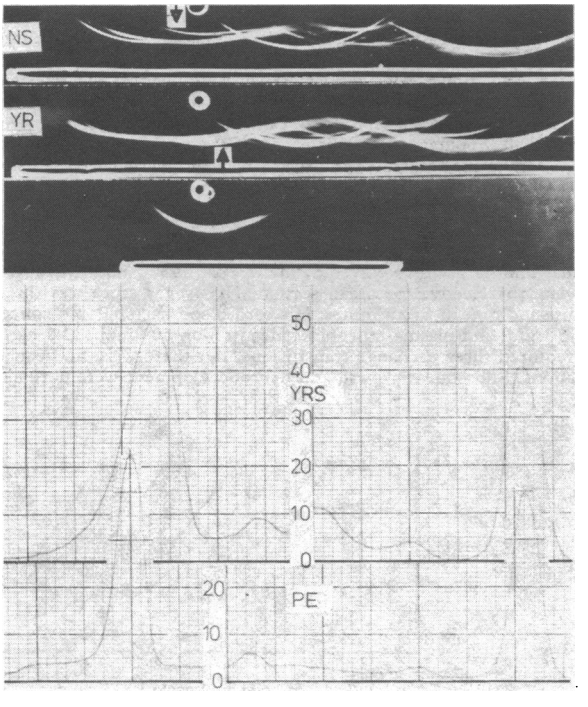
asymptomatic until eight months before her present admission, when she began to experience weakness, weight loss, and a fever of 37·5-38·C and her liver, spleen, and several cervical lymph nodes became palpable. Serological examination showed lupus erythematosus cells, antinuclear antibodies in a titre of 1/1280, and hypocomplementaemia of C3 1 g/l (normal range 0·9-2·0 g/l) and C4 0-200 mg/l (normal range 300-600 mg/l). A biopsy specimen showed a regularly shaped node with sarcoid-like granulomas. Results of other laboratory tests were unchanged except for the appearance of monoclonal gammopathy of IgG with κ chains. She underwent explorative laparotomy and splenectomy. The histopathological picture of the spleen was compatible with a diagnosis of polymorphic immunocytoma. Chemotherapy was started, and 12 months after operation she was in full clinical remission and serological tests showed antinuclear antibodies in a titre of 1/128 and lupus erythematosus cells.

Case 2—A 70 year old woman was admitted with dyspnoea, fever of 37·5°C of six weeks' duration, and recent weight loss of 15 kg. Nine years previously a routine x ray examination of her chest had shown a round lesion of her right lung. Serological tests for lupus erythematosus cells and antinuclear antibody had yielded negative results. These pathological findings were not investigated, and she had remained asymptomatic. Physical examination on admission showed pallor, dyspnoea, and dullness with loss of breathing sounds over the lower two thirds of the right lung. A chest radiograph showed that the right middle lobe was replaced by a large mass, and a moderate amount of pleural effusion was also present. Laboratory examination showed erythrocyte sedimentation rate 145 mm in first hour (Westergren), haemoglobin concentration 10 g/dl, white cell count $6·9 \times 10^9$/l, platelet count 150×10^9/l, total protein concentration 96 g/l, albumin 26 g/l, globulin 70 g/l. Electrophoresis of proteins showed a monoclonal gammopathy. Immunoglobulin concentrations were IgG 7·5 g/l (normal range 6-16 g/l), IgA 0·6 g/l (normal range 0·98-4·0 g/l), and IgM 410 g/l (normal range 2·7-2·08 g/l). The IgM was characterised as being monoclonal with κ light chains (figure). On ultracentrifugation the monoclonal IgM precipitated at 14 S instead of the usual 19 S. Serological examinations showed lupus erythematosus cells and antinuclear antibodies in a titre of 1/1280. Anti DNA antibodies were not found. At thoracotomy a solid tumour of the right middle lobe was resected and defined as immunocytoma. The postoperative course was complicated by sepsis, and she died two weeks after surgery.



Results of serum protein immunoelectrophoresis in case 2 (YR) showing unusual localisation of IgM fraction (arrow) in comparison with that in normal serum (NS) (top); and electrophoretic pattern of serum (YRS) and pleural exudate (PE) in case 2 showing a similar monoclonal fraction in both fluids (bottom).

Comment

Immunocytoma usually affects the lymph nodes. This was the case in 240 (81%) of a series of 296 patients.[2] In 130 (44%) of the patients a serum monoclonal component was detected, which in most cases was of the IgM type; in the others it was found intracellularly. The paraprotein is usually of normal structure, but monoclonal monomers of IgM (7 S on ultracentrifugation) have occasionally been described in patients with macroglobulinaemia, systemic lupus erythematosus, cirrhosis of liver, and chronic infections.[3] A light IgM was found in the serum of several patients with lymphoma, but the exact characteristics of this globulin were not defined.[4] The IgM fraction in our second patient was identified as a partially polymerised molecule that, instead of having the normal pentameric configuration, was formed of dimers and trimers alone. This type of IgM has not been described previously.

