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Case Note

Successful management of idiopathic rapidly progressive glomerulonephritis with corticosteroids and cytotoxic agent

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Abstract
A 19 years old, male patient presented with symptoms of smoky urine for 2 weeks, puffiness of face and diminished urine output for 3 weeks associated with occasional lower abdominal and flank pain. Patient's history, clinical findings and available investigations were strongly suggestive of Idiopathic Rapidly Progressive Glomerulonephritis. The patient showed excellent response to glucocorticoid and cytotoxic agent.

Key words: Idiopathic Rapidly Progressive Glomerulonephritis, Glucocorticoid, Cytotoxic agent.

Rapidly progressive glomerulonephritis (RPGN) is a form of acute glomerulonephritis (AGN), in which there is development of renal failure in weeks to months rather than years or decades as compared to other form of nephritis. Extensive extra capillary (crescentic) glomerulonephritis is the pathologic hallmark of RPGN. RPGN consists of primary or idiopathic (renal limited) crescentic glomerulonephritis (IRPGN), antiglomerular basement membrane (anti GBM) antibody disease and systemic disorder. Some important systemic causes are vasculitis, SLE, Good pastures disease and IgA nephropathy. RPGN produce very rapidly progressive and destructive glomerular disease which in the severe form terminates in renal failure in the lack of treatment. IRPGN is a form of RPGN which present as a primary glomerular disease where kidney is the only organ affected and extra renal manifestations are secondary to the disturbances of renal function. This form of disorder affects individual in wide age distribution and has predilection for male. Haematuria, oliguria, and puffiness of face are major complaints. BP remains normal or slightly elevated. Routine urine examination reveals dysmorphic haematuria and red cell casts. Proteinurea is always present and may be massive. Azotemia develops early and tends to progress rapidly. Antineutrophil cytoplasmic antibody (ANCA) is positive in majority cases.

Glucocorticoid in the form of parenteral methylprednisolone, given as pulse therapy in high dose and daily oral prednisolone in combination with cyclic cyclophosphamide has proven varying success in the management of RPGN. Our patient improved completely after 3 courses of methylprednisolone along with oral prednisolone and 6 cycles of cyclophosphamide.

Case report
A 19 year old male patient, resident of Malangawa, Sarlahi, Nepal, presented with complaints of red colour urine for 2 weeks. It was painless and there was no associated fever. He had puffiness of face and mild decrease in urine output for 3 weeks. There was occasional lower abdominal and flank pain. No significant past medical, surgical history or family history was present. On examination general condition was fair, pulse 80/min, BP 120/90 mm of Hg, afebrile, chest and CVS findings within normal limit. No definitive systemic findings were present except periorbital swelling. Initial investigations were done in which TC-10700/cumm, $P_{67\%}$ $L_{24\%}$ $M_{4\%}$ $E_{3\%}$ $B_{2\%}$, HB-8.5 grm%,ESR-0mm in 1st hr, Sugar Random-90 mg/dl, Blood Urea-54mg/dl, Serum Creatinine 1.4mg/dl, Na-135meq/L, K-3.1meq/L, Urine RME Albumin+, RBC-Plenty, Pus cell 2-4/hpf, Epi cell-1-2/hpf, RBC Cast-Few, ANCA+. Serum Urea/Creatinine was done for next consecutive 3 days, which were 78/2.6mg/dl, 94/3.5mg/dl and 109/4.6mg/dl on 2nd,3rd and 4th days respectively. USG abdomen revealed bilateral parenchymal medico renal disease. Renal biopsy was planned but could not be performed as the patient became more anxious and non co-operative. IVP studied showed both functioning kidneys with normal excretion of dye. Serum calcium and phosphorus were within normal ranges.

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On the basis of clinical findings, rapid rise in Serum Urea/Creatinine consecutively and ANCA positivity Idiopathic Rapidly Progressive Glomerulonephritis was strongly suspected. Taking into consideration of its explosive nature leading into irreversible renal damage, treatment was started immediately to salvage the kidney. Therapy with parenteral and oral steroid and cyclophosphamide were initiated on day care basis. The patient was on regular treatment for 6 months and recovered completely at the end of 6th cycle of cyclophosphamide. Routine haematology, renal function tests were done frequently and came to normal range after 6 months of treatment. The patient is still on regular follow up for maintenance therapy. The brief investigations and treatment regime are tabulated below.

