ALBUMIN PHERESIS IN A WOMAN WITH THROMBOTIC THROMBOCYTOPENIC PURPURA

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INTRODUCTION

Acquired thrombotic thrombocytopenic purpura (TTP) is usually rapidly diagnosed and treatment promptly initiated. Standard therapy includes plasma exchange with FFP or solvent detergent FFP (SDFFP). Plasma infusion was the first successful intervention in treating TTP lowering mortality rates from 90% to 37%. With the initiation of daily plasma exchange as the standard treatment, the mortality rate decreased to 22%. Plasma exchange is continued until at least 2 days after remission is achieved. Remission is defined as normal neurology, platelet count 150,000, normal LDH and rising HGB.

This is a case report of a patient who for religious reasons would not accept FFP. The presentation of this case is important. Experience with Blood Conservation Programs treating TTP with albumin replacement of plasma was uniformly unsuccessful. The literature available had no reports of treatment success under these conditions.

CASE PRESENTATION

A 45 year old previously healthy white female who developed confusion and difficulty expressing herself following a GI flu-like illness. Initial symptoms resolved spontaneously, but reoccurred a week later with lack of coordination and right hand fine motor skills diminished. Patient was admitted to a community hospital, where and MRI of the head showed multiple bilateral cortical small infarcts.

TREATMENT INITIATED AT COMMUNITY HOSPITAL				
Rituxin	Cytotoxan	Vincristine	IgG	Epoetin Alfa

Ten days later patient had a hemoglobin (HGB) of 6.3, hemianopsia and was transferred to Saint Luke's Hospital of Kansas City. The decision was supported in part by the patient's refusals of blood transfusion and the need for albumin-pheresis. (See Table 1, Day 1 at SLH for labs).

TREATMENT INITIATED AT SLH			
Methylprednisolone	Epoetin	Alfa Rituxin	Vincristine
Albumin-pheresis	IgG	Cryoprecipitate	Vitamin C
Leuprolide Acetate	Multivitamin	Folic Acid	Ferric Gluconate

All of the usual blood conservation techniques, using micro sampling and reinfusion of patient's own blood from central and arterial lines were implemented.

Ten days later patient developed chest pain and was moved to the stepdown cardiac unit. The patient had suffered an acute subendocardial MI secondary to small arteriolar occlusion, which was managed medically.

TREATMENT REGIMEN AFTER MI				
Cyclosporine	Rituxan	Vincristine	Cryoprecipitate	Albumin-pheresis

Seven days later patient developed a small abscess and cellulitis of the left gastrocnemius muscle. Patient was placed in reverse isolation. Albumin pheresis stopped. (See Table 1, Day 20 labs)

TREATMENT REGIMEN AFTER REVERSE ISOLATION			
Vancomycin	Imipenem-cilastatin	Filgrastim	Rituxin
Vincristine	Epoetin Alfa	Ferric Gluconate	

Cyclosporin stopped. One week later patient started to improve and Vancomycin and Imipenem-cilastatin was stopped and changed to Moxifloxacin and albumin-pheresis was restarted.

Two weeks later patient developed a fever; blood cultures positive for *E coli* sepsis. IV antibiotics were restarted and the patient response to treatment was noticeably improved. The patient was discharged home on day 54 after 21 albumin-pheresis procedures. Two weeks later the patient was readmitted due to a community acquired pneumonia that did not affect the TTP and following treatment was released. The patient has had no reoccurrence of her TTP for the past 9 months. (See Table 1, labs on discharge)

DISCUSSION

Autoimmune destruction of the ADAMTS13 protease is the sole defect in TTP. The body's ability to breakdown von Willebrand's factor (VWF) in the circulatory system is uniquely dependent on VWF accumulate leading to clumping and activation of platelets. The autoimmune inhibitors can now be measured and the activity of the protease is also directly tested by specialized labs. The first labs were drawn 23 days after initiating treatment and 29 days after initiation of symptoms. The inhibitor was still present although in small quantities and the activity level of the ADAMTS13 was 8% (normal 67-177%)

Aggressive treatment using multiple interventions to affect the immune system was used due to treatment failure of previous patients treated with albumin as a plasma replacement. Additionally the patient was never admitted to the intensive Care Unit but managed on a telemetry unit after her MI. The only major complications being the steroid-induced myopathy from which she is continuing to gradually improve and a small visual field defect from her initial stroke. Also of note, this patient did not have a splenectomy as she was too ill at the initial treatment and, by the time she had gained strength to the point where she would tolerate surgery, her ADAMTS13 activity level was back to normal, and the inhibitor was not measurable.

