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Original Research Paper

Pathology

CRESCENTS – CHARMING CATASTROPHES

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ABSTRACT

Background and Objectives: Crescentic Glomerulonephritis is a medical emergency because patients will progress to Rapidly Progressive Glomerulonephritis, a fatal condition. Crescentic Glomerulonephritis can be pauci immune, immune complex mediated or anti glomerular basement membrane disease.The presence of crescents indicates a poor prognosis for the patient. This paper highlights the various presentations of Crescentic Glomerulonephritis. **Study Design:** Prospective study. **Setting:** Tertiary care centre in South India. **Materials and Method:** 34 renal biopsies were received over a period of 18 months (January 2021 to June 2022). 6 cases of Crescentic glomerulonephritis have been reported. Histopathological examination, ANCA and Immunofluorescence were done for these cases.Results:Out of the 6 cases, 1 was a case of anti-GBM disease, 1 was a case of pauci immune glomerulonephritis, 2 were cases of lupus nephritis and 2 were cases of IgA Nephropathy. **Conclusion:** Crescentic Glomerulonephritis is a medical emergency.It is the duty of the Pathologist to inform the Nephrologist as soon as possible to look for the etiology and instigate appropriate therapy.

KEYWORDS : Crescentic Glomerulonephritis, Crescent, immunofluorescence

INTRODUCTION

Crescents, from time immemorial, have served as a symbol of intrigue and mysticism. Various cultures around the world have been fascinated by the half moon. It has served as a symbol of fertility and motherhood. The Greek Goddess of the hunt and motherhood Artemis is commonly associated with Selene, the Moon Goddess. Virgin Mary is commonly depicted standing on the crescent moon. The Islamic crescent is definitely the most popular representation of the moon as it served as a compass for weary travellers to traverse the desert at night.

Crescents represent good fortune and luck in many cultures. Unlike the crescents seen in the folklore around the world, the ones witnessed in pathology are a harbinger of danger and misfortune.

Crescents in the glomeruli signify doom and gloom to the patients, whereas the humble Pathologist is both morbidly delighted and dismayed at the patient's adversity.

Crescentic Glomerulonephritis is defined by the presence of more than 50% of glomeruli having crescents.(3) Although certain pathologists prefer to use to the term even if a single crescent is witnessed in the biopsy.

Regardless of the varied disputes in the definition, severity is directly proportional to the number of affected glomeruli in the biopsy. When >50 % of the renal biopsy has developed crescents, it is associated with the rapid decline of renal function which is termed as Rapidly Progressive Glomerulonephritis (RPGN).

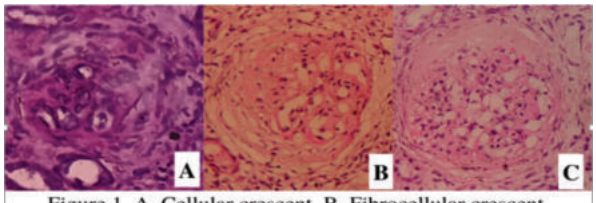

Figure 1. A. Cellular crescent. B. Fibrocellular crescent. C. Fibrous Crescent

The Crescents Of Pathology:

Crescents are defined by the presence of two or more layers of cells that either completely or partially fill the Bowman's space.

Histologically, they are classified as cellular, fibrocellular and fibrous crescents based on their cellularity and age.

The more cellular the crescent, the better the prognosis. (4) Cellularity is a sign of an active lesion. So with prompt treatment, it is possible for the condition to be reversed and bring the disease progression to a halt. When the presence of extensive glomerular necrosis exceeds 50%, patients present with Rapidly Progressive Glomerulonephritis.

How Are Crescents Formed?

A glomerulus is a cup shaped structure where the afferent arteriole pushes into the Bowman's space forming a bunch of capillary loops. The Bowman's space is lined by parietal epithelial cells.

When the glomerular capillary wall undergoes necrosis, there is a subsequent release of fibrin, proteins and red blood cells which causes proliferation of the parietal epithelial cells in the damaged area.

Cellular crescents are the result of such an injury. As healing sets in, fibrocellular and fibrous crescents are formed. (1) (Figure 1)

Cellular crescents have a cellularity of >75%. vFibrocellular crescents have a cellularity of 25 - 75%. Fibrous crescents have a cellularity of <25%.

