Pregnancy, subarachnoid haemorrhage, and the intravascular coagulation syndrome

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SYNOPSIS Two patients are described who developed subarachnoid haemorrhage during pregnancy and the puerperium. In both patients there was clinical, haematological, histological, and renal angiographic evidence of the intravascular coagulation syndrome. No source of intracranial bleeding was demonstrated by bilateral carotid angiography in either patient. We suggest that the subarachnoid haemorrhage was a result of the intravascular coagulation syndrome in both patients.

In the past 10 years, 145 female patients with subarachnoid haemorrhage have been investigated and treated in the Department of Neurology at the North Staffordshire Hospital Centre. Sixty-eight of these were of child-bearing age. Five were pregnant at the time of the haemorrhage. Investigations in the group with subarachnoid haemorrhage in pregnancy revealed cerebral arteriovenous abnormalities in two of the five and an internal carotid aneurysm in a third. The purpose of this communication is to describe the events in the remaining two patients in whom the evidence indicates that the subarachnoid haemorrhage was caused by the intravascular coagulation syndrome.

CASE 1

J.D., aged 36 years, had an uncomplicated pregnancy in 1955. She was admitted to the maternity unit of the North Staffordshire Medical Centre on 12 December 1970, in the 26th week of pregnancy with a two-week history of headache, ankle oedema, and a trace of proteinuria. Her blood pressure had been normal throughout the early pregnancy.

Forty-eight hours before admission she developed increasingly severe occipitofrontal headache, confusion, restlessness, and violent behaviour. Examination on admission to the maternity unit revealed a confused and irrational patient with severe headache and vomiting. Her blood pressure was 240/140 mmHg and she had generalized oedema and gross proteinuria. A diagnosis of eclampsia was made and she was treated with morphine, chlorpromazine, and

frusemide. Shortly after admission she was observed to have a classical fit with generalized convulsion, urinary incontinence, and loss of consciousness. Anticonvulsant and hypotensive treatment was instituted with diazepam and methyl dopa respectively. Labour was induced and a non-viable fetus was delivered. She continued in an irritable, confused, and incoherent state with a blood pressure of 180/110 mmHg. Forty-eight hours after admission she was transferred to the neurological department. At that time she showed the clinical signs of bilateral papilloedema and neck rigidity. Cranial nerve examination was normal and there were no focal neurological signs in the limbs. A clinical diagnosis of subarachnoid haemorrhage was made and confirmed by lumbar puncture, the cerebrospinal fluid

TABLE 1
HAEMATOLOGICAL DATA ON BOTH PATIENTS INDICATING
MAXIMUM ABNORMAL VALUES AND VALUES ON RECOVERY

	Case 1 (J.D.)		Case 2 (D.T.)	
	Maximum abnormal value	Value after recovery	Maximum abnormal value	Value after recovery
Haemoglobin (g/100 ml)	11.4	14.6	9.9	15.3
White cell count (/cu. mm)	13,600	6,900	16,200	3,000
Platelet count (/cu. mm)	100,000	504,000	37,000	460,000
Reticulocytes (%)	4	0	5.5	0
Abnormal cells*	+++	0	+++	0

* Burr cells, schistocytes, helmet cells, crenated cells.

TABLE 2
BIOCHEMICAL DATA ON BOTH PATIENTS INDICATING
MAXIMUM ABNORMAL VALUES AND VALUES ON RECOVERY

	Case 1 (J.D.)		Case 2 (D.T.)	
	Maximum abnormal value	Value after recovery	Maximum abnormal value	Value after recovery
Fibrinogen (mg/100 ml)	1,090	350	400	350
Fibrinogen degradation products (μ g/ml)	640	0	160	0
SGOT units (/ml)	100	30	110	15
SGPT units (/ml)	45	15	140	15
SLD units (/ml)	1,320	730	1,400	500
Albumin (g/100 ml)	2.5	3.2	2.8	4.7
Urine protein (g/24 hr)	5	0	0.6	0
Blood urea (mg/100 ml)	56	21	250	24
Blood creatinine (mg/100 ml)	1.5	0.7	8.5	0.8
Creatinine clearance (ml/min)	40	97	2	109

being uniformly bloodstained with xanthochromia at an opening pressure of 290 mm of water. Haematological, biochemical, and renal investigations carried out at that time suggested the presence of intravascular coagulation (Tables 1 and 2). Bilateral carotid angiograms revealed no site of intracranial bleeding. During the next two weeks she made a gradual and complete clinical recovery and at discharge three weeks after her admission neurological examination was normal and her blood pressure was 130/90 mmHg. All treatment was discontinued before her discharge. At outpatient follow-up four months after the acute episode the blood pressure was 100/80 mmHg and renal function was entirely normal (Table 2). The haematological manifestations of the intravascular coagulation syndrome had entirely disappeared by the fifth day after delivery of the fetus.

