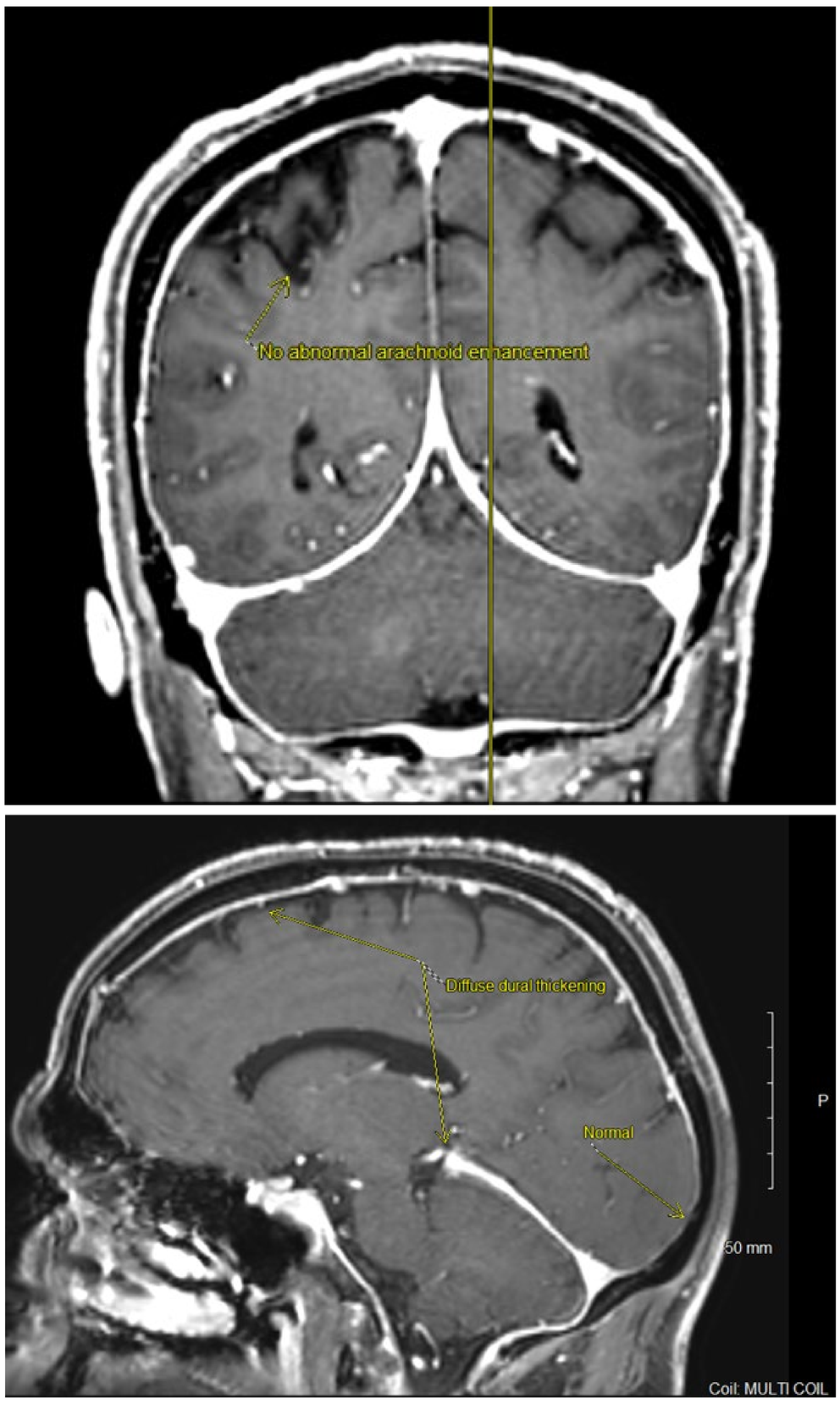

Figure 1: Isolated CNS Pachymeningeal enhancement without arachnoid involvement. Note the uniformity of thickening (non-nodularity)

