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Case Study

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SUCCESSFUL AYURVEDIC MANAGEMENT OF CRESCENTIC FORM OF IGA NEPHROPATHY WITH CONCURRENT ANTI GBM DISEASE LEADING TO ESRD-A CASE STUDY

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ABSTRACT

IgA Nephropathy is the most common form of Glomerulopathy and its incidence is steadily increasing globally. A number of studies have documented a poor prognosis in the crescentic form of IgA nephropathy. The concurrent presentation of anti-GBM disease with IgA nephropathy has been rarely reported. End Stage Renal Disease is the outcome in majority of patients with crescentic form of IgA nephropathy within 5 years. Nothing much is left to save life when ESRD is established, except Kidney transplantation or Dialysis. Here is a case study of 45 year old male subject developing RPGN, due to IgA crescentic form of Nephropathy and was unsuccessfully managed by Modern treatment by steroids, Plasmapheresis and haemodialysis, case deteriorated and landed in to ESRD, but Ayurved has successfully managed the case for more than a year and maintained him without dialysis. His ESRD/CKD-5 status has improved to CKD stage 4. He is symptomless, doing his entire job in government setting, maintaining full quality of life. This case study highlights the potential of Ayurved in treating conditions like IgA nephropathy with anti-GBM disease leading to ESRD where modern medicine has limitations.

KEYWORDS: IgA Nephropathy, Crescentic IgA Nephropathy, IgAN, Anti GBM disease, Ayurvedic management, Anuktavyadhi.

INTRODUCTION

IgA Nephropathy (IgAN) is the most common form of Glomerulonephritis and its incidence is progressively increasing globally.[1] It is an immune complex mediated Glomerulonephritis that involves diffuse mesangial polymeric forms of IgA deposits, often associated with mesangial hypercellularity. IgM, IgG, C_3 deposits or immunoglobulin light chains may be co-distributed along with IgA deposits.[2,3] Many studies documented patients with Crescetic form of the IgAN have a worse prognosis.[4]

It has been reported that the presence of crescents in IgA nephropathy increased the risk of renal failure almost 1.5-fold and that 50% of patients with crescents and diffuse mesangial proliferation reached end-stage renal disease within three to five years.[4,5,6]

IgAN is more common in males and the prevalence is 45/ 1million population in Asians.[7] IgAN is treated by Corticosteroids, Immunosuppressive drugs, ACE inhibitors/ ARBs, Diet modifications and Fish oil supplements (Omega-3)[8,9,10,11], which may slow the progress of the disease to some extent but once ESRD is established, nothing much can be done to save life, except Kidney transplantation or Dialysis. Further, if there is concurrent Anti GBM disease, unless serum antibodies are undetectable, Kidney transplantation option no longer exist because of risk of recurrence.[2]

Case study: This 45 year male subject had repeated episodes of macroscopic hematuria and hypertension was treated by one private practitioner at Nanded on 12 May 2018 and was investigated. His S. Creatinine was 1.98 mg/dL, which rapidly increased to 5.1 mg/dL on 8.9.2018 when he was further investigated by one Modern physician. He was hypertensive having B.P.-200/110 mm of Hg. His other lab findings were; Blood urea -144 mg/dL, Hb-8.8 gm/dL, WBCs-6400/Cmm, RBCs- 3.02 Million/Cmm, Platelets-2,04000/Cmm; HCT-27.99%. Urine routine and microscopic examination showed Proteins ++; RBCs-Plenty, Pus

cells-2-3/HPF, Epithelial cells-1-2/HPF. He was diagnosed as a case of Rapidly Progressive Glomerulo-Nephritis (RPGN) and referred to one renowned corporate hospital in Hyderabad. He was hospitalized from 19.9.2018 to 24.9.2018 and was thoroughly investigated. The ANCA-IgG antibodies were significantly detected under fluorescent microscopy in 1:32 dilution. Anti GBM antibodies were strongly detected under fluorescent microscopy in 1:10 dilution.

Kidney biopsy done on 21 Sep 2018 showed following findings

Serial sections studied show a core of renal cortex with up to 14 glomeruli and 1 artery.

-7 glomeruli are obsolescent with 4 of these showing associated fibrous and fibrocellular crescents. 6 of the other glomeruli show crescents which are cellular in 4 and fibrocellular in 2. The underlying tuft shows a mild mesangial widening with minimum mesangial hypercellularity and segmental sclerosis in 2

-Tubular atrophy is seen over 25% of the cortex sampled. Scattered tubules have hyaline and granular casts. The interstitium is widened with a moderately dense infiltrate of lymphocytes with occasional polymorphs.

