Details of patients with pulmonary hypertension in systemic lupus erythematosus

Case No	Age (years)	Sex	Raynaud's phenomenon	Lupus anticoagulant	Vasculitis	Pulmonary artery pressure (mm Hg)
1	47	F	+	+	+	60/25
2	41	F	—	+	—	135/25
3	31	M	—	+	+	44/20
4	19	M	+	+	!	55/25
5	25	F	+	—	+	70/40
6	21	F	—	+	—	80/40

had Raynaud's phenomenon (though this was mild in all three), raising the possibility of vasospasm as an aetiological factor.

Another possible cause of pulmonary hypertension in our patients was vasculitis. Acute inflammation of small pulmonary arteries and arterioles has been found at necropsy in patients with systemic lupus erythematosus. In our series vasculitic lesions were noted in cases 1, 3, and 5 and one patient (case 4) developed a vocal cord palsy that may have been vasculitic in origin. Our data do not, however, suggest a major pathogenetic role for vasculitis.

Platelet dysfunction has recently been suggested as another possible aetiological factor in pulmonary hypertension in systemic lupus erythematosus. This was not, however, explored in our patients.

Thromboembolic disease is a well recognised cause of pulmonary hypertension, but recurrent small thromboemboli or in situ thrombosis may be easily overlooked clinically. A hypercoagulable state is occasionally seen in systemic lupus erythematosus and has been associated with the presence of a lupus anticoagulant, which has been found in up to 23% of patients with the disease.³ This antibody, which may be detected in either the IgG or IgM fraction of the serum, paradoxically prolongs kaolin partial thromboplastin time in vitro. It has also been associated with an increased risk of spontaneous abortion, thrombocytopenia, cerebral lupus, and a biological false positive result on testing for syphilis.⁴ Lupus anticoagulant was detected in five of our six patients (table), two of whom had a history of venous thrombosis. The remaining patient was immunosuppressed, and this might have accounted for the negative test result. It is interesting to speculate on the possible pathogenetic role of this anticoagulant in view of its association with thrombosis, and to suggest that its presence may perhaps be related to the development of intrapulmonary microthrombosis with consequent pulmonary hypertension. Twenty years ago Sleeper *et al*⁵ noted that, of their series of 10 patients with primary pulmonary hypertension, three had false positive serological reactions to tests for syphilis, and this perhaps may have indicated the presence of lupus anticoagulant. Studies of this association are now in progress.

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Pregnancy complicated by gestational trophoblastic disease in a renal transplant recipient

Fertility may return after renal transplantation. Several normal and abnormal pregnancies have been reported.¹ We can find no report of gestational trophoblastic disease arising de novo in a pregnant renal transplant recipient and therefore describe such a case.

Case report

A 22 year old woman developed hypertension and uraemia from presumed chronic pyelonephritis in 1979. There was no evidence of autoimmune disease. She was maintained with haemodialysis until May 1981, when she received a cadaveric renal transplant. Immunosuppressive treatment was given as prednisolone and azathioprine. Four rejection episodes were each treated with high dose pulses of methylprednisolone, and after the third episode continuous low dose cyclophosphamide (30 mg daily) was added for three months. Six months after transplantation her serum creatinine concentration was 110 μ mol/l (1.2 mg/100 ml).

Eleven months after transplantation, and after two months of amenorrhoea, she aborted spontaneously a hydatidiform mole. Despite uterine curettage on three subsequent occasions, serum chorionic gonadotrophin concentrations remained raised (up to 100 000 IU/l). There was no evidence of extra-uterine trophoblastic disease. She was referred for cytotoxic chemotherapy. During the first course of low dose methotrexate she developed acute abdominal pain, paralytic ileus, and became shocked. Emergency laparotomy showed rupture of the uterus, and a total abdominal hysterectomy was performed. Serum chorionic gonadotrophin values rapidly returned to normal postoperatively and remained so.

Gross examination of the specimen showed a fundal mass with an overlying tear. Histological study showed villi with pronounced trophoblastic proliferation. There was invasion of the uterine muscle and extensive permeation of vessels (figure) by atypical trophoblast. There were features of an invasive mole with possible incipient evolution into choriocarcinoma.

Uterine vein invaded by atypical trophoblast cells. Haematoxylin and eosin $\times 215$ (original magnification).

Comment

Patients with renal transplants have an increased incidence of malignant disease.² A proposed reactivation of latent choriocarcinoma has been described after renal transplantation,³ as has transmission of choriocarcinoma with the cadaver kidney,⁴ but no gestational trophoblastic disease arising de novo in a pregnant transplant recipient has been noted.

