Combined Anterior Pituitary Necrosis and Symmetrical Cortical Necrosis of the Kidneys following Accidental Haemorrhage

BY

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DETAILS of a case of necrosis of the anterior pituitary and symmetrical cortical necrosis of the kidneys and of cases of cortical necrosis are submitted because of the rarity of both these conditions and therefore of the need to report such information as becomes available.

CASE 1. 3859/43, K. J.

An unmarried girl, aged 15 years 10 months, a primigravida with an uneventful previous medical history. First day of last menstrual period, February 1943, first week. Expected date of confinement, November 1943, second week.

Although she knew herself to be pregnant she had not made preparations for her confinement or had any ante-natal supervision. She is said to have been quite well until September 16th, 1943, when she had a fall. This not very serious accident was followed, within an hour, by vaginal bleeding which continued intermittently for another hour. Bleeding then ceased but began again later in the evening, accompanied by pains in the "pit of the stomach". These pains became rhythmical in character, occurring at intervals of 5 minutes, and she now thought she "might be aborting". She therefore came to hospital in the early hours of the morning of September 17th.

When seen at 3 a.m. her condition was poor, her colour was bad with the pallor of shock or possibly blood loss and she was obviously anxious. Oedema of the legs was present to the level of the knees and the face was markedly puffy. She was well developed and well nourished.

Cardio-vascular system. Heart not enlarged, pulse poor in volume, rate 110. Blood-pressure 110/65.

Abdomen. Enlarged to the size of a 36 weeks' pregnancy, the uterus palpable as a hard, tense tumour. Foetal parts could not be identified nor was the foetal heart heard. On rectal examination the cervix could be identified one finger dilated, with the vertex presenting.

Uterine contractions were occurring at intervals of 10 minutes. There was slight continuous bleeding *per vaginam*. A provisional diagnosis of toxaemia of pregnancy with accidental haemorrhage was made.

Treatment and progress. As the accidental haemorrhage had now become revealed it was hoped that there would be spontaneous delivery as uterine contractions were occurring regularly.

At 9.30 a.m. there had been little change in her condition, but uterine contractions were beginning to decrease in intensity and frequency. The uterus had not appreciably increased in size and although still tense could not be described as "woody". Labour ceased for some hours during the afternoon, but pains returned with markedly increased severity at 5 p.m. At 6 p.m. her pulse was 136 and her blood-pressure had fallen to 98/76. The cervix was now fully dilated and the small foetal head well down in the pelvis. At 7.30 p.m. she was delivered spontaneously of a macerated female foetus weighing 4 pounds 7 ounces, and measuring 19 inches in length. The placenta and membranes were expelled at 8 p.m. There was no excessive loss during delivery, but about 10 ounces of blood and clots were expelled with the placenta, which showed numerous infarcts. Blood clot was adherent to the maternal surface of the placenta. Labour had lasted approximately 24 hours.

Subsequent progress. Following delivery her condition showed some improvement and she took

fluids well and slept during the rest of the night without drugs. During the 24 hours she passed 900 ml. of urine.

On September 18th she complained of drowsiness, and during that 24 hours passed only 90 ml. of urine, although she still took adequate fluids *by mouth*. The subsequent fluid intake and output are indicated in the accompanying chart, Fig. 1, and show the sudden and pronounced oliguria. The haemoglobin on September 20th was only 22 per cent and the blood urea 184 mgm./100 on the following day.

From the 21st, there began a rapid deterioration in her condition, the blood urea had risen to 216 mgm./100 on September 24th, and she died the following day.

Throughout her illness and in spite of the very high blood-urea estimations, her mental condition remained clear. She was drowsy but could be roused sufficiently to carry on intelligent conversation.

