Introduction of Ponticelli Regimen in Sri Lanka for Idiopathic Membranous Nephropathy

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Introduction

Idiopathic Membranous Nephropathy in adults is a disease of worldwide occurrence. The outcome of the disease is variable. Spontaneous remission can occur in some patients and kidney function may be stable for many years in others, but approximately half of all patients die or have end stage renal failure within 10 to 15 years after the onset of symptoms. Various treatment protocols including high-dose alternate-day steroids and cytotoxic agents[2] (Cyclophosphamide, Imuran) have been used with varying success rates. However, today the Ponticelli Regimen is widely accepted as a successful treatment in Idiopathic Membranous Nephritis.

The Ponticelli Regimen consists of monthly corticosteroids (cycle A) alternating with chlorambucil (cycle B) for six months.[2] The monthly steroid treatment consists of Methylprednisolone in 1Gm pulses for 3 days followed by oral prednisolone (0.5 mg per kg of body-weight per day) for 27 days. At the end of the first month the steroid is discontinued and chlorambucil (0.2 mg per kg of body-weight per day) is administered for 30 days. No previous report of the use of this regimen of treatment is known is Sri Lanka.

Scheme of Therapy

Cycle A (Months 1,3,5)
1Gm iv Methylprednisolone for 3 days
Oral Prednisolone 0.5 mg/kg/day for 27 days.

Cycle B (Months 2,4,6)
Chlorambucil 0.2 mg/kg/day for 30 days.

Case Report

Mr. A, a 54 - year old Insurance Consultant from Colombo presented with nephrotic syndrome in June 1989. He had been well previously except for having suffered from an episode of acute Gouty Arthritis in 1987. He has been on Allopurinol 100 mg daily since then. He was diagnosed to have had Membranous Glomerular Nephritis after a renal biopsy performed in July 1989 in New Zealand. He was advised symptomatic treatment and came back to Colombo in September 1989. On examination he was of average build (wt - 70 k.g.) and had mild ankle and sacral oedema. His blood pressure was 150/94, JVP was not raised and heart was clinically normal. Lung bases were clear, liver and spleen were not palpable and there was no free fluid in the peritoneal cavity. There was no evidence of arthritis or cutaneous manifestations of hyperlipidaemia. He received Verapamil 40 mg tds, Frusemide 40mg bd, Moduretic 1/2 tab bd and Enalapril 5 mg daily for his hypertension and oedema. He was also prescribed Gemfibrozil 600mg bd as he had very high serum lipid levels. Unusually his serum amylase was found to be high during the initial period of his illness. He did not have any symptoms or signs of pancreatic disease and the ultrasound examination and CT scan of the abdomen were normal.

He was started on the Ponticelli Regimen in August 1990 as progressive decline in his renal function was noticed. His calculated daily dose of Prednisolone and Chlorambucil

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were 35 mg and 14 mg respectively. During the second cycle of Chlorambucil treatment he developed high fever which warranted temporary suspension of the treatment for 3 weeks. The cause of the fever was thought to have been due to viral infection. He otherwise tolerated the treatment well except for having been very anxious. He frequently complained of troublesome tremors, severe anorexia and nausea. (The T3/T4 was within normal limits). The renal function, 24 hour urine protein excretion, full blood count, blood sugar, lipid profile, Liver function test, and Serum Uric acid were closely monitored. The results are duly summarized in figures I and II.

Discussion

Since commencement of the treatment the 24-hour Urinary protein excretion has reduced markedly and considerable improvement in Serum albumin level has been noticed (Figure 1). The renal function too has shown a change in trend towards improvement. He now takes a much smaller dose of diuretic(Moduretic 1/2 tab daily). He continues to take the same dose of Enalapril, Verapamil and Gemfibrozil.

Although this treatment regimen is claimed to be quite successful in Membranous Nephropathy, it is important that the selection of patients should be rigorous (in view of the adverse effects of the drugs used). This treatment is not recommended for those patients with significant renal insufficiency and those who show signs of diffuse interstitial or glomerular sclerosis in renal biopsy[4]. Besides, this treatment may not be suitable for elderly patients, patients with infective foci and those with previous neoplasms[4]. Futhermore, at present one does not see much justification in treating patients who have Membranous Nephritis without evidence of nephrotic syndrome as they generally have a good long-term prognosis without any specific treatment.