Immunoflorescence study shows **11 glomeruli all with crescents**. There are significant linear deposits of IgG with associated mesangial deposits of IgA, C3c.

Diagnosis/Comments: Kidney (Needle) biopsy shows features of **crescentic glomerulonephritis** with linear deposits of IgG consistent with **Anti GBM disease**.

-There is associated background IgA nephropathy. There is focal global glomerular obsolescence (7 of 14) and mild to moderate Interstitial Fibrosis and Tubular Atrophy (25%) are features of chronicity. Scores: IgG-4+, IgM-Nil, IgA-3+, C_3c-3+, Kappa Lc-2+, Lambda Lc 2+

It was very clear from the Kidney biopsy that 11/14 (79%) glomeruli had crescentic glomerulonephritis with concurrent Anti GBM disease and findings were consistent with features of chronicity.

Patient was given Plasmapheresis 2 times with Haemodialysis on alternate day. Patient took discharge voluntarily from the hospital due to its exorbitant charges to the tune of > Rs. 2 lakhs in one week.

Patient was admitted again in one tertiary care hospital/ Medical College Hospital, Aurangabad from 25/9/2018-6/10/2018. He was given Plasmapheresis 9 times with Hemodialysis 9 times; he was initiated Immuno-suppressive treatment of Cyclophosphamide and corticosteroids.

Table no. 1: Lab investigations reports in Tertiary care hospital.

Investigation	25/9/18	26/9/18	27/9/18	28/9/18	30/9/18	2/10/18	4/10/18
Hemoglobin	9.8	9.0	8.2	8.8	7.4	6.8	6.1
TLC	9,400	9,650	7,990	11,370	7,510	11,670	15,260
Platelets	2,25000	2,07000	1,71000	1,62000	1,35000	98,000	66,000
Blood urea	155	218	218	212	211	207	146
S. Creatinine	6.6	6.0	5.0	4.6	4.6	4.4	5.0
Na /mEq/L		134	137	136	135	134	132
K/ mEq/L		4.6	4.1	4.1		4.3	5.1
Ca/ mEq/L		7.7	7.1	6.6		7.1	

It is evident from the table No.1, that there was hardly any improvement in the clinical/biochemical indicators of the patient. His moderate anaemia deteriorated to severe anaemia. Normal Leucocytes count increased to Leucocytosis. Platelet count decreased subnormally; Na^+, K^+ and Ca^{++} level worsened. S. Creatinine and Blood urea level was marginally decreased despite Plasmapheresis and Hemodialysis.

On 8.10.2018, Anti GBM antibodies -Significant level of antibodies were detected on intensified immunofluorescence in 1:10 dilution. It is pointed out that even after a course of 9 Plasmapheresis, there was no effect on level of Anti GBM antibodies.

Patient was referred to author on 3 Jan 2019 with following complaints.

Severe bipedal oedema/*ubhay- pad shoth*
Oedema on face/*Mukh shoth*
Severe weakness/ *Dorbalya*
Tingling and numbness in limbs/ *Chimchimayan*
Dyspnoea on slightest exertion/ *Shrama shwas*
Rash over the body

} 15 days

H/o Hypertension: 6 months, intermittent hematuria-8 months
No H/o Diabetes
No H/o Renal disease in family
Personal history: H/o Tobacco chewing 20 years, Loss of Appetite, Constipated-bowel movement every 2-3 days, Vegavrodh (Wilful holding urge of urination/defication).
Doshik prakruti-Kapha-Pittaj; Manas prakruti- Satva-Rajas
On examination: Afebrile, Pulse-90/ min, Respiration-23/ min; B.P. 140/90 mm of Hg.
Pallor +++
Oedema over feet-+++ Oedema over face-++ Rash over body ++
Systemic examination- R.S., C.V.S.-NAD
P/A- Liver just palpable; Spleen 1 finger palpable. Kidneys not ballotable. **Ascitis +**

Lab reports: **Hb-4.3 gm/dL**, WBC-9800/Cmm; RBC-2.4 million/Cmm; Platelets 1,20000/Cmm;
HCT-24% . S.Proteins- 4.1 g/dL; Albumin-1.9 g/dL

Serum Creatinine- 7.7 mg/dL, Blood urea- 166 mg/dL
Na- 134 mEq/L, K-5.3 mEq/L, Serum Calcium-7.1 mg/dL
Urine exam.- **Proteins ++++**; Sugar-Nil

RBCs- Plenty, Pus cells-8-10/HPF, Epithelial cells- 4-5/HPF; Hyaline and granular casts present.
Urine Protein -Creatinine ratio was 4.2.
HIV, HBsAg and HCV- Non-reactive.