Gestational trophoblastic disease has a range of malignant potential from hydatidiform mole and invasive mole to choriocarcinoma. The clinical course is determined by factors such as the inherent malignant potential of the trophoblastic tumour and the immunological host response.⁵

In 80% of cases of classic hydatidiform mole human chorionic gonadotrophin concentrations become normal within 60 days of removal of the tumour, reflecting effective host immunological rejection mechanisms.⁶ The trophoblastic disease in our patient increased in malignant potential from the initial hydatidiform mole. It may be postulated that transformation occurred because of immunosuppression of the host, induced to prevent rejection of the transplanted kidney.

If this is so we may expect an increase in incidence of this malignancy in the future in women with renal transplants who become pregnant.

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Intravenous indomethacin or oxycodone in prevention of post-operative pain

It is an indictment of modern medicine that prevention of post-operative pain has been neglected.¹ Pain seems to be generally accepted as an essential part of the postoperative phase, and patients may suffer intolerable pain despite the plethora of effective analgesics available. Opiates are still the most popular potent analgesics, but they are usually not administered frequently enough or are not administered until the patient complains. Increased interest has recently been shown in continuous intravenous or on demand administration of opiates.²⁻⁴ We compared the efficacy of continuously administered intravenous indomethacin and intravenous oxycodone in preventing postoperative pain.

Patients, methods, and results

Altogether 168 patients (124 women, 44 men) received a single dose of 0.5% bupivacaine as an epidural anaesthetic before operation for varicose veins or orthopaedic disorders. Immediately after the operation 148 patients

were given 25 mg indomethacin (Confortid IV, A/S Dumex, Denmark) and 20 were given 5 mg oxycodone (Oxanest, Leiras, Finland) intravenously over 10 minutes. Thereafter indomethacin (5 mg/h) and oxycodone (2 mg/h) were given as continuous injections by means of an automatic syringe pump (Hostec R-50, Finland) throughout the night after the operation. Supplementary doses of 10 mg indomethacin or 2 mg oxycodone were administered intravenously to patients who complained of pain. A five degree scale of pain (none, mild, moderate, severe, or intolerable) on a time schedule was used to record pain and its duration. Possible side effects were recorded. Patients were questioned about their pain on the morning after the operation.

The table shows the incidence and relative duration of pain with each drug. The mean dose of indomethacin was 123 mg and of oxycodone 38.1 mg. Forty one (27.7%) of the patients given indomethacin and eight (40%) given oxycodone received supplementary doses of their respective drugs. The incidence of no pain was significantly higher ($p < 0.01$) and the incidence of severe pain significantly lower in patients given indomethacin ($p < 0.01$).

Side effects comprised mild nausea (17 patients (11.5%) given indomethacin *v* four (20%) given oxycodone), vomiting (three (2%) *v* three (15%)), and mild dizziness (seven (4.7%) *v* seven (35%)). Patient acceptance of the treatment was high: 143 patients (97%) given indomethacin and 19 (95%) given oxycodone found it acceptable.

Comment

The lower incidence of postoperative pain and the longer periods without pain ($p < 0.01$ and $p < 0.05$, respectively) in patients given indomethacin show that indomethacin prevented postoperative pain more effectively than oxycodone. The mean dose of indomethacin was only 123 mg whereas that of oxycodone was 38.1 mg, which is almost the maximum daily dose.

Because of its mechanism of action and other properties it seems logical to administer indomethacin prophylactically and then to maintain a preventive concentration by continuous intravenous injection. An initial intravenous dose of 25 mg and a maintenance dose of 5 mg/h are low enough to permit additional doses when necessary. This regimen resulted in a peak serum concentration of about 2 mg/l and a steady state concentration of about 0.7 mg/l. Indomethacin has the added advantage of being non-addictive.

The type of surgery that these patients had undergone was theoretically suitable for comparing analgesia obtained with an anti-inflammatory agent and with oxycodone. In more severe and deeper pain intravenous indomethacin may be administered together with intravenous opiates because of their advantageous synergism.⁵

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Incidence and duration of post-operative pain in patients given intravenous indomethacin or oxycodone

Degree of pain*	No (%) of patients given:		P†	Duration of pain as % of total duration of treatment		P†
	Indomethacin	Oxycodone		Indomethacin	Oxycodone	
None	103 (69.6)	8 (40)	<0.01	97.1	90.0	<0.05
Mild	18 (12.2)	6 (30)	<0.05	1.6	5.0	NS
Moderate	22 (14.9)	3 (15)	NS	1.1	2.5	NS
Severe	4 (2.7)	3 (15)	<0.01	0.2	2.5	NS
Intolerable	1 (0.6)		NS	0.04		NS
Total	148 (100)	20 (100)		100	100	

* Incidence of pain was registered according to hardest pain.

† χ^2 test.