Treatment had consisted of the administration of adequate fluids, particularly glucose, which she took well. The oedema of the legs present at the

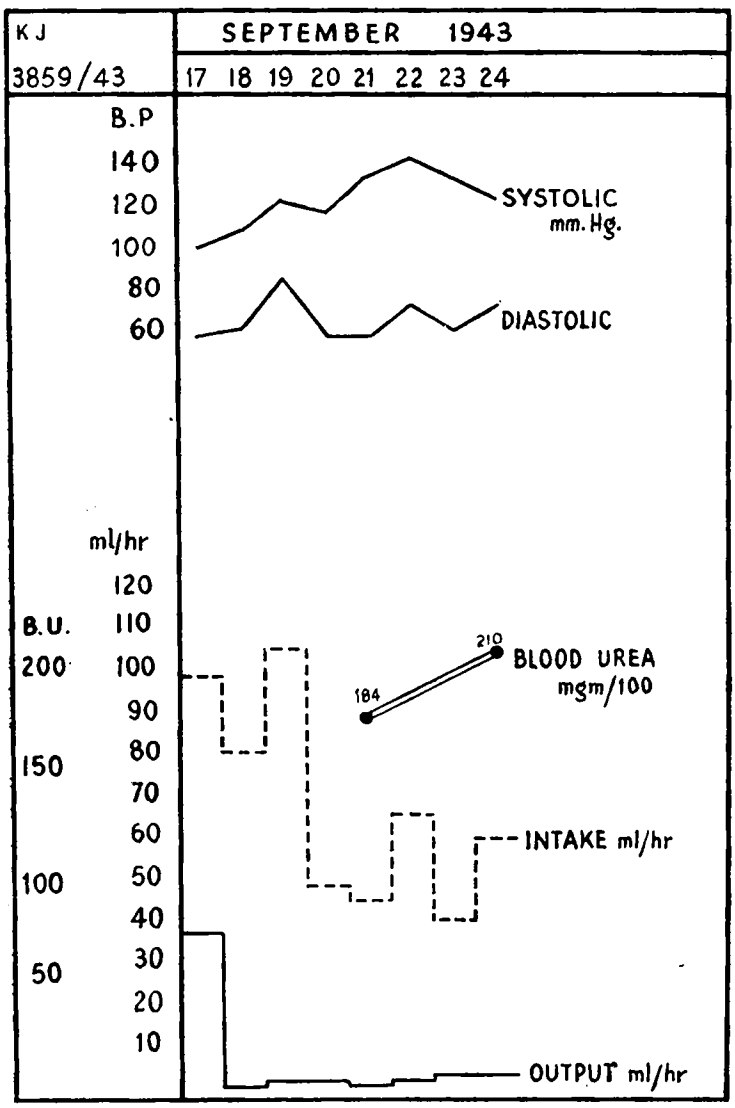

FIG. 1.

time of admission gradually disappeared, but the puffiness of the face persisted. This was the only obvious sign of fluid retention.

Postmortem examination was carried out on September 26th, and the following conditions were observed.

Kidneys. Both kidneys were enlarged and the cortex, apart from a narrow subcortical area of normal tissue, was entirely necrotic and structureless, the appearance typical of symmetrical cortical necrosis.

Liver. Not grossly abnormal.

Thyroid. Enlarged, but not abnormal.

Pituitary gland. Necrosis of anterior lobe.

Microscopical examination of sections of the kidneys showed typical and extensive cortical necrosis.

The pituitary gland showed "complete necrosis of the anterior lobe cells, with the exception of a small area anteriorly". The sections were examined by Professor Payling Wright, who commented that this form of necrosis was not uncommon in conditions of haemorrhage but not, as far as was known, previously reported in association with cortical necrosis. The extent of the necrosis is shown in Fig. 2, and is identical in type and appearance with that reported by Doniach and Walker (1946).

Discussion.

In considering this case, which was observed some 2 years before that described so completely by Doniach and Walker, the many points of similarity between the cases are at once apparent, and are shown in tabulated form in Table I.

Two similar cases are described by Hügin (1946).

The first is that of a 5-para, aged 35 years, in whose obstetric history was known evidence of toxaemia—oedema of legs in a pregnancy 11 years previously, followed by "kidney disease" in the puerperium, and hypertension (blood-pressure 160/90) in a pregnancy 2 years before that under review. In the pregnancy described, the patient is said to have been "well, and less tired than in previous pregnancies but some dyspnoea on exertion and occasional headaches and spots before the eyes, swollen ankles and itching of the hands, especially during the last weeks" are reported. Severe pain followed by vaginal bleeding occurred during the night

Table I.