CASE 2

D.T., aged 27 years was delivered normally of a healthy full-term male infant on 21 July 1970. This was her third pregnancy, her second pregnancy three years previously having been complicated by a postpartum haemorrhage. She had never been hypertensive and her general health was good. Two hours after delivery she became restless and complained of headache. Five minutes later she developed extensor spasms of the arms and legs and lost consciousness. She was transferred to the neurological unit. On examination she was deeply un-

conscious. General system examination was normal and the blood pressure was 140/90 mmHg. Neck rigidity was present, the pupils were pin-point and non-reacting. The fundi were normal, and the corneal reflexes were absent. In the limbs tone was flaccid, tendon reflexes were normal, and the plantar responses were extensor. A clinical diagnosis of subarachnoid haemorrhage was confirmed by lumbar puncture. The cerebrospinal fluid at an opening pressure of 250 mm of water was uniformly blood-stained with xanthochromia. Bilateral carotid angiograms revealed no source of intracranial bleeding. Details of all other investigations are given in Tables 1 and 2.

Twenty-four hour urinary output was persistently below 400 ml and there was no response to intravenous mannitol, confirming the presence of oliguric renal failure. A diagnosis of subarachnoid haemorrhage and renal failure associated with the intravascular coagulation syndrome was made on the basis of the clinical, haematological, and biochemical findings and treatment was started with heparin and peritoneal dialysis. Within five days of starting treatment the patient was responding to questions but was still drowsy and confused and showed difficulties in sustained concentration. Over the subsequent 10 days she became cooperative with insight and there were no abnormal signs on neurological examination. Clinical improvement was maintained and at discharge five weeks after admission she was alert and showed no intellectual deficit. Neurological examination was normal. Peritoneal dialysis was discontinued after six days but full recovery of renal function was not achieved until three months after the acute episode (Tables 1 and 2) at which time the blood pressure was 110/70 mmHg. The haematological features of the intravascular coagulation syndrome had entirely disappeared 14 days after commencing treatment.

CASES 1 AND 2: FURTHER INVESTIGATIONS

RADIOLOGY *Bilateral carotid angiography* Neither patient showed any evidence of aneurysm or angioma. In one patient (J.D.) spasm was present in the terminal portions of the internal carotid arteries and in the main trunks of the anterior and middle cerebral vessels. In the other patient (D.T.) the anterior cerebral vessels were narrowed and stretched, suggesting a degree of dilatation of the lateral ventricles. Radiographs of the chest were normal in both patients.

Intravenous pyelography This was performed on D.T. three weeks after the onset of the subarachnoid haemorrhage. It showed normal renal function with residual pregnancy dilatation of the upper urinary

FIG. 1. (a) Late arterial phase of selective renal angiogram (right) showing focal peripheral arterial disease characterized by beading (white arrow) and cork-screw appearance (black arrow) of peripheral interlobar arteries. (b) Nephrogram phase of the same series of renal angiograms showing a small peripheral infarct (arrow) in the lower pole with associated stasis of the contrast medium in this area.

tract on the right side. The pyelogram performed on the second patient (J.D.) two weeks after the onset of subarachnoid haemorrhage was normal.

Selective renal angiography The main renal vessels and their segmental branches were normal in both cases. Bilateral focal peripheral vascular abnormalities were present in both cases, characterized by tortuosity and narrowing of the terminal interlobar vessels giving a beaded appearance (Fig. 1a). In addition, stasis of contrast medium was noted in the lower pole of one kidney (D.T.) (Fig. 1b) and an area of probable cortical ischaemia was observed in the left kidney of the other patient (J.D.).

RENAL BIOPSY Percutaneous renal biopsies were performed at the same time as selective renal angiography. The findings for each patient are detailed below.

J.D. Serial sections showed that about one-third was medulla. The remainder was cortex containing an average of 11 assessable glomeruli. There were no abnormalities of the arterioles or of one small muscular artery included at the junction of the cortex and medulla. There was widespread minimal tubular degeneration, most marked in the convoluted tubules whose cells were about half their normal thickness. In the medulla the tubules appeared nor-

mal but many contained small cellular 'casts'. Two glomeruli showed slight pericapsular fibrosis. Adhesions between tuft and capsule were seen in the majority. One showed a small focal area of sclerosis at the site of attachment of the tuft. There were no other abnormalities. The glomerular capillary loops were all patent and there was no hypercellularity nor were any microthrombi seen. No completely sclerosed glomeruli were included in this biopsy.

