Cellular immune variables in patient, other long-term (over three years) kidney transplant recipients, and controls

Lymphocytes in differential count												
White cell count ($\times 10^9/l$)	Total		Early E rosettes		E rosettes		Proportion bearing IgM		Proportion bearing IgG			
	No ($\times 10^9/l$)	%	No ($\times 10^9/l$)	%	No ($\times 10^9/l$)	%	No ($\times 10^9/l$)	%	No ($\times 10^9/l$)	%		
Patient												
36 months after transplantation	9.0	1.6	18.0	0.24	15.0	0.32	20.0	0.23	14.0	0.23	14.0	
41 months after transplantation	7.5	0.9	12.0	0.22	23.0	0.49	54.0	0.09	10.0	—	—	
47 months after transplantation	7.1	1.5	21.0	0.18	12.0	0.72	48.0	—	—	0.15	10.0	
Other transplant recipients												
Mean $\pm$ SE	7.6 $\pm$ 0.60	1.6 $\pm$ 0.17	21.6 $\pm$ 2.0	0.58 $\pm$ 0.08	39.8 $\pm$ 3.4	0.88 $\pm$ 0.12	54.0 $\pm$ 3.3	0.10 $\pm$ 0.02	6.0 $\pm$ 1.1	0.11 $\pm$ 0.02	7.2 $\pm$ 1.2	
Range	4.1-15.0 (n = 19)	0.6-3.5 (n = 19)	7.0-37.0	0.2-1.3 (n = 17)	17.0-64.0	0.25-2.2 (n = 19)	23-78	0.02-0.25 (n = 13)	1.0-16.0	0.01-0.24 (n = 12)	1.0-17.0	
Controls												
Mean	7.5 $\pm$ 0.42	2.4 $\pm$ 0.23	32.9 $\pm$ 2.3	1.03 $\pm$ 0.15	41.6 $\pm$ 3.2	1.46 $\pm$ 0.14	60.5 $\pm$ 1.4	0.23 $\pm$ 0.03	9.6 $\pm$ 0.6	0.22 $\pm$ 0.037	8.9 $\pm$ 1.1	
Range	5.1-13.1 (n = 25)	1.4-3.5 (n = 25)	18.0-52.0	0.3-1.8 (n = 22)	23.0-63.0	0.78-2.6 (n = 25)	47.0-77.0	0.08-0.31 (n = 21)	5.0-13.0	0.06-0.49 (n = 13)	2.0-14.0	
Other recipient v controls*		P<0.01	P<0.001	P<0.025		P<0.005		P<0.01	P<0.01	P<0.02		

*Student's *t* test used for comparison.

that some patients might have their immunosuppressive treatment withdrawn without any untoward effects.

Patients, methods, and results

The patient, a 17-year-old girl, began haemodialysis in January 1974 and five months later received a cadaver kidney allograft. Matching for HLA histocompatibility was poor (donor: B+, HLA-A2, A10, B5, —; recipient: B+, HLA-A10, —, B8, —). Routine immunosuppressive treatment included corticosteroids, azathioprine, and antilymphocyte globulin. Peritoneal dialysis and haemodialysis were performed once. The postoperative period was uneventful. She had never had a rejection episode, and only three mild infections were recorded. In August 1975 she stopped her immunosuppressive treatment without informing the medical staff. When seen in 1977 she had good renal function, with serum creatinine concentration 72.5 μ mol/l (0.8 mg/100 ml); serum non-protein nitrogen concentration 42 mmol/l (59 mg/100 ml); no proteinuria; and a daily urine output of 1500 ml. The other patients in the series were taking azathioprine (1.5–3.0 mg/kg/day) and methylprednisolone (16 mg on alternate days).

Serum concentrations of IgG, IgM, and IgA (ICL Scientific) and C3, C4, and C3 proactivator (Behringwerke) were determined with commercial single radial diffusion plates. Whole serum haemolytic activity was measured. The ¹²⁵I-Clq-binding assay was used to detect circulating immune complexes in serum. Mononuclear cells were isolated from heparinised blood by Ficoll-Isopaque (MSL, Eurobio) density-gradient centrifugation. The E rosette test and early E rosette test were performed. Immunoglobulin-bearing lymphocytes were detected with fluorescein-labelled antisera (anti-IgM, anti-IgG; Cappel laboratories).