	Doniach and Walker	Grasby
Duration of pregnancy	28–30 weeks	28–30 weeks
Blood-pressure:		
Maximum	155/95	150/80
Minimum	130/80	110/65
Albuminuria/1000 ...	7.5	8
Oedema	Legs and face (slight)	Face, legs and lower abdomen (slight)
Shock	Severe	Severe
Haemoglobin gm. per cent	5	3
Blood urea, mgm./100	106–216	182–216
Lactational changes	nil	nil
Death-day of illness	7th	7th

and on admission to hospital her condition was grave. Only a few ml. of pale urine were obtained by catheterization. Foetal heart sounds were not heard. Hysterotomy was performed and separation of a normally situated placenta discovered. The placenta showed numerous infarcts. There was complete anuria after operation, in spite of bilateral renal decapsultation, and death occurred 7 days later with a mounting blood urea. Postmortem examination revealed the typical changes of symmetrical cortical necrosis, necrosis of the anterior pituitary cells, the gland showing an apparent attempt at new formation of capillaries and thrombosed vessels, but without changes in the vascular wall which were found in other organs, notably the kidneys. The liver showed the changes of eclampsia, while the breasts showed lactational changes.

The second case is that of a primigravida aged 29 years, with no previous history of severe illness or abortions. Two antenatal examinations revealed no abnormalities. Severe epigastric pains occurred without warning and were followed by the cessation of foetal movements, the onset of abdominal pains and regular contractions. The patient was unable to void any urine. Vaginal bleeding then followed, the pains diminished and she fell asleep, only to be interrupted by sudden eclamptic convulsions. A recently dead foetus was extracted with forceps, the placenta showing "extensive infarcts". Decapsulation of the kidneys was performed for complete anuria and the patient died on the 15th day after delivery. Postmortem examination showed the typical changes of symmetrical cortical necrosis, necrosis of the cells of the anterior pituitary—"not a nucleus visible"—and eclamptic changes in the liver. The kidneys also showed "nephrosis and haemorrhagic nephritis, with extensive cast formation and fatty degeneration". The blood urea is given as 300 mgm./100.

Unfortunately the brief reports of these cases do not give the blood-pressure readings, haemoglobin or biochemical findings. The summary of the pathological findings is given as "eclamptic necrosis of the liver, softening of the brain substance, cortical necrosis of the kidneys, necrosis of the anterior pituitary and intrauterine death of the foetus. The changes were not so marked in the second case, i.e. the renal vessels were hardly changed, there were no thromboses, and although there was haemorrhagic necrosis of the anterior pituitary there were no proven changes in the walls of the vessels or thromboses".

In these 4 cases—the first to be recorded—those described by Hügin show interesting variations, notably the previous history in each of his 2 cases of pregnancy toxaemia and the postmortem eclamptic changes, confirmed microscopically in the liver. No such changes were demonstrated in the case reported by Doniach and Walker nor in the case above described. A further interesting feature is the report by Hügin of apparent attempts at "reorganization" in the pituitary and, in the second case, an apparently less severe degree of necrosis, coincident with a longer period of survival after the onset of acute symptoms of retroplacental bleeding.

Variations in the severity and rapidity of onset of symptoms of pituitary insufficiency following postpartum haemorrhage are well recognized, from the slowly developing condition originally described by Simmonds (1914) to the mild types of pituitary emaciation described by von Bergmann (1934) and others. Sheehan (1938; 1939) who particularly investigated and described postpartum pituitary necrosis considered the thrombosis of the vessels due to the haemorrhage and collapse during delivery but that recovery was pos-

sible in the less severe cases. Recovery is in fact accelerated by the occurrence of a subsequent pregnancy. Sheehan and Murdoch (1938; 1939) have reported not only symptomatic improvement but, in a patient (Case 5) who was given intensive hormonal therapy (gonadotrophic and oestrogenic) to render pregnancy more probable and who did become pregnant, immediate and subsequently permanent improvement of the pituitary insufficiency. It is suggested that this improvement is due to the physiological hypertrophy of the remaining undamaged anterior pituitary cells occasioned by the subsequent pregnancy.

Such possible variations in the degree of pituitary necrosis may explain the less extensive disease and evidence of lactational changes in the cases described by Hügin. Similar variation in severity is recognized in symmetrical cortical necrosis, which, as Doniach and Walker point out in their detailed review is explicable by a relatively simple pathology—reflex vasoconstriction following severe haemorrhage in an already anaemic patient, leading to vascular degenerative changes and thrombosis—which can equally well be applied to explain the pituitary necrosis.

