MPO-ANCA associated necrotising glomerulonephritis in an eight year old girl with preceding history of bilateral orbital lymphoid hyperplasia.

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Introduction

- Myeloperoxidase anti-neutrophil cytoplasmic antibody (MPO-ANCA) associated glomerulonephritis is an unusual presentation in the paediatric population.
- We describe the case of an eight year old girl, presenting with severe acute renal failure, a high titre of myeloperoxidase anti-neutrophil cytoplasmic antibodies (MPO-ANCA) and necrotising glomerulonephritis on renal biopsy.
- The index case had presented fifteen months prior with bilateral orbital masses. Biopsy showed reactive lymphoid hyperplasia. Orbital lesions resolved with a short course of oral corticosteroid therapy.
- We postulate the potential link between both presentations and describe her unusual case.

Case presentation

- An eight year old female was referred to our unit with acute renal failure, on a background of a six day history of vomiting, mild non-bloody diarrhoea and oliguria.
- This was complicated by a recent varicella zoster virus (VZV) infection, with ongoing crop eruption.
 - Past medical history was remarkable for an unusual presentation fifteen months prior, with bilateral orbital lid masses, which following biopsy (Fig 1a) was successfully treated with a short course of oral corticosteroids.
 - Family history was negative.
- Clinical examination findings were minimal. The patient was normotensive, with mild dehydration and a rash consistent with VZV. There were no orbital findings. She was anuric but remarkably well.

Investigations

- Investigations indicated severe renal failure with
 - **Creatinine 1398umol/l**
 - **Urea 68umol/l**
 - **Hyperkalaemia.**
 - Urine microscopy revealed granular and white cell casts.
- Immunological studies showed positive perinuclear anti-neutrophil cytoplasmic antibody (P-ANCA) with **Myeloperoxidase (MPO) titre of 9.3IU/ml (0.0-3.4).**
- Previous orbital biopsy slides were reviewed and showed a mixed lymphoid infiltrate without granulomata or neutrophils and no evidence of vasculitis, necrosis or neoplasia.
- Renal biopsy was performed

- Renal biopsy obtained 78 glomeruli, 16 of which were sclerosed.
- 56 of the remaining 62 showed cellular crescents and segmental necrosis.
- Tubulointerstitial inflammation was noted with red cells and red cell casts.
- It was difficult to assess interstitial fibrosis due to the severity of interstitial oedema and inflammatory cell infiltrate.

- Infectious disease, rheumatology, ophthalmology and histopathology input was sought. She was treated with haemofiltration, plasmapheresis, methylprednisolone and subsequent immunosuppression.
- She had a remarkable response to treatment and measured creatinine recovered to 53umol/l. There is no evidence of other system involvement to date.

Conclusions

- ANCA (Anti neutrophil cytoplasmic antibody) associated vasculitides are extremely rare in childhood though, are associated with significant morbidity, mortality and treatment challenges.
- Paediatric data remains limited with most knowledge derived from larger adult studies. We describe the case of a young girl with severe acute renal failure and a previous presentation with bilateral orbital inflammatory masses associated with MPO-ANCA positivity.
- We postulate a link between both presentations. Fortunately she demonstrated an excellent response to treatment and continues to progress well without relapse.
- Further paediatric research is needed to ascertain true prognosis in this group.

