ovary. Radiotherapy in the form of external irradiation together with intrauterine irradiation may be advised as an insurance if continuing ovarian function is not thought necessary; but the same considerations apply as for surgery.

Summary

Of 100 patients with ovarian neoplasms treated by unilateral ovarian cystectomy or oophorectomy 63 were followed up from 7 to 14 years after operation; 50 had benign neoplasms and in 13 the tumour was malignant.

In some cases—two in this series—distinction on pathological grounds between the benign and the malignant is not always clear, and "borderline" cases should come under consideration for a proper follow-up with limited treatment.

Against a background of a further 140 patients with bilateral ovarian carcinoma, of whom 39 (28%) survived, only one patient from whom a benign cyst was removed showed evidence of any further neoplastic activity; one borderline case recurred, and 9 out of 13 with definite carcinomas survived five years or more. Two patients reassessed as borderline cases survived.

It is suggested that no further treatment, surgery, or irradiation is necessary in the majority of patients in whom carcinoma is an incidental finding in an ovarian cyst in a young woman.

We gratefully acknowledge the approval of the Medical Committee, Chelsea Hospital for Women, to use case records of their patients.

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Medical Memoranda

Maternal Complications of Rhesus Iso-immunization

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The maternal complications associated with rhesus iso-immunization are the results of different pathogenic mechanisms. The occurrence of afibrinogenaemia after the prolonged retention of a dead foetus probably follows the release of placental thromboplastin into the maternal circulation. Hydramnios can result when the mouth and fauces of the hydropic foetus are so oedematous as to interfere with the swallowing of liquor amnii. The high incidence of pre-eclamptic toxæmia is probably related to the state of "hyperplacentalosis"; and defective placental implantation, or the mechanical problem of accommodating a bulky hydropic placenta, may be the cause of antepartum haemorrhage (Scott, 1958). No mechanism has been suggested to account for the sudden onset of massive dependent oedema of the mother's legs, with no other signs of toxæmia, which sometimes occurs between the 28th and 36th week of a pregnancy complicated by hydrops foetalis.

There is a further rare but well-accepted maternal reaction to a foetus with an incompatible blood group *in utero*. It was first described nearly 50 years ago and re-emphasized by Scott in 1958. This reaction, the onset of which is acute, is manifested by a general illness, and signs of jaundice, pruritus, haemolytic incidents, and oliguria or anuria. Death may supervene. The clinical picture is very similar to that seen after a transfusion of incompatible blood, and it seems likely that in cases of rhesus iso-immunization the syndrome results from foetal red cells, or the products of their haemolysis, passing into the maternal circulation. The following case illustrates the syndrome.

CASE REPORT

A woman, aged 25, conceived for the first time in 1955. During that pregnancy her blood group was found to be O rhesus-negative. No rhesus antibodies were detected in her serum. The pregnancy was uneventful and at term she delivered a healthy, unaffected male child weighing 8 lb. (3.63 kg.).

In 1957 the patient delivered normally and at home a second baby, a daughter weighing 6 lb. 12 oz. (3.06 kg.). During this pregnancy her blood was not examined for rhesus antibodies.

In 1960 the patient attended the Liverpool Maternity Hospital at the eighth week of her third pregnancy. Examination of her blood at that time revealed the presence of rhesus antibodies when the test was performed on both saline and albumin suspensions. At 37 weeks' gestation a positive antibody test was obtained on serum diluted 1 in 4 volumes. The patient remained well, did not develop oedema, proteinuria, or hypertension, and delivered a female child normally at term. The baby weighed 6 lb. 13 oz. (3.09 kg.), and immediately after birth its cord blood gave a positive Coombs test, and showed a haemoglobin concentration of only 83% (12.3 g./100 ml.) and a serum bilirubin level of 7 mg./100 ml. An immediate exchange transfusion was carried out and the child subsequently made good progress.

Investigation in 1960 of the patient's husband showed his blood group to be O rhesus-positive, the probable genotype being CDe/cDE.