Details of 2 cases of cortical necrosis are reported to illustrate less severe degrees of the condition.

CASE 2. 4966/43 N.A.

Married, aged 40 years; 5-para; the last pregnancy terminated in miscarriage at the 28th week, no cause being known. She had not had antenatal supervision in any of her pregnancies, which had been normal, and there was no history of serious illness.

First day of last menstrual period not known, but was early in May 1943. Expected date of confinement early February 1944.

The patient stated that the pregnancy had appeared to be quite normal until December 3rd, 1943, the day before admission to hospital, when "she started losing". There was no pain with this haemorrhage, but she thought she may have lost almost 10 ounces of blood. She did not look upon this as particularly serious and did not call in her doctor until the following day. Information could not be obtained as to her previous condition or blood-pressure.

On admission to hospital on December 4th, 1943, the patient was well nourished; good build; mucous membranes very pale; general condition fair; no shock; oedema of legs as high as the knees.

Cardiovascular system. Heart normal in size, no bruits; blood-pressure 190/140.

Respiratory system. No abnormalities discovered.

Urine. Albumin, plus 3 (9/1000 in Esbach).

Abdominal examination. Immediately below the umbilicus was a small haematoma of the abdominal wall, 1½ by 1 inch in size, and apparently quite superficial. The patient believed it had appeared the previous day. The abdomen was enlarged to the size of a 36 weeks' pregnancy, the uterus on palpation being hard, tense and tender. There was no area of localized tenderness. Foetal parts could not be identified nor could any foetal heart be heard. Contractions of the uterus could not be felt and the patient did not appear to be in labour. On rectal examination the os could be felt undilated. There was a continuous slight haemorrhage from the vagina, which had continued since the first haemorrhage on the previous day. A diagnosis of toxaemia with accidental haemorrhage (mixed) was made.

Treatment. The membranes were ruptured and 15 ounces of clear liquor amnii were run off without difficulty and without discomfort to the patient. A course of injections of pitocin 2 units every half hour was also commenced and continued for 5 injections. Good uterine contractions ensued with no increase in the amount of blood loss from the vagina.

At 9.30 p.m. she was delivered spontaneously of a macerated male foetus weighing 2 pounds 9 ounces, and measuring 14 inches in length, corresponding with a 29 weeks pregnancy. There was no bleeding with the delivery of the foetus. The placenta and membranes were delivered intact half an hour later, and were accompanied by 12 ounces of dark blood and old blood clot. The uterus contracted well after delivery and the patient's

condition at the end of the third stage was quite satisfactory. Temperature 98°F., pulse 100; respiration 20.

The placenta was found to contain numerous small infarcts and much old blood clot adherent to the maternal surface. The retroplacental haematoma had not ruptured into the amniotic cavity.

Subsequent progress. The patient's condition on the following day, December 5th, was quite satisfactory. The blood-pressure was 160/100, there had been no bleeding during the night and she had passed urine on 2 occasions.

On December 6th, she appeared rather drowsy, her tongue was dry and coated, and she did not appear as well as was to be hoped. During the 24 hours she passed 450 ml. of urine only and this oliguria was particularly noted because she had taken fluids well. The blood urea was estimated and found to be 232 mgm./100.

The fluid intake and output and the blood urea estimations are recorded for convenience in a chart (Fig. 3), and show a progressive oliguria and rising blood urea, with fluid retention until December 16th, when there commenced a sudden polyuria. This markedly increased urinary output continued, with, however, a gradual fall in total fluids excreted until December 27th, when she again passed large quantities of dilute urine. She was by now unfortunately incontinent and exact measurement of the amounts was impossible. This second polyuria coincided with a remarkable fall in the blood urea.

The following are abstracts from the day to day records:—

7.12.1943. Intravenous dextrose 10 per cent, 550 ml.; intravenous dextrose 25 per cent, 10 ml.

8.12.1943. Drowsy, but quite rational and taking fluid well. Oedema, plus 3; fluid output, 230 ml.; blood-pressure, 210/130; haemoglobin, 35 per cent; intravenous dextrose, 50 per cent, 60 ml.