The table summarises the results in the patient, the other transplant recipients in the series, and a group of normal controls. No appreciable difference in any variable was observed between the patient and other transplant recipients except in the concentration of serum polyclonal IgMs, which was noticeably increased in the patient (10 g/l). Circulating immune complexes were detected in low concentration. There was a significant difference in most variables examined between the other transplant recipients and controls.

Comment

This patient stopped her immunosuppressive treatment because she was worried about its effect on her growth. (She and her mother admitted this spontaneously, so we have no reason to doubt it.) Nevertheless, she had good renal function. The lack of any clinical and immunological difference between the patient and kidney transplant recipients who were taking their immunosuppressive treatment suggests that the degree of immunosuppression was the same. This raises questions about the persistence of immunosuppression without immunosuppressive treatment, the possibility of graft acceptance without immunosuppressive treatment, and the relation between graft acceptance and immunosuppression. The persistent immunosuppression may have resulted from the massive immunosuppressive treatment given after transplantation. HLA histocompatibility matching was poor, so that spontaneous acceptance of the cadaver kidney allograft was unlikely.

Azathioprine is commonly discontinued to avoid bone marrow and liver toxicity,^{2,3} and some workers⁴ recommend stopping azathioprine two years after transplantation. Naik *et al*⁵ withdrew prednisone

after two years without untoward effects in renal transplant recipients given this treatment alone. Our findings confirm that this may be possible and suggest that some specific immunosuppression occurs in organ transplantation. Rejection may occur after stopping treatment,³ however, so that criteria must be sought to establish the real need for long-term immunosuppressive treatment after transplantation.

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Polle syndrome: children of Munchausen

We report on a family in which the mother, who had the Munchausen syndrome, fabricated two different illnesses in her son and daughter in a highly systematic way. She was not suspected for six months, as her behaviour seemed normal.

Case reports

The daughter—This child was admitted in May 1976 aged 22 months with a five-day history of polydipsia, polyuria, and weight loss. Her urine contained 2% sugar. A glucose tolerance test was performed. The curve was an odd shape but definitely abnormal. She was diagnosed as having diabetes mellitus with a low renal threshold. She was stabilised on diet and Monotard insulin, and subsequent control was satisfactory.

The son—This 5-year-old boy was first seen in July 1976. Two months previously he had been accidentally knocked out. Soon afterwards he developed attacks of fever associated with headache, vomiting, abdominal pain, and diarrhoea. Later polyuria, polydipsia, and nocturia developed. His mother had seen blood and pus in his underpants and gravel in his urine. He

was admitted to hospital in August. Each afternoon he became febrile, ataxic, and irritable and then after about an hour fell into a deep sleep. On one occasion his speech was slurred and the left side of his body twitched. He also had transient blank spells. By October his notes contained results of 119 investigations, most of which were normal. An electroencephalogram had shown excess fast activity: the parents denied the possibility of drug ingestion. Anticonvulsants were ineffective. Eventually prednisolone was started empirically with dramatic improvement. The child was briefly discharged but returned acutely confused. Myoclonic jerks were associated with a generalised paroxysmal abnormality on the electroencephalogram. Urine taken on admission contained a phenothiazine metabolite, and repeated specimens confirmed high concentrations of the substance.

The mother—This 29-year-old woman had spent every day but one with her son on the ward and seemed to us to be a very good mother. Her hospital notes were therefore startling. She had been admitted to Frenchay Hospital in 1975 for investigation of a right hemiparesis. The history obtained there, partly from her and partly from other hospitals, left no doubt that she suffered from the Munchausen syndrome. A psychiatrist had considered her "a gross hysterical psychopath with self-destructive tendencies."

