Case Report

A Young Female with Renal Cortical Necrosis Treated with Intravenous Immunoglobulin in a Resource Poor Setting : A Case Report

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Renal Cortical Necrosis (RCN) is a rare cause of Acute Kidney Injury (AKI) characterized by diffuse or patchy ischemic coagulation necrosis of the cortex. One of the important causes is Acute Thrombotic Microangiopathy (TMA). It is very crucial to diagnose & treat it early to avoid morbidity & mortality. There is limited therapy available in resource poor setting. Here we report a case of TMA with Renal Cortical Necrosis (RCN) with poor response to Plasmapheresis & Steroid, treated with Intravenous Immunoglobulin (IVIG). To the best of our knowledge, this is the first report of successful treatment of adult patient of Dialysis dependent Renal Cortical Necrosis (RCN).

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Key words **: Intravenous Immunoglobulin (IVIG), Thrombotic Microangiopathy (TMA) Ab-Antibody, Antinuclear Anti-body (ANA), Anti Complement Factor H (anti CF-H).**

Thrombotic Microangiopathy (TMA) is one of the most important causes of Renal Cortical Necrosis (RCN) and Rapidly Progressive Renal Failure (RPRF). It can be classified into Primary (hereditary or acquired) & Secondary TMA. Acquired Thrombotic Thrombocytopenic Purpura (TTP) is an Autoimmune Disorder caused by inhibitory effects of autoantibodies on ADAMTS13 (cleaves vWF multimers that are secreted from Vascular Endothelial Cells) thereby decreasing enzymatic activity and includes classical acquired primary idiopathic TTP (ADAMTS13 deficient), hemolytic-uremic syndrome [Shiga toxin-mediated (HUS)], atypical HUS (drug-mediated TMA and complement-mediated)[1-4]. Other causes are Systemic Infections, Disseminated Malignancy, Severe Preeclampsia, Hemolysis Elevated Liver Enzymes and Low Platelets (HELLP) Syndrome, Malignant Hypertension, Autoimmune Disorders [eg, Systemic Lupus Erythematosus (SLE), Systemic Sclerosis (SS), Catastrophic Antiphospholipid Syndrome (CAPS)] and Hematopoietic Stem-cell (HSCT) or Organ Transplantations.

There are limited treatment options available till date for Acute Cortical Necrosis, which in most cases caused by TMA. Plasmapheresis, Steroid & Dialysis are the only options available in a resource poor setting. If not treated early, Acute Cortical Necrosis lead to long term Dialysis dependency, morbidity and mortality.

Case Report

A 30-year female presented with Rapidly Progressive Renal Failure (RPRF) with anuria without extrarenal organ involvement features, no fever, diarrhea, any history suggestive of active source of infection, no features of Autoimmune Disease or recent drug history or vaccination, recent or current pregnancy or abortion. She didn't have any history of previous Comorbidities. On evaluation she was found to have Hypertension, pallor and normal systemic examination. She found to have deranged Renal parameters with Serum Creatinine 10 mg/dl, serum urea 206 mg/dl, Metabolic Acidosis, Severe progressive anemia with mild Thrombocytopenia with peripheral smear no any evidence of Hemolysis or Schistocytes, raised serum LDH, mild indirect hyperbilirubinemia with normal liver enzymes, normal coagulation parameters with low C3, normal C4, negative immunological markers & Anti Phospholipid Antibodies. Her imaging of the abdomen shown normal renal anatomy, no evidence of obstruction & normal color doppler of renal vessels. She got started on Hemodialysis, through right Internal jugular vein hemodialysis catheter. Renal Biopsy was done which was suggestive of focal areas of cortical tissues coagulation necrosis with ghost outlines of Glomeruli and Tubules. The glomeruli were blood-less with organizing thrombus in afferent arterioles and fibrinoid necrosis of capillary loops. There was no segmental sclerosis/double contouring/endocapillary hypercellularity/crescent. Tubules was showing moderate tubular injury with sloughing of epithelial cells and regenerative atypia of lining epithelial cells nuclei. Interstitium shown inflammation to <10% of biopsied cortex & IFTA <10%. Arterioles & medium sized vessels

Editor's Comment :

- In a resource poor setting, complement & genetic studies may be not always possible, so we should avoid delay in treatment.
- In a case of Acute TMA with cortical infarct, IVIG may help if there is partial or failure to response to standard therapy.