11.12.1943. Some improvement in general condition, patient talking and quite rational. Taking fluids well but fluid output less than 300 ml. for 3 days. She passed no urine during the last 24 hours. No oedema. Blood urea 312 mgm.5/100; blood-pressure, 200/120.

13.12.1943. Condition not so good. There has been a return of the odema, and although she is completely rational she is obviously uraemic, with gasping respiration, lack of interest in her surroundings, and severe skin irritation. Blood-pressure, 196/130; blood urea, 496 mgm./100; urine urea, 1,480 mgm./100; standard urea clearance 3.9 per cent average normal.

15.12.1943. Blood urea 408 mgm./100; condition much worse.

16.12.1943. Sudden polyuria; output 1,700 ml. in 24 hours; blood-pressure, 130/90; outlook seems more hopeful.

17.12.1943. Still maintaining a good fluid balance, but there is no improvement in her condition. No oedema.

20.12.1943. She is still drowsy, disinterested, pale and now beginning to look cachetic. The skin irritation persists. Intake and output approximately equal at 1,400 ml.; blood-pressure has risen from 140/95 to 170/105.

21.12.1943. Blood urea, 932 mgm./100; urine urea 1,720 mgm./100; urea clearance 3.2 per cent average normal.

22.12.1943 to 2.1.1944. Gradual deterioration in patient's condition. Still passing from 1,000 to 1,500 ml. dilute urine, specific gravity c. 1008, and taking fluids quite well. Her mental condition is getting confused and although she recognizes people around her she is roused only with an effort. Towards the end she became incontinent, but the polyuria was even more marked.

On December 26th she passed 400 ml. urine which contained one third part by volume of pure pus. Until then the urine had contained no pus cells but occasionally a trace of albumin. Cause for this pus was not discovered.

On December 29th the blood urea was 464 mgm./100; but there was no improvement in her condition and she died on January 2nd, 1944.

Treatment during this period was purely symptomatic.

Microscopical examinations of the urine during the course of the illness revealed red blood corpuscles and granular casts on 2 occasions only, namely the second and third days of oliguria.

A postmortem examination was made and revealed the typical kidney damage associated with symmetrical cortical necrosis confirmed by microscopical examination. Other organs were not grossly abnormal and there was little evidence of toxaemia of pregnancy. The uterus was not infected.

In reporting on the sections Dr. de Nevasquez

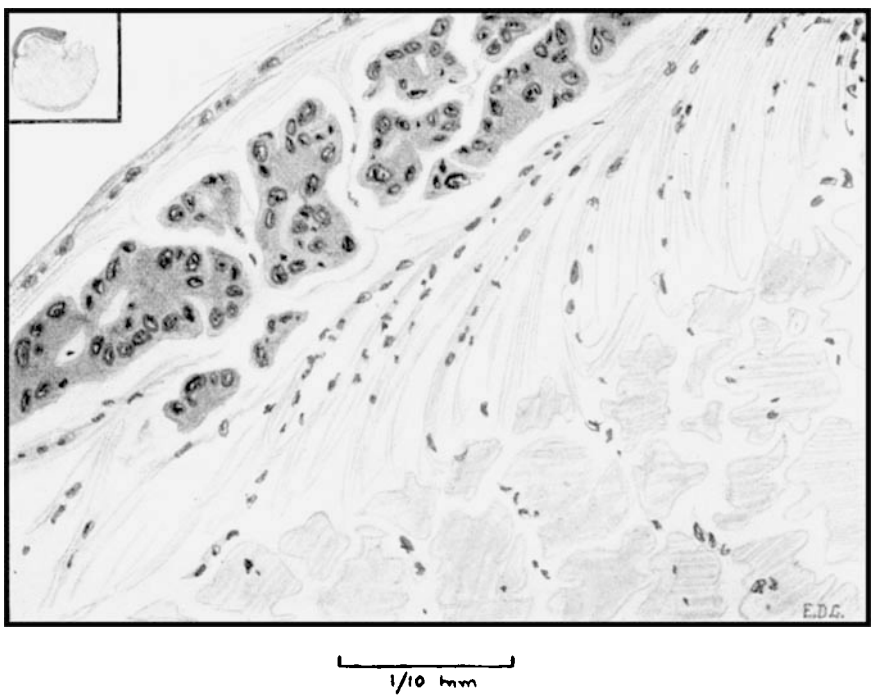

FIG. 2.