- MR C/T spine found no extension of pachymeningitis into the spinal cord
- ANA 1:160, pANCA 1:160, MPO >8
- Placed on high dose steroids (Solumedrol 1g qday), with long taper as an outpatient with immediate impressive improvement in ambulation (to cane)
- 05/2018: Steroid wean caused increased gait instability, headaches, new diplopia on downward gaze. MR unchanged, ?worse. Escalated to high dose steroids, urgent Rheumatology consultation

Updates

- Patient was placed on high dose steroids to cyclophosphamide
- Dysequilibrium improved, but not back to baseline
- MPO decreased from 8 to 1.1, repeat MR head is pending

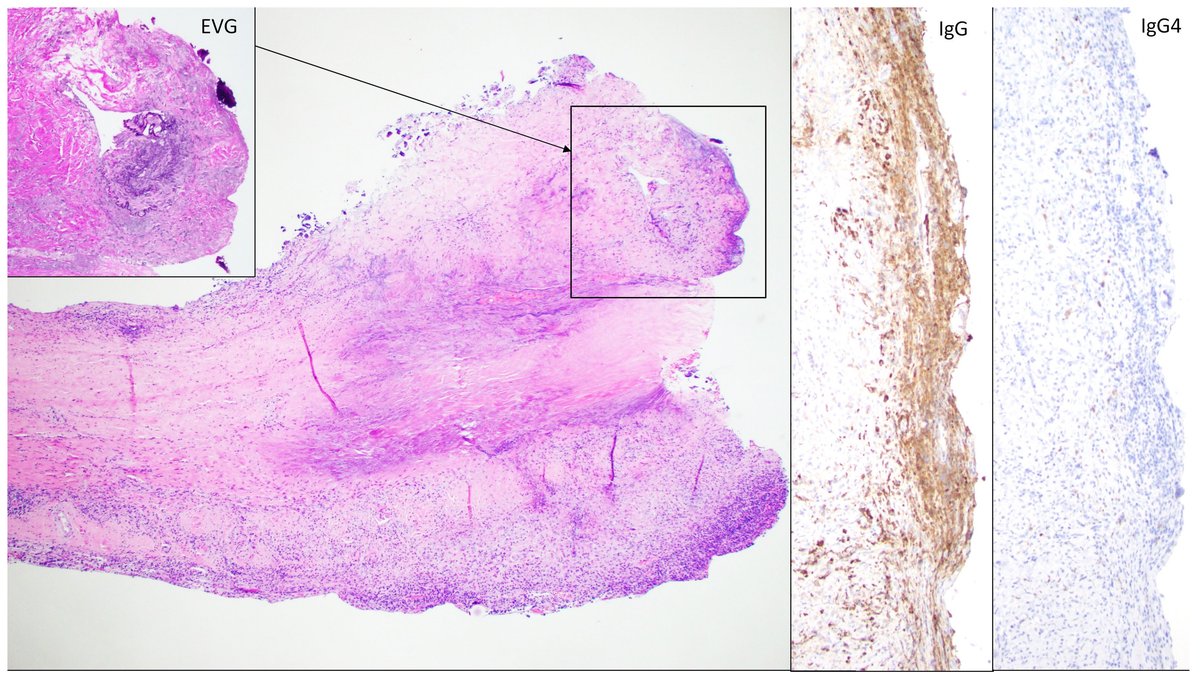

Figure 2: Dural Biopsy 6/29/2018: H&E section show a hyperplastic dura with fibrosis, fibrinoid necrosis, and marked lymphoplasmacytic inflammation. An elastin stain (EVG, inset image) shows obliteration of a thick walled artery. Immunohistochemical analysis with IgG and IgG4 (right) show that IgG4-positive plasma cells representing ~20% of the plasma cell population. Special stains to evaluate for microorganisms are negative (not shown).