References

1. Sacri AS, Chambaraud T, Ranchin B, et al. Clinical characteristics and outcomes of childhood-onset ANCA-associated vasculitis: a French nationwide study. Nephrol Dial Transplant. 2015;30:104–12.
2. Jennette JC, Falk RJ, Bacon PA, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum. 2013;65:1–11.
3. Iudici M, Quartier P, Terrier B, et al. Childhood-onset granulomatosis with polyangiitis and microscopic polyangiitis: systematic review and meta-analysis. Orphanet J Rare Dis. 2016;11:141.
4. Watkins A, Kempen J, Choi D, et al. Ocular disease in patients with ANCA-positive vasculitis. J Ocul Biol Dis Inform 2010; 3:12–19.
5. Martinez-Gutierrez J, Mencia-Gutierrez E, Gutierrez-Diaz E, et al. Bilateral idiopathic orbital inflammation 3 years before systemic Wegeners granulomatosis in a 7 year old girl. Clinical Ophthalmology 2008;2(4) 941-944.
6. Rosenbaum j, Choi D, Wilson D, et al. Orbital pseudotumor can be a localized form of granulomatosis with polyangiitis as revealed by gene expression profiling. Exp Mol Pathol. 2015;99(2):271-278.
7. James K, Xiao R, Merket P et al. Clinical course and outcomes of childhood- onset granulomatosis with polyangiitis. Clin Exp Rheumatol. 2017 ; 35(Suppl 103) : 202-208
8. Watts RA, Mahr A, Mohammad AJ, et al. Classification, epidemiology and clinical subgrouping of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis. Nephrol Dial Transplant. 2015;30:14–22.
9. Grisar S, Yuen GW, Miettunen PM, Hamiwka LA. Incidence of Wegener's granulomatosis in children. J Rheumatol. 2010;37:440–2.
10. Sacri AS, Chambaraud T, Ranchin B, et al. Clinical characteristics and outcomes of childhood-onset ANCA-associated vasculitis: a French nationwide study. Nephrol Dial Transplant. 2015;30:104–12.
11. Uh M, McCormick IA, Kelsall JT. Positive cytoplasmic antineutrophil cytoplasmic antigen with PR3 specificity glomerulonephritis in a patient with subacute bacterial endocarditis. J Rheumatol. 2011;38:1527–8.
12. Mirsaeidi M, Syed F, Jaffe ES. Antineutrophil Cytoplasmic Autoantibody Associated Systemic Vasculitis is Associated with Epstein-Barr virus in the Setting of HIV Infection. Infect Dis Clin Pract (Baltim Md). 2013;21:50–3.
13. Calatroni M, Oliva E, Gianfreda D et al. ANCA-associated vasculitis in childhood: recent advances. Italian Journal of Paediatrics (2017) 43:46.
14. Iudici M, Quartier P, Terrier B, et al. Childhood-onset granulomatosis with polyangiitis and microscopic polyangiitis: systematic review and meta-analysis. Orphanet J Rare Dis. 2016;11:141.
15. Abdou N, Kullman G, Hoffman G, et al. Wegener's granulomatosis. Survey of 701 patients in North America. Changes in outcome in the 1990s. TJ Rheumatol. 2002;29:309-316.
16. Kubasi B, Samra A, Foster S et al. Granulomatosis with polyangiitis (Wegener's disease):An updated review of ocular disease manifestations. Intracatble & Rare Diseases Research 2016;5 (2) 61-69.
17. Hoffman GS, Kerr GS, Leavitt RY, et al. Wegener granulomatosis: an analysis of 158 patients. Ann Intern Med. 1992;118:488–98.
18. Yates M, Watts RA, Bajema IM, et al. EULAR/ERA-EDTA recommendations for the management of ANCA-associated vasculitis. Ann Rheum Dis. 2016;75:1583–94.
19. ames KE, Xiao R, Merkel PA, Weiss PF. Variation in treatment of children hospitalized with antineutrophil cytoplasmic antibody-associated vasculitis in the United States. Arthritis Care Res (Hoboken). 2016.
20. Jayne DR, Gaskin G, Rasmussen N, et al. Randomized trial of plasma exchange or high-dosage methylprednisolone as adjunctive therapy for severe renal vasculitis. J Am Soc Nephrol. 2007;18:2180–8.
21. Jayne D, Rasmussen N, Andrassy K, et al. A randomized trial of maintenance therapy for vasculitis associated with antineutrophil cytoplasmic autoantibodies. N Engl J Med. 2003;349:36–44.
22. Langford CA, Talar-Williams C, Barron KS. Use of a cyclophosphamide-induction methotrexate-maintenance regimen for the treatment of Wegener's granulomatosis: extended follow-up and rate of relapse. Am J Med. 2003;114:463–9.
23. Guillevin L, Pagnoux C, Karras A, et al. Rituximab versus azathioprine for maintenance in ANCA-associated vasculitis. N Engl J Med. 2014;371:1771–80.
24. Iudici M, Puéchal X, Pagnoux C, et al. Brief Report: Childhood-Onset Systemic Necrotizing Vasculitides: Long-Term Data From the French Vasculitis Study Group Registry. Arthritis Rheumatol. 2015;67:1959–65.
25. Noone DG, Twilt M, Hayes WN, et al. The new histopathologic classification of ANCA-associated GN and its association with renal outcomes in childhood. Clin J Am Soc Nephrol. 2014;9:1684–91.
26. Arulkumaran N, Jawad S, Smith SW, et al. Long-term outcome of paediatric patients with ANCA vasculitis. Pediatr Rheumatol Online J. 2011;9:12.