Classification Of Crescentic Glomerulonephritis:

Crescentic Glomerulonephritis can be classified based on the pattern of Immunofluorescence staining as follows.(3) (Figure 2)

- Type 1(anti-glomerular basement membrane [GBM] disease) - linear deposits of immunoglobulin G (IgG)
- Type 2 (immune-complex mediated) - granular deposits of immunoglobulin
- Type 3 (pauci-immune) presents with few or no immune deposits
- Type 4 – combination of types 1 and 3
- Type 5 – ANCA negative, pauci-immune renal vasculitis.

Type 1 – Anti Glomerular Basement Membrane Disease:

Anti-GBM disease is mediated by the presence of autoantibodies against type IV collagen that is a normal

constituent of the glomerular basement membrane. This results in the deposition of the antibodies on the GBM which elicits an inflammatory response. The glomerular capillary wall is damaged and crescents are formed in nearly all the glomeruli.

Anti- GBM disease shows a linear staining of IgG and sometimes C3c along the glomerular basement membrane.
If there is pulmonary involvement along with renal dysfunction, it is termed as Goodpasture's Disease.

Type 2 – Immune Complex Mediated Glomerulonephritis:
This category involves all the immune complex mediated glomerulonephritis like Post-infectious glomerulonephritis, IgA Nephropathy, Lupus Nephritis, Henoch-Schonlein Purpura. It may also occur superimposed on a primary glomerulonephritis like Membranous glomerulonephritis, C3 glomerulonephritis or Membranoproliferative glomerulonephritis.

There is a granular deposition of immunoglobulins depending on the underlying condition on the glomerular basement membrane or the mesangium.

This type of glomerulonephritis cannot be treated with plasmapheresis and requires treatment of the underlying condition.

Type 3 – Pauci-immune Glomerulonephritis:
These patients may have circulating p-ANCA or c-ANCA. Anti Neutrophil Cytoplasmic Antibodies can have either cytoplasmic or perinuclear staining. c-ANCA or PR3-ANCA (antibodies against neutrophil protein proteinase – 3) and p-ANCA or MPO-ANCA (against neutrophil myeloperoxidase) are commonly elevated in this type but a small number of patients may not have them.

There is no or very minimal immunofluorescence staining noted in this type, hence the term pauci-immune glomerulonephritis.

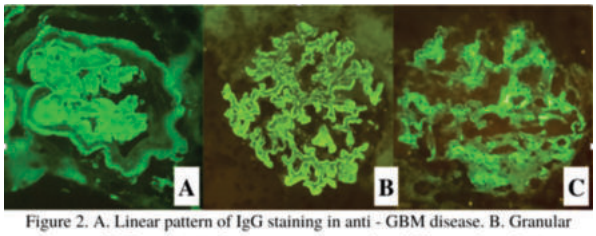

Figure 2. A. Linear pattern of IgG staining in anti - GBM disease. B. Granular pattern of IgG staining in Immune complex mediated Glomerulonephritis. C. Mesangial IgA deposits seen in IgA Nephropathy.

A prospective study was conducted with 34 renal biopsies received over a period of 18 months (January 2021 to June 2022).

6 cases of Crescentic glomerulonephritis have been reported. Histopathological examination and Immunofluorescence were done for these cases.

Stastistical Analysis:
Out of the 6 cases, 1 was a case of anti-GBM disease, 1 was a case of pauci immune glomerulonephritis, 2 cases of IgA Nephropathy and 2 cases of Lupus Nephritis.

DISCUSSION:
In this case series, Type 2 Immune complex mediated crescentic glomerulonephritis was most commonly seen. There was a slight male predominance.

All the patients had hypertension.

Type 1 and Type 3 crescentic glomerulonephritis had the most severe clinical presentation with nephritic syndrome. Both cases did not respond well to therapy and succumbed rather swiftly after diagnosis.

The Type 2 crescentic glomerulonephritis cases had varying degrees of proteinuria and hematuria.

The more serious presentations at the time of biopsy i.e. with increased hematuria and serum creatinine levels had poorer prognosis.

CONCLUSION:
Anti – GBM disease and Pauci immune crescentic glomerulonephritis have the worst prognosis. Early detection of these conditions by renal biopsy will definitely improve the patient's condition and response to therapy. Timely diagnosis and treatment of Immune complex mediated Crescentic glomerulonephritis can benefit the patient immensely. Therefore, crescents should be considered as a medical emergency. It is the sworn duty of a pathologist to inform the nephrologist of the presence of crescents as soon as possible.

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