Necrosis of anterior pituitary gland, the few remaining undamaged cells are shown to the left, the necrotic tissue to the right. *Inset*: Drawing to show the exceedingly small fringe of remaining healthy tissue in the pituitary gland (shaded dark in the upper left quadrant).

E.D.Y.G.

noted that although the kidneys showed typical cortical necrosis the extent of the lesion was rather less than that usually seen.

Other features of particular interest in this case were the evidence of arterial spasm to which

CASE 3. 2506/45, R. P.

This patient was a 2-para and did not give any history of illness or abnormality in either of her previous pregnancies. Her previous medical history was equally uneventful.

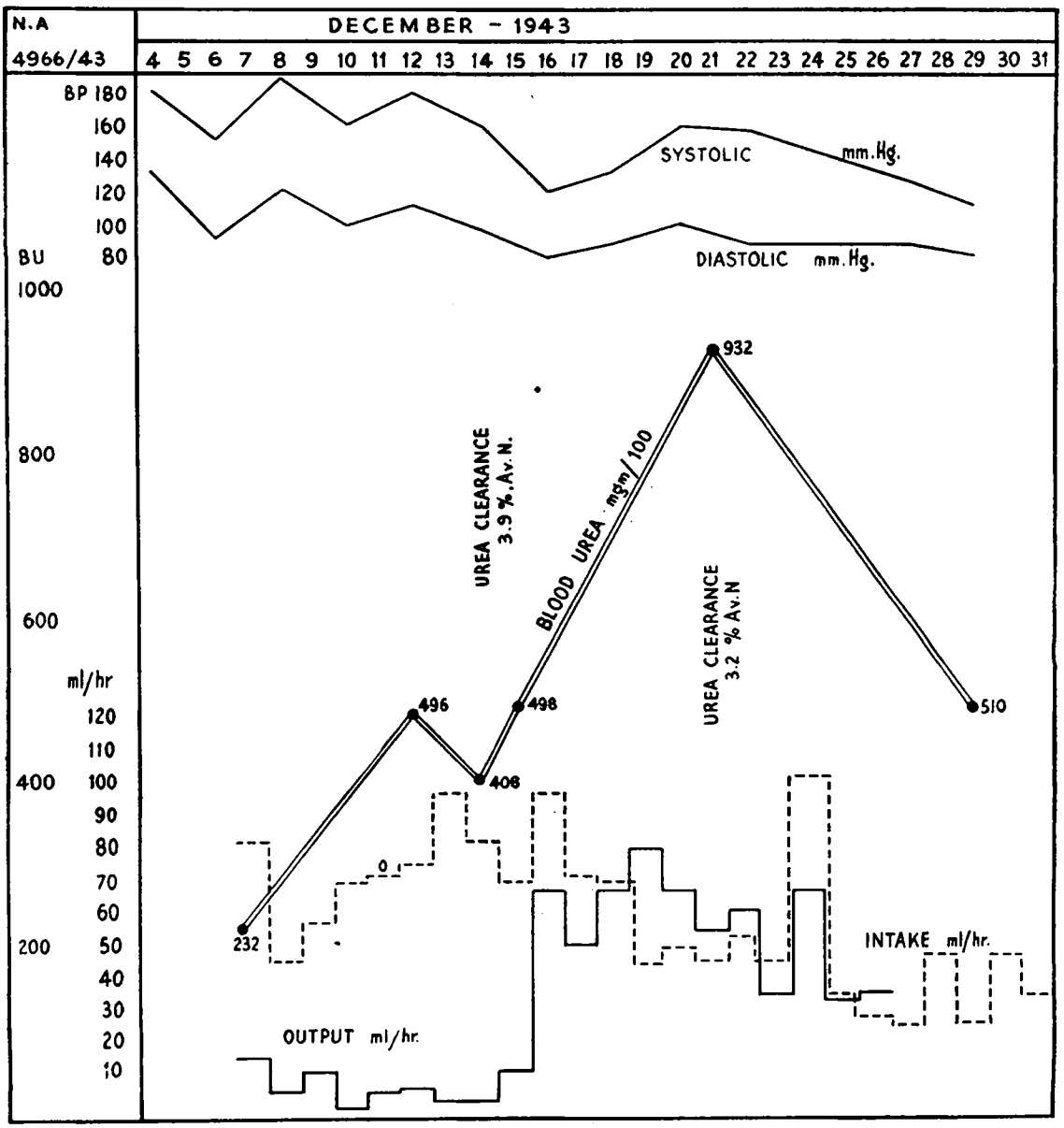

FIG. 3.