Differential Diagnosis Considerations

- Classification for GPA/Microscopic Polyangiitis is currently in flux
- GPA- associated with granulomatous inflammation, cANCA/PR3
- MPA- associated with necrotizing vasculitis without granulomas, pANCA/MPO
- These may be different spectra of the same disorder- ANCA type (MPO vs PR3) may have more prognostic and clinical meaning rather than formal MPA vs GPA delineation

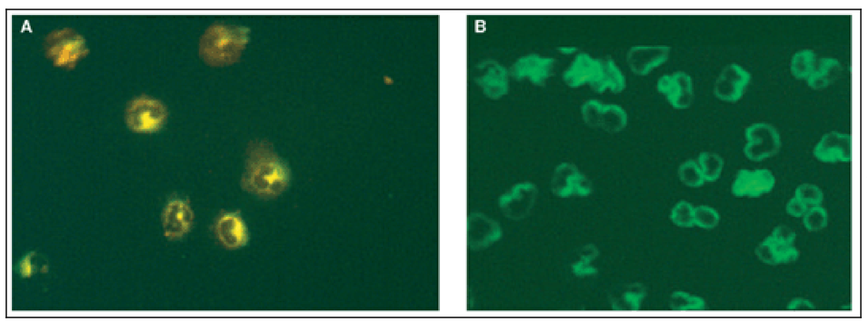

Figure 3: Demonstrates the staining patterns of (A) cANCA with granular, cytoplasmic staining pattern vs (B) pANCA with perinuclear staining pattern

New Entity? Isolated pANCA/+MPO Pachymeningitis

- Granuloma formation results in isolated dural enhancement
- Questionable whether different cytokines are preferentially located in different meningeal layers
- Literature Review in 2004 found 15 biopsy-proven cases in the literature
- In Japan, unclear association between pANCA and complex CNS disease
- Clinical syndrome with severe headache, cranial neuropathies, isolated CNS pachymeningitis, dural biopsy with granulomatous necrotizing inflammation
- Rapid response to prednisone/cytotoxic medications

Conclusions

- This case report highlights a rare but increasingly described clinical phenomena of a steroid/immunoresponsive ANCA-associated isolated pachymeningitis
- This case illustrates the differing molecular makeup of the different meningeal layers, with possible significance for targeted therapies

References/Contact

1) Chin RL, Latov N: Central nervous system manifestations of rheumatologic disease. *Curr Opin Rheumatol* 2004, 17:91-99

2) Fam AG, Lavine E, Lee L, et al.: Cranial pachymeningitis: an unusual manifestation of Wegener's granulomatosis. *J Rheumatol* 2003, 30:2070–2074.

3) Gaffo AL: Diagnostic Approach to ANCA-associated vasculitides. *Rheum Disease Clinics of North America*, 36(3), 491-506

4) Kono H, Inokuma S, et al: Pachymeningitis in microscopic polyangiitis (MPA): a case report and review of central nervous system involvement in MPA. *Clin and Exper Rheum,* 18 (3): 397-400

5) Murphy JM, Gomez-Anson B et al: Wegener Granulomatosis: MR Imaging Findings in Brain and Meninges. *Radiology* 1999, 213: 794-799

6) Nagashima, T. , Maguchi, S. , Terayama, Y. , Horimoto, M. , Nemoto, M. , Nunomura, M. , Mori, M. , Seki, T. , Matsukawa, S. , Itoh, T. and Nagashima, K. (2000), P-ANCA-positive Wegener's granulomatosis presenting with hypertrophic pachymeningitis and multiple cranial neuropathies: Case report and review of literature. *Neuropathology*, 20: 23-30. doi:10.1046/j.1440-1789.2000.00282.x

7) Uptodate

8) The experience and wisdom of our Rheumatology fellows, infectious disease/Neurology attendings

9) http://www.vasculitis.org.uk/about-vasculitis/glossary-of-blood-test-monitoring

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