USG Abdomen- Normal sized kidneys, echotexture normal, no e/o of calculus or hydronephrosis; Liver- E/o Coarse echotexture; Mild Splenomegaly.

Table No.2: Treatment chart.

Type of Treatment	From	To	Details of treatment
Deepan-Pachan	03.01.2019	07.01.2019	Sitopaladi + Avipattikar churna Half TSF BD before meals twice daily
	08.01.2019	10.01.2019	Pimpali (Piper longum) churna 0.5 gm in warm water followed by Erandpatra swaras (Juice of Castor leaves/Ricinus communis)) 3TSF early morning
Niruh basti	11.01.2019		Niruh: Dashmool+ Erandmool+ Punarnava 450 ml quath + Saindhav 5 gm + Honey 5 ml. + Narayan tail 20 ml.
Rakta-basti	12.01.2019	14.01.2019	60 ml. blood from previously screened donor given per rectally 48 hours apart.
Shaman chikitsa	08.1.2019	26.7.2020	Sitopaladi + Avipattikar churna Half TSF BD before meals twice daily Drakshadi kashay +Sarivaidyasav 3TSF BD Chandan(Santalum album) churna 2 gm+ Sariva (Hemidesmus indicus) 2 gm+Bhumyamalki (Phyllanthus niruri) 2 gm+ Gokshur (Tribulus terresteris) 2 gm+ Punarnava(Boerhavia diffusa) churna 2 gm BD along with Koshna jal/warm water. Milk boiled in Shatavari (Asparagus racemosus)+Gokshur+Vasa (Justicia adhatoda) 40ml BD for 8 days, then Milk boiled in Shatavari+Gokshur -40ml BD
	08.01.2019		Tab Punarnavadi mandur 2 BD Tab Gokshuradi guggul 2 BD
		09.02.2019	Tab Neeri 2 BD Majune dabi Dulward + Jawarise jalinus 1TSF each TDS
	28.7.2019	28.9.2019	Tab Hridayarnav rasa 1BD Churna of Haritaki (Terminalia chebula)50 gm +Guduchi (Tinospora cordofolia) 50 gm + Deodar(Cedrus deodara)50 gm + Punrnava50 gm + Sunthi 25 g+ Gokshur 50 gm + Amalki (Emblica officianalis)50 gm + Sariva 25 gm +Arjun(Terminalia arjuna) 50 gm+ Maka (Eclipta alba) 50gm + Shatawari 50 gm +Nagarmotha (Cyperus rotundus) 50 gm 1TSF BD with Koshna-Jal. Gandharva hastyadi Kashay 3 TSF+ jaggery 2 gm+ Rocksalt 500 mg BD Drakshadi kashay 3 TSF BD
	29.9.2019	till date	Sitopaladi + Avipattikar churna Half TSF BD before meals twice daily Shatvari+ Gokshur siddha kshirpak 40 ml. BD Gokshuradi guggul 2BD Guduchyadi Kashay One and half TSF BD Drakshadi Kashay One and half TSF BD

DISCUSSION

Case presented with accelerated hypertension. Many studies have reported hypertension as the main presenting feature and up to 20% presented with accelerated hypertension (mean arterial pressure >150 mmHg)[3]. Similarly Tumlin *et al* reported the clinical presentation of 20 patients having IgAN with at least 10% cellular crescents, and demonstrated that all had

hypertension as a presenting feature.[8] The present case had presented with accelerated hypertension having > 75% crescents and that reconfirms the findings of the researchers. The case had Anti GBM antibodies detected, that revealed that this was an autoimmune disorder in which the circulating antibodies are directed against an antigen normally present in the Glomerular Basement Membrane. This was the probably reason of Rapidly Progressive Glomerular Nephritis which progressed to End Stage Renal Disease within a span of few months.[12] In addition, the presence of Anti-Neutrophilic Cytoplasmic Antibody (ANCA) was responsible for accompanied vasculitis observed in autoimmune disorder. Providentially the case was spared of the pulmonary involvement as commonly observed in Goodpasture Disease. The combination of RPGN due to IgA nephropathy with concurrent Anti GBM disease is very rare. There are only 5 cases reported in the literature earlier having RPGN with Anti GBM disease.[13]