Doniach and Walker specifically draw attention, the severe anaemia and the unusually high blood urea.

First day of last menstrual period was early in March 1945. Expected date of confinement about second week December 1945.

She had had no antenatal supervision but stated she had been well until October 5th, 1945, when she had an attack of vomiting associated with epigastric pain. The pain became worse and she was seen by her doctor on October 7th when the pain was severe in the abdomen and back. Her blood-pressure was then found to be 160/110 and the urine found to contain a trace of albumin. She was admitted to hospital with a tentative diagnosis of accidental haemorrhage and toxaemia.

On admission to hospital on October 7th, 1945, her condition was very shocked and pale. Pulse poor in volume; rate below 105. Generalized oedema; blood-pressure, 110/90; urine contained albumin, heavy cloud. The uterus was enlarged to correspond with a 32 weeks' pregnancy. It was

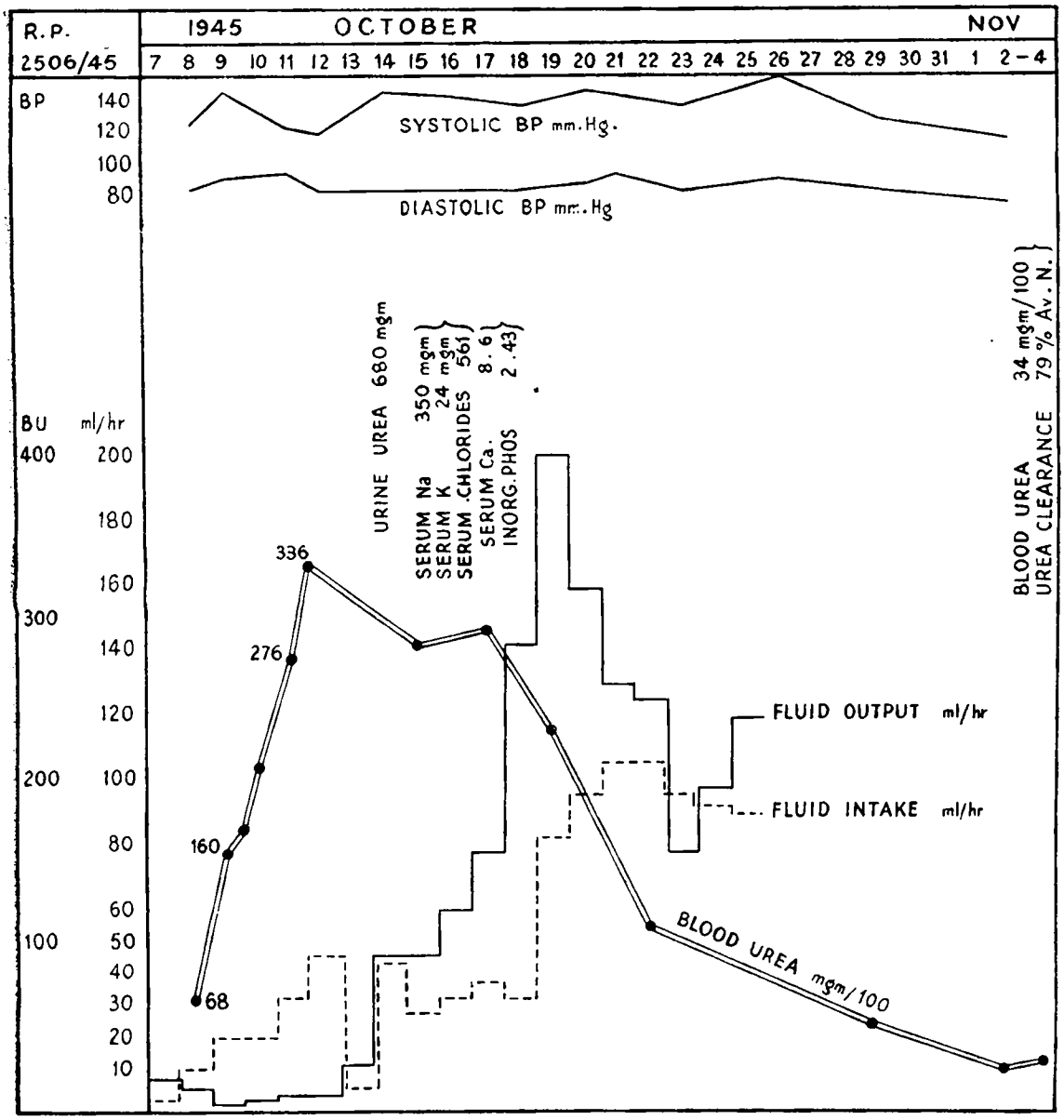

FIG. 4.

tense and hard, and tender. Foetal parts could not be palpated nor could the foetal heart be heard. There was a slight loss *per vaginam*.

In the belief that there had been a considerable intrauterine haemorrhage a blood transfusion of cross-matched blood was given, and later in the evening the membranes were ruptured.

On the following morning she expelled a macerated male foetus of about 28 weeks' duration. The placenta and membranes were expelled complete and without further haemorrhage, the placenta showing multiple infarcts and some old blood clot adherent to the maternal surface. The uterus contracted well and her general condition was much more satisfactory. The blood-pressure was 130/90. She had not passed urine since admission and at 10-30 p.m. she was catheterized and 70 ml. of urine withdrawn. There was no blood in the urine. It was decided, because of the oliguria, to give 370 ml. of 50 per cent glucose solution intravenously. On October 9th catheterization yielded 15 ml. of urine containing albumin but no blood. The oedema persisted and there was now papilloedema of the fundi, more marked in the right disc. She was given 50 ml. of 50 per cent glucose intravenously followed by 1,100 ml. of 3.4 per cent sodii sulph. solution.

