

# Castleman disease presenting as membranous glomerulonephritis in a middle aged Indian female

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## Introduction

Castleman disease is a multi-system disorder with a wide range of presentations<sup>1</sup>. It has gone from being an ill defined lymphoproliferative disorder to one which is firmly placed in the shared domain of haematology and immunology with the recognition of IL-6 driven cytokine storm as the main driver of its pathogenesis<sup>2</sup>.

The recently proposed consensus diagnostic criteria have helped to advance our knowledge of the disease and have also established clear cut histological criteria with grade<sup>3</sup>. This will increase the specificity of the diagnosis and ensure greater uniformity in studying the disease in clinical trials thereby improving the confidence of results.

## Case Summary

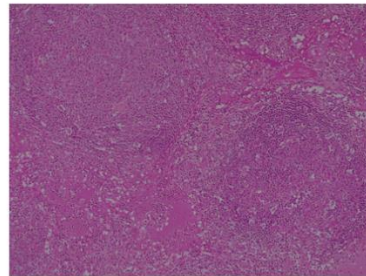
Ms X, a 55 year old female presented to our clinic with nephrotic syndrome. Her 24 hour urine protein was 3.5gm and her serum albumin was 2.3gm/dL. Her renal biopsy showed histological features of membranous glomerulonephritis with PLAR negativity. A thorough search for secondary causes was undertaken and her CECT chest and abdomen revealed the presence of significant, generalised lymphadenopathy involving nodes on both sides of diaphragm. The lymph node histology showed hyperplastic germinal centres with sheet like plasmacytosis in interfollicular region, concordant with the hyperplastic histological subtype. She met both the major criteria of the proposed diagnostic criteria; and six of the minor. She had anemia, thrombocytopenia, anasarca, hypoalbuminemia, elevated CRP, ESR and constitutional symptoms of fever and fatigue. Her IL-6 levels were also elevated which supported the diagnosis under consideration. All the disease mimics of iMCD were excluded. HHV-8 was negative.

Finally patient was started on corticosteroids and Rituximab. After two months her repeat CT chest showed dramatic regression of lymphadenopathy and a parallel decline in proteinuria. The improvement was sustained at six months and she was declared to be in remission.

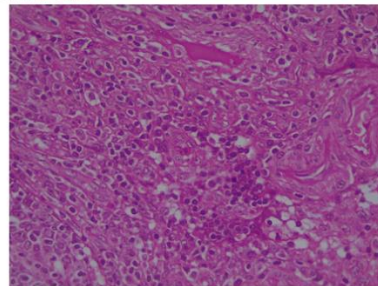
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## Figures



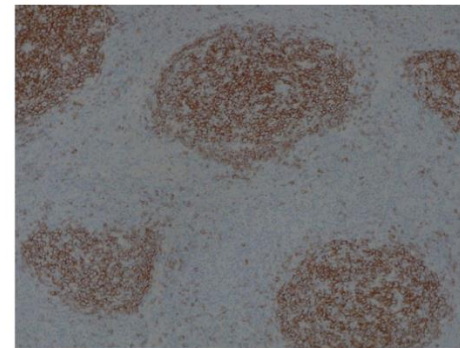
Hyperplastic germinal centres



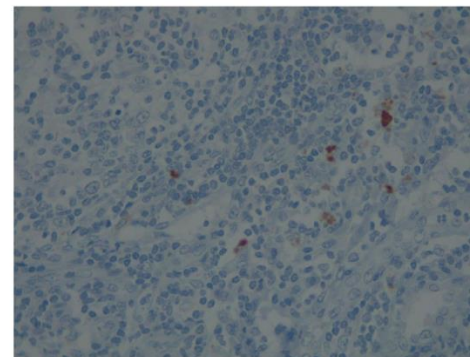
Interfollicular area with plasma cells and immunoblasts



Bcl-2 negative centres



CD-20 immunoreactive centres



CD-30 immunoreactive immunoblasts in interfollicular area

## Discussion

Renal dysfunction is a known complication of Castleman disease but presentation with frank nephrotic syndrome is rare with few known case reports in literature<sup>4,5,6</sup>. Our case highlights the importance of 'pattern recognition', a familiar rheumatological concept, in aiding the diagnosis of this multi-system disorder. It is especially relevant in cases which present with a primary renal complaint.

The other important issue highlighted in our case is the significant overlap which exists among the various described subtypes of this disease. Our patient also fulfilled the diagnostic criteria of TAFRO syndrome but her histology and renal lesions were not typical of it<sup>7</sup>. TAFRO is usually associated with hyaline-vascular histological subtype and among the renal manifestations MPGN and TMA are the typically described lesions<sup>8</sup>.

Finally, it is important to mention the relevance of the newly proposed diagnostic criteria in both case recognition as well as increasing the diagnostic confidence of the treating physician. It definitely allowed for earlier initiation of treatment in this case.

## Take away messages

- 1) The need to educate and sensitise physicians to keep iMCD in mind as a possible diagnosis in cases of nephrotic syndrome. If properly looked for in this subset of patients, the case yield has the potential to increase.
- 2) To try and study the underlying pathogenesis of renal injury in iMCD, a few case reports have highlighted the importance of IL-6 - VEGF axis, but it requires more extensive evaluation.
- 3) The recognition that there is considerable overlap among the proposed subsets at present points towards the need for better delineation of the same.
- 4) With the recent recognition of IL-6 as an important cytokine in infection induced cytokine storms as was seen in COVID-19 it might be interesting to look for other conditions which cause persistent IL-6 elevation and prospectively evaluate them as possible triggers for MCD like presentations.

## References

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