Present case received Corticosteroids, Immunosuppressant drug (Cyclophospamide), Plasmapheresis as mentioned by researchers.[9,10,11] But the disease could not be controlled and case deteriorated as evidently obvious from Table No.1. Even after administering course of Plasmapheresis there was no reduction in circulating Anti-GBM antibodies. The cost of treatment incurred to patient -a financial loss of Rs 4-5 lacs within 20 days. He was fortunate that he approached Ayurved and was treated effectively with bare minimum cost.

Samprapti: IgA nephropathy is Anuktavyadhi (Not described in classical literature). It may be called as *Vishamay (Aam) Vrikka-rog* which occurs due to toxins accumulated from different foods and medicines.[14] Free radicals and Reactive Oxygen Species (R.O.S.) are unstable molecules as a by-product of cellular metabolism and when produced in large amount, it may cause extensive damage to various cells. Aam may be termed as the combination of free radical damaged physiochemical and cellular material, accumulated due to various internal and external toxic stimuli. Autoimmune disease like Anti GBM disease with IgA nephropathy may be viewed as Aam related pathogenesis.

There is correlation between symptoms of *Vrikka-rog* (ESRD) and symptoms of *Annavahsrotas dushti*. Vagbhatta mentioned symptoms of *Aam as follows*.
Srotorodh Balabhransh Gaurav Anilmudhata II
Aalasyapakti-nisthiva Malasangha-Aruchi-Klumah I
Ling Malanam Samanam Niramanam Viparyayah II
Vagbhatta Sutrasthan 13/23-24

Patient used to consume *Guru, Snigdha, Abhishandi, Atilavan, Dugdhjanya aahar, Adhyashan,* etc *Santarpanjanya* aahar-hetu and tobacco chewing, *Atap sevan, Vegavarodha,* sedentary life style etc. *vihar hetu sevan* were observed, that resulted in to *Agni dushti* due to production of *Kapha Kleda* i.e. *Aam,* causing *Jatharagnimandya*. Therefore the nourishment of *Uttarottar dhatus* suffered and that created *Dhatvagnimandya*. Due to *Agnimandya, Strotorodhjanya Vat prakop* occurred in *Annavah, Udakvah (Rasa, Rakta, Lasika, Mutra and Sweda), Pranvah strotas*, this type of Vat prakop is termed as ***'Avrutta vat.'*** It caused obstruction to the gati of various *dhatu pravah*, therefore their *Parinaman* is halted. If this state remains for some time, the *Sanchit doshas* travel in opposite direction & produce lakshanas like *Trishna, Shoth, Shwas, Udar,* etc. In this *Vat prakop*, instead of treating *Vat* alone, chikitsa of *Kapha* and chikitsa of *Rakta & Meda* has to be made because it is the *Partantra* type of *Vat prakop.*

***Chikitsa sutra*:-**Patient was treated with following treatment principles:

1. ***Nidan-Parivarjan***
2. ***Deepan-Pachan***
3. ***Shaman and Vatanuloman***
4. ***Rakta basti-Bruhan /Rasayan chikitsa.***

1. *Nidan-Parivarjan*: The case was addicted to tobacco. It is documented that Tobacco chewing contributes to the development of renal impairment leading to renal disorders.[15] He left this habit by repeated counselling. He was asked to avoid *Guru, Snigdha, Vidahi, Abhishandi, Atilavan, Dugdhajanya, Adhyashan, Tikshna/Ushna aahar* and asked to consume *Laghu-Supachya aahar*. He was asked to avoid *Vegavrodh*. We asked to taper off the dose of steroids within 3 weeks. Cyclophosphamide was stopped completely by gradually reducing the dose.

2. *Deepan-Pachan*: Removing *Agnimandya* & increasing *Agni (Kshudha*/Appetite) was the main purpose of *Deepan/ pachan dravyas*. Sitopaladi churna and Avipattikar churna are having *Deepan-Pachan* properties that reduced *Rasa-Rakta dhatugat 'Samata'*, and therefore they were used.