Table 1: Investigation Summary

Time of Investigation	TC/cu mm	DC	HB gm%	Urea/ Creatinine	Urine Routine	USG Abdomen
Prior to Initial Therapy	10700	$P_{67\%}$ $L_{24\%}$ $M_{4\%}$ $E_{3\%}$ $B_{2\%}$	8.5	109/4.6mg/dl	Albumin+,RBC Plenty, Cast Few Pus Cell 2-4, Epi. Cell 1-2	Bilateral Medico renal disease
During 2nd Cycle	10500	$P_{62\%}$ $L_{29\%}$ $M_{4\%}$ $E_{2\%}$ $B_{3\%}$	9	68/2.6mg/dl	Albumin+,RBC Few, Cast Few Pus Cell 2-3, Epi. Cell 1-2	
During 3rd Cycle	10850	$P_{65\%}$ $L_{26\%}$ $M_{3\%}$ $E_{4\%}$ $B_{2\%}$	9.5	45/1.5mg/dl	Albumin Nil, RBC Nil, Cast Nil, Pus Cell 1-2 Epi. Cell 1-3	
During 4th Cycle	11100	$P_{60\%}$ $L_{31\%}$ $M_{4\%}$ $E_{4\%}$ $B_{1\%}$	10.1	38/1mg/dl	Albumin Nil, RBC Nil, Cast Nil, Pus Cell 0-2 Epi. Cell 1-2	
During 5th Cycle	10650	$P_{69\%}$ $L_{24\%}$ $M_{5\%}$ $E_{2\%}$ $B_{0\%}$	10.8	32/1mg/dl	Albumin Nil, RBC Nil, Cast Nil, Pus Cell 0-1 Epi. Cell 0-1	
At the end of 6th Cycle	10500	$P_{66\%}$ $L_{24\%}$ $M_{5\%}$ $E_{3\%}$ $B_{2\%}$	11.6	28/0.9mg/dl	Albumin Nil, RBC Nil, Cast Nil, Pus Cell 0-1 Epi. Cell 1-3	Normal Scan

Table 2: Initial Treatment Schedule

Days	Drug Given	Dose /Route
1st Day	Inj. Methyl Prednisolone	1 gram/IV
2nd Day	Inj. Methyl Prednisolone	1 gram/IV
3rd Day	Inj. Methyl Prednisolone	1 gram/IV
4th Day	1st Cycle of inj. Cyclophosphamide	750mg/IV
	Tab. prednisolone	60mg/PO

Tablet prednisolone was given for total 30 days and inj. Cyclophosphamide was given for total 6 cycles at monthly interval.

Discussion

Rapidly progressive nephritis without obvious immune deposit or concomitant systemic disease has been defined as Idiopathic Rapidly Progressive Glomerulonephritis (IRPGN). IRPGN has also been described and known as pauci-immune crescentic nephritis. Patient with this condition usually have antineutrophil cytoplasmic antibody (ANCA).

The renal involvement in systemic vasculitis has many features common with those of idiopathic rapidly progressive glomenelonephritis. Even some patient with IRPGN have ultimately been observed to develop feature of systemic vasculitis .IRPGN has also often been described as renal limited form of small vessel vasculitis due to recognition of similar autoantibody response. There is little percentage of patients where ANCA is not present.

The outcome of treatment of renal lesion in IRPGN is equivalent to that in systemic vasculitis, provided that evaluation is made between patients with equal degree of renal involvement. The clinical feature of the disease is less evident as compared to other renal or systemic disease, so the patient present late to seek the treatment which lead to less response to treatment. The treatment response of these patients is complex to evaluate, however studies have shown 1 year survival with use of corticosteroid and cytotoxic agent is more than 70%.Patients rarely recovers renal function once they become significant oliguric. Therefore, it has been advised rational to treat with aggressive immuno suppressive therapy. Commonly used drugs for the management are methylprednisolone, prednisolone, cyclophosphamide, and azathioprine. Besides plasmapheresis and dialysis has often been practiced. Dose and duration of the treatment varies and it is wise to be individualized. Maintenance therapy is usually necessary to prevent relapse.

In our case, daily rise of Serum Urea/Creatinine, ANCA positivity and other sign and symptoms led us to consider IRPGN. Renal biopsy would be more useful for the diagnosis but the patient was not sufficiently cooperative. ANCA can be a valuable serological marker in IRPGN where renal biopsy cannot be done.

Conclusion

IRPGN is a relatively common variant of RPGN with variable clinical outcome. Prompt diagnosis and management is mandatory to prevent irreversible kidney damage.

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