CONCLUSION

- Remission of acute TTP is common when treated with plasma exchange.
- Plasmapheresis with albumin replacement alone has not been effective in treatment of TTP
- Cryoprecipitants have been proposed previously as an alternative to FFP to correct fibrinogen deficiency
- Rituximab treatment has been followed by sustained remission in two cases of acute TTP and five of six cases of chronic TTP but remission cannot be assumed to be a response to Rituximab treatment
- Course of TTP is unpredictable
- Even though successful in this case the use of multiple immune modulators does not allow conclusion as to the effectiveness of the individual agents
- Corticosteroids, vincristine, cyclophosphamide, cyclosporine and splenectomy have been used empirically for treatment of relapsing TTP, but there has not been systematic evaluation of these treatments in either acute or chronic TTP
- The identification of ADAMTS13 deficiency, and an IgG autoantibody, associated with idiopathic TTP may help clarify diagnosis and treatment response.

Due to the infrequent number of patients with TTP it would be important to encourage the reports in the literature about the management of these cases, so some day there could be a review of cases since a controlled study to look at the role of immunosuppressants in the treatment of acute TTP as an adjuvant to plasma exchange could be very difficult to accomplish.

FLOW RECORD

Date 2003	LABS										TREATMENTS	COMMENTS
	WBC	HGB	Platelets	LDH	Fibrinogen	Cytoxan	Steroids	Vincristine	IVIG	Rituxin	Pheresis	
Day 1 @ SJH	10.7	12.7	15									St. Joe admit labs
Day 7	8.6	12.4	13	725								Sept. 9th - Admitted to St. Joe with garbled speech, multiple CVA's x2, MRI
*Day 1 @ SLH	2	6.3	87	499								Admitted to St. Luke's Stroke Ctr. - Neurology/Hematology Consult
Day 2	1.3	7.7	88				Solumedrol 125mg IV q 6h					
Day 4	2.1	7.4	86	1456							X	
Day 5	2	7.4	69	1045							X	Vaginal Bleeding - Lupron Depot
Day 6	2.3	7.4	44	864			Cyclosporin 200mg BID daily	X	X	X		Started Cyclospoirin
Day 8	5.5	7.5	27	1308	97				X			
Day 10	4.4	7	12	1423							X	
Day 11	5.8	7.5	11									Chest pain/EKG/Nitro/MSO4/Cardiology/Rehab Consult
Day 12	7.7	7.6	9	1110	87						X	
Day 15	9.5	7.1	21	681	201			X 2mg		X 375	X	
Day 16	5.7	7.4	19	564	74						X	
Day 18											X	Fevers 102.8/Pain and cramping in L calf
Day 19	0.9	5.5	13	427			Prednisone 60 mg PO daily				X	Consult Infectious Disease/CXR/Venous Duplex negative
Day 20	0.3	4.7	9	360								20,000 daily/Reverse isolation/No code/hypotension/increase fluids
Day 21				566				2 mg		375		
Day 24												DC reverse isolation and add labs
Day 26	6.0	4.2	41	397			Prednisone 40 mg PO daily					
Day 28	4.9	4.9	134	776							X	
Day 29	4.9	4.7	134	610							X	
Day 39	6.1	7.6	65	494							X	Sepsis with Ecoli started Avelox
Day 54	3.8	8.8	91	481			Epo 40,000 units					Discharge to home
Day 78	9.7	10.8	412	945								Readmitted for Community Acquired Pneumonia
7 months later	6.4	13.4	308	490								