Subsequent developments—We obtained place of safety orders, and the mother was forbidden to visit. The son's symptoms disappeared, and his urine became free of the substance that was later identified as a promethazine metabolite. He was subsequently completely well. The "diabetic" daughter's glucose tolerance test was repeated and was normal. She had no further signs or symptoms of diabetes. An insulin bottle that the mother had been using was discovered at home: although labelled Monotard it contained sterile water. Glucose and acetone were also found at home. Four days after taking the place of safety orders the mother claimed to have taken paraquat and was admitted. One week later she was transferred to a local psychiatric hospital.

Comment

This family is similar to those described by Meadows¹ as having Munchausen syndrome by proxy. We named this the Polle syndrome²—that is, a child of a patient with the Munchausen syndrome who is at risk. A boy that presented in a manner similar to that in our case has been reported.³ When such a bizarre illness is being investigated examining the urine for drugs and inquiring fully into the medical and social histories of both parents should be priorities. Objective information should be sought from other medical practitioners.

This syndrome is one variation of child abuse. Children of parents with the Munchausen syndrome are at risk and should be included as such in child-abuse registers.

We are grateful to Mr C N Chapman of the department of clinical chemistry, Southmead Hospital, for the toxicological studies on the urine. Requests for reprints should be addressed to Dr D Burman.

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Prophylactic appendicectomy during caesarean section in a developing community

Appendicitis constitutes a particularly serious problem in developing countries because of the inherent lack of facilities. Nevertheless, incidental appendicectomy during caesarean section is controversial,¹ though the procedure is safe.²⁻³ We have tested its effect in a developing community in Nigeria.

Patients, methods, and results

From 1976 patients undergoing elective and emergency caesarean section under the care of one of us (WOC) were included in the series unless contra-indicated by technical problems or clinical condition. After caesarean section and uterine closure the appendix was carefully removed and the stump invaginated. All patients in our practice routinely receive prophylactic antibiotics postoperatively. We analyse here the first 100 cases, using as controls the antecedent 100 cases of elective caesarean section in which appendicectomy was not performed. Results were compared with the χ^2 test and two-way contingency tables with Yates's correction for continuity.

Details of the two groups and results of study

	Caesarean section only (100 cases)	Caesarean section and appendicectomy (100 cases)
Mean age (years)	27	29
Mean parity	2.1	2.4
Mean duration of hospital stay (days)	10.8	10.4
Incidence of febrile morbidity (%)	7	10 (NS)
Incidence of wound infection (%)	5	4 (NS)
Incidence of healing by secondary intention (%)	9	6 (NS)
No of emergency cases	25	25
No with adherent appendix	22	22

NS = Not significant ($P > 0.05$).

The table summarises the results. Mean age, parity, and the duration of hospital stay postoperatively were similar in the two groups. Of the study group, 75 were elective and 25 emergency cases. The morbidity rate in the 75 elective cases was 8%. Of the 10 cases of febrile morbidity in the study group, four were due to urinary tract infections and one to a large injection abscess. The corrected febrile morbidity rate was therefore 5%. There was no significant increase in the incidence of infected wounds or healing by secondary intention in the study group. Of the 100 appendices, 22 showed periappendicular adhesions. We encountered no case of paralytic ileus, postoperative haemorrhage, or faecal fistula, and there were no maternal deaths.

Comment

In developing countries with a predominantly rural population, poor medical facilities, and inadequate communications and transportation and where drug abuse and self-medication are common early cases of acute appendicitis, especially in pregnancy, may not compel serious attention until too late. We therefore believe that prophylactic appendicectomy should be considered as the best treatment available. Knowing that the appendix had been removed also helps in the differential diagnosis of any subsequent abdominal pain, particularly in pregnancy.

Our corrected febrile morbidity rate of 5% contrasts with the 15% reported by Larsson⁴ but agrees with the rate (5.7%) reported by Boyd and Hofmeister.⁵ We have performed repeat caesarean sections on nine of the patients, and none showed adhesions.

Our results show that appendicectomy during caesarean section does not prolong hospital stay, increase morbidity, or delay wound healing. We believe that it is safe and worth while in selected cases provided that no undue difficulty is encountered in locating the appendix and the procedure is not contraindicated by the patient's condition. We also believe that whenever possible this opportunity for prophylaxis should be taken.

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