fluorescent staining for IgG was positive. A cadaver renal transplant was performed in August 1975, but this subsequently failed and the patient has now returned to regular haemodialysis therapy.

Discussion

Massive proteinuria with nephrotic syndrome has been reported in vesicoureteric reflux and in chronic pyelonephritis.[1 2] Possibly the association is purely coincidental, but this would seem unlikely. Membranous glomerulonephritis has been produced experimentally by the injection of homologous renal tubular epithelial antigen,[3] and tubular epithelial antigen has been demonstrated deposited on the glomeruli in membranous glomerulonephritis.[4] Possibly tubular epithelial antigen is released into the circulation in reflux as a consequence of renal tubular injury, or, contact with immune competent cells is via the inflammatory cell infiltrate. Whatever the mechanism, failure to recognise the antigen as "self" might result in antibody formation. With persistent antigenic stimulation, immune complexes would form, thus providing the mechanism of glomerular injury. Tubular epithelial antigen was not demonstrated in the glomeruli of this patient but this does not necessarily invalidate the postulate.[5]

We suggest that measurement of proteinuria may be indicated in vesicourethral reflux. When massive proteinuria is found, a renal biopsy should be performed as the finding of glomerulopathy may well alter the natural history of the reflux.

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Responses to vincristine in refractory idiopathic thrombocytopenic purpura

Recent reports indicate that the periwinkle alkaloid vincristine, by producing thrombocytosis, may be useful in the treatment of idiopathic thrombocytopenic purpura (ITP).[1 2] Adult patients with ITP who are resistant to steroid treatment present a problem, especially when they require surgery or develop bleeding complications. Splenectomy produces a response in only about half of adults, and the other commonly used immunosuppressants, cyclophosphamide and azathioprine, are slow in producing an effect.

We have assessed the response to vincristine in nine patients with chronic ITP who were wholly or partly refractory to steroids. The history of thrombocytopenia ranged between one and 18 years. Vincristine was given by weekly intravenous injections of 2 mg until either a response was obtained or the patient experienced unacceptable side effects. The details of the patients are listed in the table. The platelet counts are shown before vincristine and one to two weeks and one to two months after the first injection.

Patients treated

Patient 1 responded very rapidly, the platelet count rising from 34×10^9/l to 360×10^9/l even after her steroids were tailed off; previously she had required a maintenance dose of 40 mg of prednisolone a day. Patients 2, 3, 4, and 5 had a good response, with the platelet count rising to over 100×10^9/l, but they relapsed within three weeks of the first injection. Of these four patients, only patient 3 had ever responded to steroids and she required 60 mg of prednisolone a day to obtain a satisfactory platelet count. Patients 6, 7, 8, and 9 had a poor temporary response. The patients who responded showed an increase in platelet count a week after the first injection but this was sustained with further weekly doses in only three patients.

None of the patients developed any evidence of bone-marrow suppression on this dose and the limiting factor to further administration of vincristine was the recognised side effect of peripheral neuropathy, the symptoms of which appeared to be unusually prominent. It was not possible to predict the response to vincristine from the previous failure to respond to splenectomy.

Discussion

Treatment with vincristine may produce a significant rise in the platelet count in refractory ITP. The mechanism by which it is produced is incompletely understood. Despite the fact that many cases of ITP have an autoimmune basis and that vincristine is known to produce immunosuppression in animals,[3] it is not established that production of thrombocytosis is mediated through this action. In rats sublethal doses of vincristine have produced initial megakaryocyte suppression followed by reactive megakaryocytopoiesis and thrombocytosis. Low doses produced thrombocytosis only, but the authors postulated that the same rebound mechanism obtained.[4]

In our six patients with an initial moderate response the rise in platelet count was not maintained by continuing weekly vincristine at normal doses (0·025 mg/kg) and so little further benefit would result from long-term low-dose maintenance therapy. As suggested by Ahn *et al*[2] vincristine may tide the patient over until an immunosuppressive such as azathioprine, with fewer side effects but delayed action, produces a response.

In view of the temporary effect and the high incidence of side effects, routine use of vincristine in uncomplicated ITP is not indicated as primary treatment. Nevertheless, in refractory cases it may produce sufficient response to enable surgical techniques to be undertaken or be used as an interim measure in the management of bleeding complications.

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Summary of clinical details and response to vincristine

Case No	Age	Sex	Splenectomy	Antinuclear factor	Platelet count ($\times 10^9$/l)			Total dose vincristine (mg)
					Pretreatment	Max response (1-2 weeks)	Post-treatment (1 month)	
1	65	F	No	Negative	34	360	115	4
2	45	F	1960	Positive 1/10	3	120	8	8
3	66	F	No	Negative	20	120	10	6
4	40	F	No	Negative	64	144	52	6
5	80	M	No	Negative	54	136	10	7
6	57	F	No	Negative	18	71	20	7
7	66	F	No	Positive 1/40	28	50	40	3·5
8	43	M	1956	—	18	28	8	8
9	53	F	1975	Weak positive	30	60	20	2