On October 10th there was, perhaps, slight improvement although she was drowsy and the oedema remained unchanged. Catheterization yielded 25 ml. of urine containing no obvious blood and only occasional red blood corpuscles on microscopical examination. The oliguria continued with gradual deterioration in her condition until October 14th, when she passed 1,100 ml. urine of low specific gravity (1005–1006). The diuresis continued and there was an immediate and dramatic improvement with increased mental acuity, improved vision and lessening of the oedema, and this improvement was maintained. She finally made a complete recovery and was discharged from hospital on November 8th. When seen 3 weeks later her condition was quite satisfactory, her blood-pressure was 120/80, there was no albuminuria and her urea clearance was 79 per cent average normal. The day to day record of fluid intake and output, and clinical and biochemical findings are recorded in the chart (Fig. 4).

The diagnosis in this case was considered to be symmetrical cortical necrosis following toxaemic accidental haemorrhage, although, as in so many reputed recoveries from this condition, the diagnosis rests only on the similarity between these cases and known cases proved at autopsy. Dexter and Weiss (1943) comment that the evidence for the diagnosis in the majority of reported recoveries is very inadequate but although biopsy of the kidneys, to put the question of diagnosis beyond doubt, was not performed in any of their cases, apparently genuine cases of recovery have been reported by Gibberd (1936), Dingle (1943) and more recently by O'Sullivan and Spitzer (1946) who also give a complete bibliography.

The 3 cases here described would, therefore, appear to represent variations in severity of the same clinical and pathological syndrome, the first culminating in combined cortical necrosis and pituitary necrosis, the second presenting the classical features of symmetrical cortical necrosis with, however, clinical evidence that recovery might have occurred and pathological evidence of less renal destruction than is commonly seen, while the third case probably demonstrates a recovery.

SUMMARY.

1. A case of combined anterior pituitary necrosis and symmetrical cortical necrosis of the kidneys following concealed accidental haemorrhage is described.

2. A case of symmetrical cortical necrosis of the kidneys with clinical evidence of a less severe form of the syndrome is described, with confirmatory pathological evidence.

3. A probable recovery from established symmetrical cortical necrosis of the kidneys is reported.

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