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## Waldenstrom's Macroglobulinaemia: Modified Plasmapheresis as Treatment Option in a Nigerian Setting.

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### ABSTRACT

We describe a case of Waldenstrom's macroglobulinaemia in a 56 year old Negroid male, to whom modified plasmapheresis-plasma exchange was offered with good control of symptomatic hyperviscosity.

Amelioration of the clinical status and objective assessment of response was evident by dramatic reduction in monoclonal immunoglobulin M (IgM) from 100g/L to 14.7 g/L, and a fall in erythrocyte sedimentation rate from 130mm/hr to 80 mm/hr with this therapy.

This highlights the need to adopt a modification of manual plasmapheresis in the treatment of the hyperviscosity syndrome complicating this B-cell disease in his environment.

**KEYWORDS:** Waldenstrom's macroglobulinaemia; Modified plasmapheresis; Nigeria.

### INTRODUCTION

Waldenström's macroglobulinaemia (WM) is a relatively rare disorder, but often remains a major health problem. It is described as a clonal lymphoid disease that is characterized by lymphoplasmaeytic bone marrow proliferation and expresses a peak in serum protein electrophoresis consisting essentially of monoclonal immunoglobulin M (mIgM)<sup>1,2</sup>. The disease usually affects older persons and may produce anaemia, lymphadenopathy, elevated serum viscosity or a combination of these<sup>3</sup>. The disease accounted for 2% of haematologic cancers and affects approximately 1,500 Americans each year<sup>1</sup>. However the incidence in Nigeria has not been documented.

Chemotherapy using alkylating agents/steroid combination has induced responses in approximately 50% of previously untreated patients. With a subsequent median survival of about 5 year<sup>4</sup> other treatment options offered and shown to have yielded good result is plasmapheresis.

Plasmapheresis, however is unique and it is the treatment of choice in this patient with

hyperviscosity syndrome. In WM, there is elevation of circulating Ig M level, cryoglobulinaemia<sup>4</sup> and/or peripheral neuropathy<sup>5</sup>.

Plasmapheresis is performed with specialized equipment e.g Haemonetics model 30 or V 50 (as an intermittent - flow cell separator) or IBM/Cobe 2997 (as a continuous flow device)<sup>5</sup>. With the advent of structural adjustment programme in Nigeria, funding of tertiary Health care center has been a problem. With the peculiarities in this environment in mind, there is the need to adopt a local measure to offer our needy patients in order to reduce their sufferings.

In this report we describe the first case of WM to be treated with modification of plasmapheresis as a treatment option in our setting. The procedure resulted in drastic reduction in the serum paraproteins which thereby enhanced the well being of the patient. This treatment option may also play an important role in the treatment of the hyperviscosity in this B-cell disease in our environment.

### CASE REPORT

A 59 year old negroid male, was first seen at university college hospital, Ibadan 12 months ago. He presented with a 3 month history of pain the neck and a peculiar sensation in his right hand with shooting pain down right side of his head. Systemic review revealed that there was no backache, no weight loss in the last 6 months, no drenching night sweat, no numbness in the hands and feet, no tingling sensation, no weakness and no stamping gait. The appetite was good and there was no vomiting, bowel habits were normal, there was no pruritus. There was a positive history of passage of holly urine but there was a normal functioning gonithalia. There was no blurring of vision or abnormalities with his vision.

Physical examination revealed that the patients general health was good. He was well nourished, not in any distress, afebrile, mildly pale, mucous membranes moist and well hydrated. He had no

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palpable peripheral lymphadenopathy. The liver and spleen were not enlarged. He has a normal gait.

Laboratory data were as follows: Haemoglobin 12.1gm/dl, erythrocyte sedimentation rate (ESR) 119mm/hr (Plasma viscosity of 2.31 mpa (1.50-1.72 and marked rouleaux formation was observed on blood film review. Bence jones protein was negative. Immunoglobulin M. (Kappa light chain type) was 69 g/L [0.4-2.3], IgG of 12.8g/L [7.0-16.0], IgA of 1.0 g/L [ 0.7-4.0] Serum Beta - 2 microglobulin of 2.3 mg /L [ 0-1.9]. Serum Calcium 2.47 mmol/L[2.20-2.60] Urea of 45mg/100ml, and creatinine of 1.8mg/dl.

The bone marrow confirmed slight increase in plasma cells. Trepine biopsy revealed a hypercellular marrow, with preservation of architecture. Immunohistochemistry carried out in England confirmed CD79a positive cells accounting for 5-10% of all cells, and within sinusoids were seen CD20 positive cells. The presence of both CD20+, CD 79a + B cell and CD 20-, CD 79a + plasmacytoid cells confirmed lymphoplasmacytic lymphoma.