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shown fibrinoid necrosis of vessel wall & thrombi in varying stage of organization. These changes were suggestive of a diagnosis of acute TMA with patchy cortical necrosis (Figs 1-4). We considered the possibility of atypical HUS, Anti CF-H antibody had been sent, as this is one of most common cause of this kind of presentation & complete genetic analysis was not possible due to economical restraint. She was started on alternate day Plasmapheresis (PLEX) with pulse steroid Injection Methylprednisolone 500 mg for 3 days, then Tablet Prednisolone 1mg/kg/day. She responded to this partially & Urine output improved, but she remained dialysis dependent with severe progressive anemia requiring blood transfusion. She then received IV Immunoglobulin (IVIG) 2 gm/kg total. Her clinical course improved following this and within 48 hours her renal parameters started improving with no further need for dialysis or blood transfusion. She is currently off dialysis & hematological & renal parameters improving with S Creatinine approximately 2 mg/dl. Repeat Renal biopsy not done, as patient refused in view of clinical & biochemical recovery. Her anti CF-H antibody report was reported as negative. After patient follow-up, to prognosticate risk of recurrence & ESRD, genetic panel for analysis of aHUS was sent & result came after 1 month, as no abnormal gene detected.

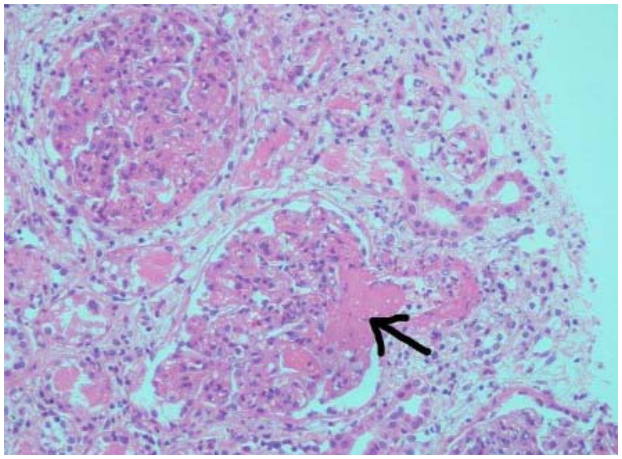

Fig 1 — Glomeruli showing Fibrin thrombi (H&E, 100x)

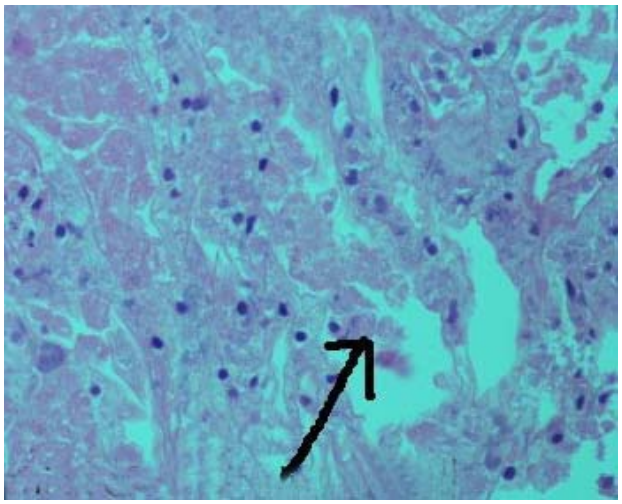

Fig 2 — Tubular injury and sloughing of the tubular lining cells (H&E, 100x)

Perspective

This young female mother of two kids, with Acute Cortical Necrosis, in a resource poor setting in rural South India with logistical challenges to do complete complement workup, ADAMTS13 activity and nonavailability of costly drugs, with risk of mortality & ESRD, was managed successfully by following clinical course and response in arriving at a probable etiological diagnosis & early treatment initiation.

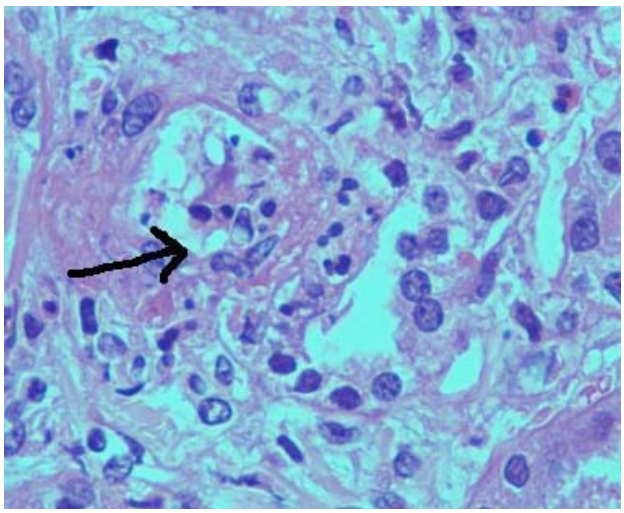

Fig 3 — Fibrinoid necrosis (H&E, 400x)