Figure I

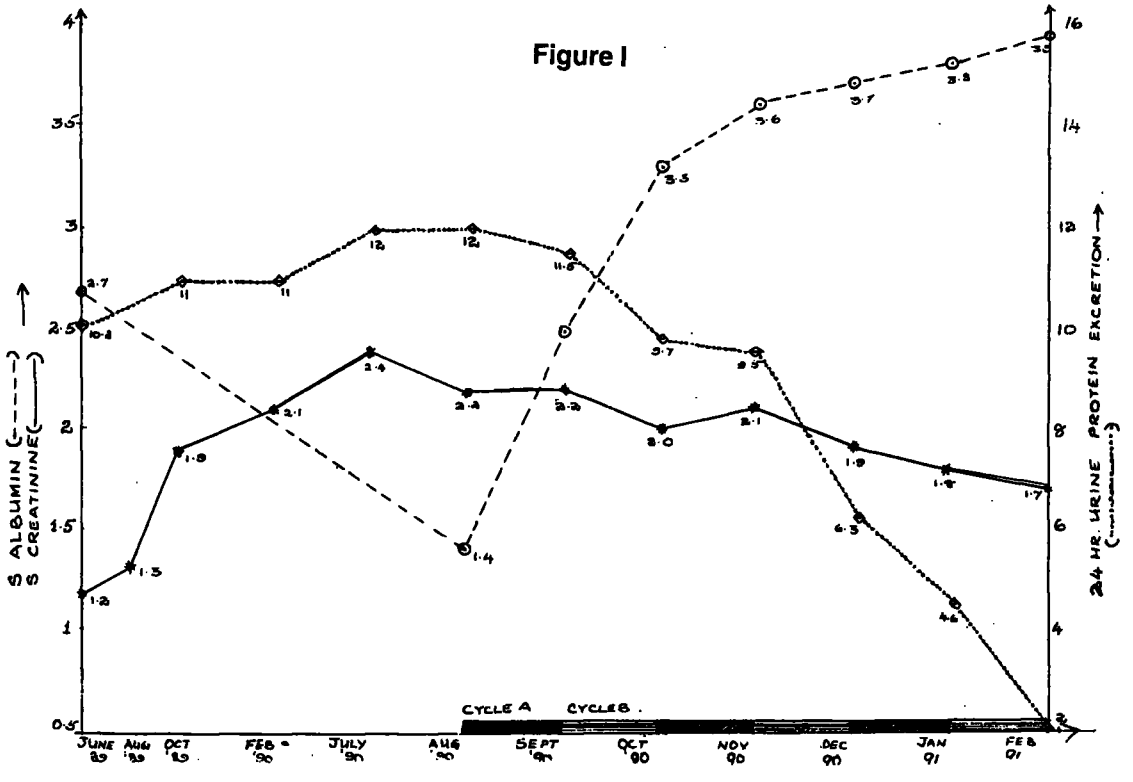

Figure II

	June 89	*Dec 89*	*July 90*	*Aug 90*	*Sep 90*	*Oct 90*	*Nov 90*	*Dec 90*	*Jan 91*	*Feb 91*
E S R (mm)	122	121	85	100	136	103	40	44	130	132
Creatinine Clearance (ml/mt/m^2)	75	70	68.6	56.3	67	79.7	67.8	84	73	78.5
S. Chol (mg/dl)	436	403	385	303		281	286	243		235
S. Tg (mg/dl)	408	282	315	146		130	145	100		170
S. Ldl (mg/dl)	387	298	100	203		196	199	184		159
S. Hdl (mg/dl)	28	33	35	72		59	52	39		42
Chol/Hdl	15.51	13.2	11	4.2		4.7	5.3	6.2		5.5
S. Amylase (Somogi units/dl)	325	433	953	780	735	75		100		120

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