D.T. Semi-serial sections at two levels showed that the biopsy consisted of one-third medulla and the remainder cortex, which contained an average of 20 glomeruli. The interstitial tissues showed focal slight increase of fibrous tissue, and one area of round cell infiltration, surrounding glomeruli that showed pericapsular fibrosis and atrophy of the tuft. Many of the remaining glomeruli appeared entirely normal, a few showed pericapsular fibrosis, and some showed some mesangial thickening with small foci of hypercellularity. No active lesions were present. There was some tubular damage, possibly associated with the more severely affected glomeruli. The remaining tubules appeared normal. About 50% of the glomeruli seen in this specimen were unaffected. No microthrombi were seen.

DISCUSSION

The majority of observers agree with Walton's (1955) conclusion that the occurrence of subarachnoid haemorrhage in normal pregnancy is a coincidence. In eclampsia, however, subarachnoid haemorrhage is a recognized complication (Donnelly and Lock, 1954). The figures for incidence vary from 1 in 2,000 (Cannell and Bottrell, 1956), to 1 in 11,000 pregnancies (O'Leary *et al.*, 1962); the variation would appear to be an expression of the observer's interests rather than social or racial factors. Subarachnoid haemorrhage may occur at any time in pregnancy and the management and treatment is that routinely practised in the non-gravid female; the morbidity and the mortality is the same in both groups (Pool, 1965). Although the cause of subarachnoid haemorrhage may be either a berry aneurysm or a congenital arteriovenous malformation, negative angiograms are not uncommon so that the cause of bleeding is frequently uncertain.

In the two patients described, haematological, biochemical, and histological evidence indicates that the intravascular coagulation syndrome was

responsible for both the subarachnoid haemorrhage and the other clinical features observed in both patients. In neither patient was a vascular anomaly demonstrated by bilateral carotid angiography and in the clinical circumstances vertebral angiography was not considered justifiable. In both patients the haematological criteria set out by Brain *et al.* (1962) were satisfied and in both an elevation in the concentration of the serum fibrin degeneration products was demonstrated.

The widespread nature of the disorder was apparent from the involvement of the lungs, brain, liver, and kidneys. Selective renal angiography showed unequivocal abnormalities of the interlobar vessels in both patients (Fig. 1a and b). Minimal abnormalities of the intrarenal vascular pattern were demonstrated on histological examination of the renal biopsies. The absence of intravascular microthrombi could be accounted for by the fact that the renal biopsies were carried out after recovery from the acute episode. The renal histological findings in both patients were similar to those noted in other patients who have been studied after recovering from the intravascular coagulation syndrome (Shinton *et al.*, 1964; McKay, 1969; Moncrieff and Glasgow, 1970) and we have observed identical renal angiographic appearance in other patients with this syndrome (Boyd, unpublished data).

Although the 'triggering' factor responsible for initiating intravascular coagulation in one patient (J.D.) seems to have been associated eclampsia, which is the commonest cause of subarachnoid haemorrhage during pregnancy (Donnelly and Lock, 1954), the precipitating cause in the second patient was by no means clear. In this patient the onset of acute renal failure in the early puerperium was similar to that reported by Robson *et al.* (1968) in four patients in whom there was histological evidence of partial or complete occlusion of interlobular arterioles and glomerular capillaries by fibrin thrombi. Unlike our patients, congestive cardiac failure associated with a 'cardiomyopathy' was a prominent feature in all four patients of Robson *et al.* (1968) and indeed it was this rather than renal failure that was responsible for the death of two patients. When their data were examined, there was evidence of thrombocytopenia and haemo-

lytic anaemia associated with many abnormal red cells in the peripheral circulation, supporting the possibility that intravascular coagulation may also have played a part in determining the clinical features.

On the basis of our two patients it is interesting to review the early pathological observations of McKay *et al.* (1953) who presented arguments in favour of intravascular fibrin deposits in arterioles and capillaries as one mechanism for the disseminated tissue necrosis and haemorrhage and the bilateral renal and pituitary necrosis observed in 21 patients who died from toxæmia of pregnancy. Reviewing their postmortem findings, there were two patients with primary subarachnoid haemorrhage, two with subarachnoid haemorrhage and intracerebral haemorrhage combined, and one patient with primary intracerebral haemorrhage alone. It is not unreasonable to suggest that the underlying mechanism for subarachnoid haemorrhage in these individuals was similar to that observed in our patients.

Our decision to treat one patient with post-partum subarachnoid haemorrhage with heparin was taken after the diagnosis of the intravascular coagulation syndrome associated with acute renal failure had been confirmed and after cerebral angiography had failed to disclose either a berry aneurysm or other intracranial vascular malformations in the carotid circulation. Until a controlled trial of this form of therapy has been carried out in a wide range of patients with the intravascular coagulation syndrome it is clear that a degree of caution is still called for before one can justify this potentially hazardous form of treatment.

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