Pippali is the main drug having action of *Deepan & Pachan* at cellular level and hence it was used. Pippali carries out *Vatashaman* due to its *'Snigdha guna'* & functions as *Rechan of Pitta* owing to its *'Sar' guna* properties. Pippali having its *Kaphaghna* and *Vatanuloman* properties, removes *Vibandh*/obstruction. Pippali has specific action for *Raktavahstrotas & Pranvah strotas*. Due to its *Katu rasa & Madhur Vipak*, & being *Raktagami*, that increased *Rakta-agni* and acted as *Raktavardhak.* Therefore *Raktotpatti*/ Haemopoiesis also improved.

Erandpatra is having *Vataghna, Kaphaghna, Mutrakrichhghna, Gulma/Bastishoolharam &* ***Saptavidha vriddhiharam & Adhobhagharam (Rechan)* properties.**

3. *Shaman and Vataluloman*:- Patient had macroscopic Hematuria. In Ayurved, it is termed as *Adhog-raktapitta* and *Vaman*/ Emesis is the best remedy advised to treat it.

Adhovahe Raktapitte Vamanam Param uchyate...I Charak Sanhita Chikitsasthan 4/60
But before provoking *Vaman, Bala-bal* (fitness) has to be ascertained. The patient was very weak with severe Anemia. He was not fit for *Vaman* procedure; therefore we decided not to administer *Vaman*. We used *Agnipradeepak, Pachak,Virechak, Raktashodhak/ Raktaprasadak, Shothaghna, Swedal, Mutral, Anulomak* and *Dhatu bal- vardhak* herbal drugs as mentioned in treatment chart.

4. Raktabasti:- Patient was severely anaemic with Hb 4.3 gm/dL. Author had successfully treated anaemia in ESRD study subjects by Raktabasti, earlier. In this study 39 ESRD study subjects with severe anaemia were given 60 ml of blood and repeated after 48 hours. The average rise in Hb% after two Raktabasti was found to be 1.65 gm/dL.[16] With respect to the present case, we administered 60 ml blood of a previously screened healthy donor to the patient per rectum and repeated it after 48 hours. Hb was estimated after 48 hours and it was revealed that Hb was 6.4 gm/dL (an increase of 2.1 gm/dL) with just 120 ml of donor's blood. Raktabasti is a Bruhan basti, that reduced S.Creatinine from 7.7 mg/dL to 5.4 mg/dL within 48 hours.

Patient responded very well to the Ayurvedic treatment. Within one month most of his symptoms disappeared. He has been maintained free of dialysis for last 16 months. His Serum creatinine has been stabilized around 3.5 mg/dL. There is no Proteinuria. His ESRD/CKD-5 status has improved to CKD stage 4.

Modern Medicine has strong conviction that ESRD is irreversible. But Ayurved has shown that it's a myth. Author had conducted one clinical trial on 50 study subjects of Chronic Renal Failure in which 39 study subjects were of ESRD. Out of these 39 ESRD study subjects, improved kidney function was notable in 12 (31%) study subjects; out of them, 9 subjects were shifted to CKD stage 4, 2 subjects shifted to CKD stage 3B and one subject shifted to CKD stage 2. This study has proved that ESRD is reversible by Ayurvedic line of treatment.[17] Where Modern science has limitations, Ayurved has a lot of potential to show its pre-eminence.

Follow-up:-Patient is symptomless, doing his entire job in government setting, with full capacity. Ayurved has fully restored his quality of life. He is totally free of dialysis since Ayurved treatment started from Jan 2019. This case study is a ray of hope to thousands of sufferers of crescentic form of IgA nephropathy with a message to them that Ayurved has a definite role to play in its effective management.

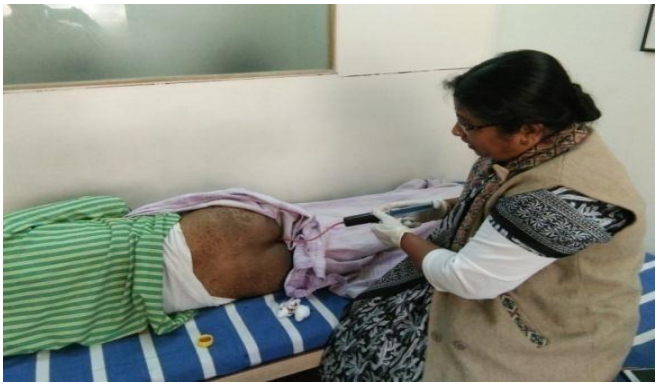

Fig.No.1: Author administering Raktabasti.

Fig. No.2: After 6 months of treatment.

Fig. No.3: After 16 months of treatment.

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