In November 1962 the patient, then aged 32 years and pregnant for the fourth time, was once more booked for confinement at hospital. Examination of her blood at the tenth week of pregnancy again revealed the presence of rhesus antibodies when the serum was tested against cells suspended in either saline or albumin solutions.

Until the 31st week of gestation the pregnancy continued uneventfully and the patient was physically well in every respect.

At the 32nd week, however, it was noted that her feet and legs had become very swollen, with gross pitting oedema. But the blood-pressure and urine remained normal. The haemoglobin level was 73% (10.8 g./100 ml.) and the rhesus antibody test positive at a titre of 1 in 10 volumes. On abdominal examination at that time the uterus was found to be tense and its size was that of a 36 weeks pregnancy. Foetal heart sounds were not audible and no foetal movements were felt. This sudden increase in uterine size was attributed to hydramnios, and subsequently this diagnosis was confirmed by a torrential gush of liquor following rupture of the membranes during labour.

Radiological examination at the 32nd week of pregnancy showed a foetus of corresponding maturity whose attitude *in utero* was typical of hydrops foetalis.

At the 33rd week the patient was admitted to hospital for induction of labour. She was given a soap enema, and, as the foetus was already dead, four doses of quinine sulphate, 5 gr. (325 mg.) orally, at half-hourly intervals. This produced no uterine response, so an intravenous infusion of 10% dextrose, containing two units of oxytocin (Syntocinon) in one litre, was started. The patient was in

labour eight hours later, and was given 100 mg. pethidine intramuscularly when the cervix was half dilated. Within four hours of this injection a stillborn hydropic child weighing 5 lb. (2.27 kg.) was born spontaneously. The placenta was pale and oedematous and weighed 1 lb. 1 oz. (482 g.). Post-mortem examination showed the changes typical of advanced haemolytic disease in both the foetus and its placenta.

Approximately two hours after delivery the patient began to feel ill, and complained of a dull pain in her back. Within the next hour it was noted that she had become extremely pale and that the oedema, previously affecting only her legs, was evident in her hands also. The pulse rate was then 106 per minute and the temperature 100.4° F. (38° C.). The blood-pressure was 140/90 mm. Hg, and remained at this level throughout her illness. Examination of the respiratory and central nervous systems and of the abdomen gave negative findings.

Morphine 1/6 gr. (10 mg.) and chlorpromazine 25 mg. were given intramuscularly and the patient's general condition gradually improved. Her blood-pressure was maintained at 140/90 mm. Hg, but nine hours after the onset of her illness the patient had become slightly jaundiced. The oedema had increased and had spread to affect the face, lips, hands, legs, and feet. Both renal angles were tender on palpation, but no other abnormality was detected on abdominal and vaginal examination. Debris taken from the cervical os with a sterile swab was subsequently examined bacteriologically and no pathogenic organisms were discovered. Catheterization produced only 6 oz. (170 ml.) of dark-yellow urine; this contained protein and pus cells, and on culture yielded a small growth of *Escherichia coli*. Samples of maternal blood were taken for microscopic, biochemical, and bacteriological examination. The blood urea reading was 35 mg./100 ml. and the haemoglobin level was 77% (11.4 g./100 ml.). Blood cultures subsequently proved to be sterile. Electrocardiography and radiographs of the chest performed later the same day showed normal findings.

On the day after delivery the patient was still slightly jaundiced. Her serum bilirubin was 1.3 mg./100 ml. and the haematocrit was 29%. Within 48 hours the jaundice and oedema disappeared and by the third day the patient's temperature was normal. Her blood-pressure was 125/85 mm. Hg. Severe oliguria persisted for seven days, only 5 oz. to 7 oz. (142 ml. to 198 ml.) of urine being secreted in each 24 hours. During this time the patient's blood urea rose to 207 mg./100 ml., and the serum potassium to 7 mEq/l. Meanwhile the haemoglobin fell to 55% (8.14 g./100 ml.).