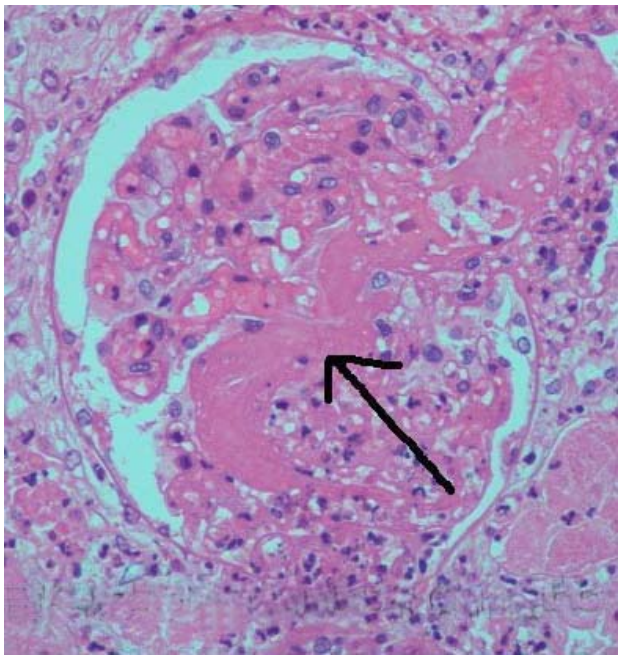

Fig 4 — Organising Thrombus (H&E, 400x)

Discussion

Renal Cortical Necrosis is one of the rare but critical causes of irreversible renal failure. It can be histologically classified as diffuse and focal or patchy. There are various etiologies mainly classified as Obstetric and Non-obstetric causes, eg, Pre-eclampsia, Septic abortion, Placenta previa, Sepsis, Gastroenteritis, Snake Bite, Pancreatitis, Shock, Drugs, Organophosphorus poisoning, SLE, APLA Syndrome, vasculitis, TMA & other causes of RPRF[6]. TMA is one of important causes of Acute Renal Cortical Necrosis, which should be suspected and treated early. TMA is clinically suspected in cases presenting with Microangiopathic hemolytic anemia, anemia with thrombocytopenia with normal coagulation profile and end organ damage, commonly renal and brain, but other organs like lung, heart also can be involved. TMA can be primary or secondary. Primary causes are TTP, HUS, Secondary causes may be malignant hypertension, drugs, autoimmune disorder, pregnancy related complication or abortion. Anuria with dialysis dependency are bad prognostic markers for case of TMA with cortical necrosis, if there is delay in diagnosis or treatment. There are few case reports of partially reversible Acute Renal Cortical Necrosis[7].

In this instance, we describe a case of Acute Renal Cortical Necrosis presenting with RPRF with anuria, dialysis dependent, found to have TMA, negative workup for common causes of Secondary TMA. The most common cause in in this setting was atypical HUS. Though ADAMTS13 level, antibody test against ADAMTS 13, genetic workup and antibody against complement factor like CF-H Antibody should be done in each patient, but it will take lots of time (mostly month in our setting) and requires resources & cost to treat such cases, with limited success rate. We sent genetic analysis test & anti CF-H antibody analysis. This case was refractory to treatment to standard therapy. She had partial response to standard of care treatment for TMA (PLEX with pulse steroid and oral steroid,) and Hemodialysis. We kept a possibility of antibody mediated aHUS & started treatment with IVIG, without wasting time to wait for result. Though her anti CF-H Antibody was negative & because of poor resources, we could not do complete antibody panel for complement gene. In this case she responded to treatment with IVIG, probably secondary to antibody against complement. Though we got the report of genetic analysis showing no abnormal gene detected against aHUS.

There is no case report to the best of our knowledge till date in adult dialysis dependent case of Acute Cortical Necrosis. In one case report in a pediatric age group, the patient of TMA of unknown etiology, was treated with IVIG, after failed response to standard therapy. But child had developed dialysis dependency, ESRD and had undergone Renal Transplantation[5].

Secondary TMA needs to be evaluated for assessment of complement activation, where alternative complement pathway will be dysregulated & C3 low & C4 will be normal. If there is evidence of complement activation, Eculizumab (complement C5 inhibitor) needs to be initiated. Other secondary causes need to be need to ruled out.

Conclusion

In a case of Acute TMA with cortical infarct and probable diagnosis is secondary TMA (aHUS secondary to antibody mediated against complement factor) and secondary causes has been properly evaluated and ruled out, IVIG may help if there is partial or failure to response to therapy. In a resource poor setting, complement & genetic studies may be not always possible and the use of IVIG when standard of care fails might prove to be a reasonable option and use of limited resources when a full work up for TMA might not be possible.

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