Two-chlorodeoxyadenosine (Cladribine) was commenced at 1.65 mgs in a continuous infusion over 24hours. This was followed by intravenous Cladribine 7.92mg, for the subsequent 5 days. It was observed that after 28 days, there was no reduction in IgM, because of this plasmapheresis was carried out. The reduction in IgM however became noticeable 3 months after the initiation of therapy. However, the minimum level of IgM obtained was 28g/L and patient was subsequently discharged.

He represented 10 week after with worsening feature of hyperviscosity syndrome, which were pains in his neck and in his right hand which shoots down to the right side of his hand. His haemoglobin was 10.8gm/dl, erythrocyte sedimentation rate was 130mm/1<sup>st</sup> hr, urinary IgG 448mg/dl, urinary protein electrophoresis showed faint gamma and albumin bands. Immunoglobulin M of 100g/L, IgG 1046 mg/dl [ 1272 - 2713mg/dl] IgA 116 mg/dl (20 - 456mg/dl). In view of the unavailability of the drugs used in the first cycle, modified plasmapheresis was offered to the patient.

Before each treatment cycle and 24 hours after procedure the following laboratory investigations were carried out. Full blood count, erythrocyte

sedimentation rate and serum immunoglobulin quantitation. The patient has had 4 sessions of modified plasmapheresis at 4 weekly intervals until the ESR was 80mm/1st hr and IgM was 14.7g/L

Modification of plasmapheresis /plasma exchange was carried out as indicated below.

**Step**

1. 500 mls of normal saline is infused into patient.
2. 450 mls of blood is phlebotomized into a CPD-A plastic blood bag.
3. 500 mls of normal saline is infused into patient.
4. The blood removed in 2 is spun at 300 rpm for 15 minutes) in a cold centrifuge, the plasma is transfused into another blood bag and discarded.
5. The packed cells in 4 is transfused into the patient.
6. The procedure in 2 and 4 are repeated twice at each session

The above procedure was carried out monthly for 4 visits. The patient has remained in steady state with ESR 80mm/1st hr, IgM of 14.7g/L. He also has no neurological complaints.

**DISCUSSION**

WM or Lymphoplasmacytic lymphoma is a slowly progressive clonal lymphoid disorder, in which macroglobulinaemia or IgM monoclonal gammopathy poses a significant problem. IgM paraproteins increases blood viscosity more than equivalent concentration of IgG or IgA and small increases above 30 g/L in concentration will lead to increases in blood viscosity. The increase blood viscosity will result in increase resistance in the flow of blood and these will manifest as hyperviscosity syndrome.

No therapy is needed for patient without symptoms, but when IgM level exceeds 30g/L or if macroglobulin is a cryoglobulin then feature of cryoprecipitation ensues and these calls for emergency intervention.

In emergency situations, plasmapheresis has been a viable option because 80% of the total paraprotein are found within the intravascular space. In this report the monoclonal immunoglobulin M level were 100 g/L and erythrocyte sedimentation rate was 130 mm/hr coupled with the clinical state which was suggestive of a hyperviscosity syndrome. Table 1

Table 1. Variables used to Assess Response

	Pre Plasma exchange	Post Exchange					
		Post 1 <sup>st</sup> Session	Pre 2 <sup>nd</sup> Session	Post 2 <sup>nd</sup> Session	Pre 3 <sup>rd</sup> Session	Post 3 <sup>rd</sup> Session	Pre 4 <sup>th</sup> Session
Hb level (g/L)	11.0	23.1	23.1	21	21	20	14.7
ESR (mm/hr)	130	110	120	110	90	80	80
Plasma (g/L)	31	35	31	31	30	32	33
Hb (g/dl)	10.8	11.6	10.8	10.8	10.3	10.9	11.0
WBC per mm <sup>3</sup>	2,700	2,600	3,000	3,500	5,000	7,000	3,000
Platelet per mm <sup>3</sup>	16,000	130	195,000	190,000	100,000	59,000	148,000

After the series of plasmapheresis, patient was observed to have responded well to this treatment option with a fall in the level of serum IgM to 14.7 g/l from 100g/l and erythrocyte sedimentation rate to 33mm/hr from 130m/hr. There was also improvement in the clinical state. These observations have been reported by other workers who have had similar experiences<sup>10</sup> in their patients that had plasma exchange with automated apheresis. The plasmapheresis (automated devised) to the patients as assessed, if tolerability and is cost's effective. However, the setback in this treatment modality is that it requires the services of trained personnel and as such, it is not situated for primary and secondary health care centers. It is laborious, time consuming and it require hospitalization to monitor and resuscitate the patient if the need arises.

A marked reduction in serum paraproteins was observed in addition to improvement in the clinical well being of the patient. This gives credence to the usefulness of this treatment modality.

Lastly, this treatment modality is palliative and therefore is not curative. So there is need to frequently carry out the procedure.

#### CONCLUSIONS AND SUGGESTIONS

Modified plasmapheresis has shown that, in this environment, it can be given safely, it is effective and could contribute to the prolonged

disease free survival of the patient. We therefore suggest its adoption in our locality in managing hyperviscosity syndrome

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