In our two patients serological findings suggested that systemic lupus erythematosus had preceded the diagnosis of immunocytoma by years. To our knowledge these are the first reported cases of this association.

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Does ethamsylate increase the incidence of venous thrombosis?

Ethamsylate, a drug which increases capillary strength and reduces small vessel haemorrhage, has been shown to decrease blood loss in patients undergoing transurethral resection of the prostate.[1] It is also used to control menorrhagia. A study using the drug in vaginal surgery reported a significant increase in the incidence of postoperative deep vein thrombosis.[2] That study was subsequently criticised[3] on the basis that more of the patients in the ethamsylate treated group than in the placebo group were obese or had received vasoconstrictive agents and several different surgeons had performed the operations. In addition, it was pointed out that "the incidence of 26% positive which was noted in the ethamsylate group corresponds to a figure of 29% positive which has been reported for a series of patients undergoing major gynaecological surgery"; and the most surprising fact was the total absence of deep vein thrombosis in the placebo group.

The following study was therefore undertaken to reassess any effect that ethamsylate might have on the incidence of postoperative deep vein thrombosis after vaginal surgery and on the amount of surgical blood loss and postoperative morbidity.

Patients, methods, and results

Fifty one patients undergoing vaginal hysterectomy for benign conditions were studied. Patients with a history of thrombosis or bleeding diathesis were excluded. None of the patients included in the study were receiving or had recently been treated with an oestrogen/progesterone preparation. The mean age of the 24 patients in the ethamsylate group was 56·5 years and of the 27 patients in the placebo group 57·8 years. Eight patients in the ethamsylate group and 10 in the placebo group were premenopausal. In addition to a vaginal hysterectomy, 20 patients in the ethamsylate group and 24 in the placebo group had a vaginal repair. The mean weight of patients in the ethamsylate group was 62·0 kg and of those in the placebo group 66·5 kg. Two patients in each group smoked cigarettes. Four patients in the ethamsylate group and five in the placebo group had varicose veins. There was thus no significant difference between the groups for any of these factors (Student's t test and χ^2 test, as appropriate).

One gram ethamsylate or placebo was injected intravenously at the time of induction of anaesthesia and 500 mg intramuscularly every six hours for 48 hours postoperatively. Prerandomised coded ampoules were used in a double blind manner and the code was not broken until the study was completed. None of the patients received prophylactic antibiotics or any prophylactic measures against venous thrombosis. All the operations were carried out by me, and blood loss was measured by laboratory estimation of the haemoglobin content of swabs used at operation.

None of the patients received epidural anaesthesia or vasoconstrictive drugs, nor did any patient receive dextran for fluid replacement. All the patients were accommodated on the same postoperative ward and fully mobilised by the third postoperative day. Deep vein thrombosis was diagnosed using ^{125}I labelled fibrinogen, as described by Negus *et al.*[4] Measurements of radioactivity were taken at 10 cm intervals along the medial surface of the thigh and calf of each leg on postoperative days 1, 3, and 6. A difference of 15% or more between adjacent sites, or at identical sites between limbs, was regarded as a positive result.

Fourteen patients showed increases greater than 15% at one of the measured sites during the postoperative period. Five of these (21%) occurred in the ethamsylate group and nine (33%) in the placebo group. This difference was not statistically significant ($p > 0.8$; Fisher's exact test). None of the patients showed clinical signs of thrombosis. The table lists the postoperative morbidity of the patients.

Postoperative morbidity

Morbidity	Ethamsylate Group (n = 24)	Placebo Group (n = 27)
Mean (SD) surgical blood loss in ml	162·8 (99·3)	168·2 (93·8)
Mean (SD) No of postoperative days with maximum temperature > 37·2°C	2·42 (1·56)	2·44 (1·60)
Vaginal haematoma (day 5 clinical assessment)	0	0
Deep vein thrombosis (^{125}I-fibrinogen method)	5	9

Since the data for blood loss showed some departure from normal they were log transformed before comparison using Student's t test ($t = 0.36$; $df = 49$; $p > 0.05$). There was no significant difference between the two groups in terms of surgical blood loss or postoperative fever (table), and no case of vaginal haematoma occurred in either group.

Comment

Attempts at explaining the haemostatic mechanism of ethamsylate are as yet hypothetical. It seems likely that ethamsylate encourages the formation of long chain mucopolysaccharides in the capillary wall, thereby increasing capillary strength and reducing the bleeding time. There is no effect on cell counts or on fibrinogen or prothrombin concentrations and therefore no theoretical reason for any increased tendency to thrombosis with administration of ethamsylate.