During the oliguric phase the patient's daily intake of fluid was restricted to 500 ml. plus a volume equivalent to the urine passed during the previous 24 hours. She was allowed a diet rich in carbohydrate and given penicillin intramuscularly prophylactically, as well as norethandrolone orally. Lactation was suppressed. She eventually required treatment with tetracycline to eradicate the urinary infection.

On the seventh day of the puerperium the patient started a diuresis and thereafter her condition improved rapidly. She was discharged from hospital one month after delivery, when the results of all her blood tests were within normal limits; but at that time repeated water-concentration tests showed the maximum specific gravity of the urine to be 1002, despite 12 hours of restricted fluids.

COMMENT

The clinical picture presented by this patient was similar to that following an incompatible blood transfusion. It was mentioned earlier that a syndrome of this type is sometimes the result of the entry of incompatible foetal red cells into the maternal circulation, and an attempt to demonstrate such a thing happening in this patient was made by examining specimens of maternal blood for foetal red cells 12 and 18 hours after delivery. No foetal red cells were demonstrated in either specimen, but this negative finding is not necessarily significant. After an interval of 12 to 18 hours it is possible that any foetal red cells within the maternal blood stream had

already been destroyed. Nevertheless, as the foetal circulation in this case had ceased at least seven days before the maternal reaction occurred, the placental transfer of foetal red corpuscles seems a less likely causal mechanism than the transfer of the products of their degeneration.

Because of the apparent rarity of this type of maternal reaction to rhesus immunization, a study was made of the records of patients delivered in the Liverpool Maternity Hospital between January 1959 and June 1963, previous years having been covered by Scott (1958). During the four and a half years under review 173 women with demonstrable rhesus antibodies in their blood were delivered. Thirty-three had stillborn babies showing evidence of hydrops foetalis, and another 18 delivered babies so severely affected by haemolytic disease that they survived only a few hours.

Eight of the mothers (25%) carrying a hydropic foetus developed pre-eclampsia, as manifested by moderate oedema and hypertension, at approximately the 32nd week of pregnancy, but another seven mothers suddenly developed gross oedema of the feet at this time without any other signs of toxæmia. One patient developed slight hydramnios at the same time.

Among the 17 women who had severely affected, though not obviously hydropic, babies, none developed pre-eclampsia, but there were three mothers who, in the absence of hydramnios, developed this syndrome characterized by the sudden onset of gross dependent oedema at approximately the 32nd week of pregnancy. The clinical significance of such oedema in cases of rhesus iso-immunization was emphasized by Cohen (1960), who concluded that its appearance usually indicated that the foetus will succumb. If the oedema is an early sign of the toxæmia syndrome, characteristic of hydropic changes in the placenta (Scott, 1958), this clinical observation would be readily understandable.

Three patients, all carrying hydropic fetuses, had unusual systemic upsets during pregnancy. One developed jaundice two days before the delivery of a stillborn affected foetus, but the jaundice disappeared spontaneously during the first two days of the puerperium. Sudden and generalized pruritus was recorded in the other two cases. In both the symptoms first appeared during the week preceding foetal death *in utero* and persisted until soon after delivery. In all these cases it is not unreasonable to suppose that the maternal conditions were the results of an accumulation in the blood stream of bile acids and bilirubin which traversed the placenta after a haemolytic incident had occurred in the child, or following the destruction of foetal red cells within the maternal circulation. Yet if a massive foetal bleed into the uterine sinuses did occur in any of the patients reviewed it was never followed by the serious systemic reaction and oliguria which were features of the case prompting this report. Such a reaction, as judged by our experience, must be an extremely rare complication of rhesus iso-immunization. Nevertheless, it is a serious and potentially fatal one and its possible occurrence is one more reason for regarding a pregnancy complicated by hydrops foetalis as hazardous to the mother as well as to the child.

I would like to thank Professor T. N. A. Jeffcoate, under whose care this patient was treated, for his encouragement and advice, and for permission to report this case.

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