This study showed no evidence of any increase in the incidence of postoperative deep vein thrombosis with ethamsylate. This conclusion corroborates the results of a clinical trial using ethamsylate in post-partum patients,[3] which showed that the drug had no thrombogenic effects. The present study failed to show a reduction in blood loss or postoperative morbidity in ethamsylate treated patients undergoing major vaginal surgery, probably because the large vessels concerned are not affected by a drug acting at capillary level.

I am very grateful to Mrs M Dove, of St Mary's Hospital, Portsmouth, for the blood loss estimations and to Mr C A R Lamont, St Mary's Hospital, Portsmouth, for allowing me to study his patients.

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In utero resuscitation after cardiac arrest in a fetus

Although birth asphyxia is an important aetiological factor leading to neonatal death and perinatal brain haemorrhage, several studies on the resuscitation of babies with perinatal cardiac arrest have shown that the outcome is generally good when the heart beat returns within five minutes after birth.[1] We report on a hydropic fetus with severe rhesus isoimmunisation that was successfully resuscitated in utero by external cardiac massage, after cardiac arrest for three minutes during fetoscopic intravascular blood transfusion at 19 weeks' gestation.[2] Real time ultrasonography ruled out cerebral oedema and periventricular or intraventricular haemorrhage, and the baby was delivered in good condition several weeks later.

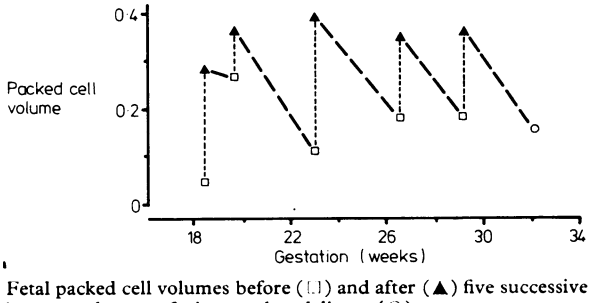
Case report

A 28 year old woman, whose blood group was A Rh negative, was in her ninth pregnancy. The first four had been uneventful and had resulted in normal deliveries at term. After the fourth delivery, however, she was found to have anti-D antibodies. In the subsequent four pregnancies the fetuses had severe rhesus isoimmunisation, which resulted in two neonatal deaths at 36 and 33 weeks' gestation followed by two intrauterine deaths at 30 and 26 weeks' gestation.

In this pregnancy the maternal antibody concentration was 17 IU/ml at 14 weeks and 213 IU/ml at 18 weeks despite thrice weekly plasmapheresis. Spectrophotometric measurements of amniotic fluid (change in optical density at 450 nm) at 17 and 18 weeks were 0·116 and 0·127 respectively ("mildly affected" zone of an extrapolated Liley's chart[3]). She was referred to this unit at 18 weeks after ultrasound examination showed a fetus with scalp oedema associated with large pericardial, pleural, and ascitic effusions.

At 18, 19, 23, 26, and 29 weeks fresh packed (packed cell volume 0·6-0·8) group O Rh negative blood was infused into an umbilical cord artery under direct fetoscopic vision. The figure shows the fetal packed cell volume before and after each transfusion. After the first transfusion the fetal oedema and pleural and pericardial effusions resolved rapidly but there was some residual ascites. During an otherwise uneventful second transfusion sudden, severe fetal bradycardia culminating in cardiac asystole within two minutes was seen on real time ultrasound scanning. She was turned into the left lateral position, and, under continuous ultrasound guidance, the fetal heart was massaged at 40 compressions a minute by digital pressure through the maternal abdomen, the fetal chest being compressed against the posterior uterine wall. Spontaneous cardiac activity resumed in three minutes.

The rest of the pregnancy and subsequent intravascular transfusions were uneventful. Serial real time ultrasound scans of the fetal brain and measurement of the anterior and posterior horns of the lateral ventricles[4] ruled out cerebral oedema and periventricular or intraventricular haemorrhage and their sequelae of hydrocephaly and porencephalic cysts. Fetal growth was normal, and the ascites resolved. At 32 weeks a 1932 g non-hydropic boy was delivered by elective caesarean section. His Apgar score was three at one minute and nine at five minutes. His cord blood haemoglobin concentration was 6·1 g/dl and plasma bilirubin concentration 60 μmol/l (3·5 mg/100 ml). He required three exchange transfusions, but there were no neonatal complications. Subsequent growth and neurodevelopment were normal.



Fetal packed cell volumes before (□) and after (▲) five successive intravascular transfusions and at delivery (○).

Comment

This case shows how the advent of fetoscopic intravascular transfusions has greatly improved the outlook for fetuses with severe rhesus isoimmunisation that develop hydrops at an early gestational age.[5] Furthermore, the successful outcome of antepartum cardiac massage in utero suggests that this technique might be incorporated in the management of intrapartum fetal death. As cardiotocography is used to monitor most women in labour fetal cardiac arrest can now be recognised immediately. External cardiac massage may therefore be performed under real time ultrasound guidance while arrangements