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GENERAL STAFF MEETING
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CONTENTS

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I. CASE REPORT

RETAINED PLACENTA. ANURIA.
Path. Koucky.

No history of toxemia of pregnancy,
delayed delivery of placenta (Crede),
due to contraction ring (pituitrin, ergot?)
response of vasomotor collapse,
followed by rather sharp urinary suppression,
with marked clinical and laboratory uremia,
without any cause for obstruction (extra-renal),
failure of sustained efforts to promote diuresis,
and clear cut death due to uremia.

The case is that of a white female, 28 years of age, admitted to the University Hospitals 3-18-32 and died 3-24-32 (6 days).

Normal pregnancy - delivery

3-18-32 - 7:00 P.M. - Patient delivered a normal female infant at home . In labor three hours. Gravida iv, para iii. No toxic symptoms present during pregnancy. Immediately postpartum, was bleeding so attending physician gave pituitrin by hypodermic and ergot by mouth.

Retained placenta

Placenta could not be expressed. Sent to the hospital. 11:45 P.M. - Admitted to University Hospitals. Blood pressure 80/0. Pulse 72. 1000 c.c. 10% glucose given intravenously followed by 200 c.c. of 25%. During this time grouping of the patient was done and donors were found.

Transfusion - Crede

3-19-32 - 2:00 A.M. - 530 c.c. whole blood given. Was oozing slightly with uterus ballooned out with blood and difficult to massage into contraction. 4:00 A.M. - Put on delivery table under anesthesia. 4:58 A.M. - Placenta was expressed by the Crede method. The uterus and vagina were packed with mercurochrome dressing. 5:00 A.M. - Blood pressure dropped to 86/0. 500 c.c. 10% glucose started intravenously. 5:15 A.M. - Medical transfusion of 480 c.c. of citrated blood. (Grouping of patient not stated). Cross matching showed some rouleau formation at the end of 20 to 25 minutes. Pituitrin 1 c.c. and ergot 1 c.c. given by hypodermic after the removal of the placenta.

Improved

Patient returned to ward with blood pressure of 120/80. 4:45 A.M. - 1000 c.c. urine removed from bladder. A mushroom catheter left in bladder. Examination of urine - amber-red color, cloudy, 3+ albumen. 8:00 A.M. - Fundus 3 fingers below umbilicus. Only slight bleeding from vagina. 1:30 P.M. - Packing removed from uterus and vagina. No bleeding. Patient slept most of afternoon. Complains of slight tenderness in abdomen.

Urinary suppression?

3-20-32 - Bladder irrigated with boric solution. Since admission only about 200 c.c. of urine passed. It was felt that this might be due to edema and swelling around bladder and ureters due to Crede expression because considerable trauma was necessary to deliver the placenta.

Diarrhoea

Patient very drowsy and seems somewhat weaker. Is having severe diarrhoea, passing 9 or 10 stools a day which are liquid and very foul. Paregoric and bismuth given. Boric solution injected into bladder to test out the possibility of rupture. Same amount that was put into the bladder was recovered. There is some tenderness of the corpus of the uterus.

Anuria

3-21-32 - Patient very drowsy. Face is somewhat edematous. No urine has been passed since yesterday. Takes fluids well. Lochia is normal. Temperature subnormal. Pulse 90 to 100. B.U.N. - 81+ with 3.19 creatinine.

No obstruction

6:00 P.M. Cystoscoped. Bladder is normal. No evidence of rupture. Catheters are passed up both ureters with ease but no urine is obtained. Hot packs and warm blankets to the trunk are advised. Intravenous

glucose, 20% solution, recommended. 12:00 P.M. - Drowsy but responds when questioned. Face still edematous and somewhat flushed. Watery stools persist. No urine obtained through the ureteral catheters. Blood pressure ranges from 150/90 to 160/90. Possibility of anuria on basis of cortical necrosis of the kidneys is considered.

Spinal anesthesia

3-22-32 - Has not excreted any more urine. B.U.N. - 95.1. Uric acid 6+. Very drowsy, sleeping most of the time, no pain. Temperature subnormal, ranging to 97. Seen by Surgical Service, advised adrenalin, diathermy and, if necessary, spinal anesthesia. Eyes - fundi, diffuse edema of retinae; disc margins indistinct; no exudate or hemorrhage; probably slight vascular spasm. Adrenalin M viii at 8 A.M., M viii at 9:20 A.M., M xii at 11 A.M. No urine excretion resulted. 1:20 P.M. - Given 200 mg. novocaine crystals, intraspinally. (Level of anesthesia not stated.) Blood pressure dropped to 65/35. Adrenalin given to bring up blood pressure. Diathermy given at 8:25 A.M. and 3:20 P.M.

Uremia continues

3-23-32 - Considerably weaker. Breathing very deep (Kausmaul type). Has had 44 watery stools in past 4 days. Catheterization of bladder has resulted in only 2 to 3 c.c. of urine. Examination of urine - loaded with rbc's, no casts, 2 to 3+ albumen. B.U.N. 112. Sleeps most of time and occasionally has hiccoughs. Perineum is edematous. There is slight bleeding. Intravenous fluids continued.

Capsulotomy

3-24-32 - Face more edematous. No edema noted in rest of body. Lips and mouth very dry. Has vomited a small amount of fluid. Is taking some fluid by mouth. No evidence of jaundice. 1:15 P.M. - A capsulotomy of the right kidney was done under local anesthesia. Because of very poor condition, the left kidney was not decapsulated. Returned to her room somewhat weaker.

Exitus

4:00 P.M. - almost completely comatose. 5:00 P.M. - Eyegrounds - slight retinal edema present before but absent now; media is becoming cloudy. 5:10 P.M. Exitus. On this day the B.U.N. has been 147, Uric acid 8.4, Creatinine 2, Alveolar oxygen 30.
The eyegrounds were examined by the Head of Ophthamology and Otolaryngology at postmortem who stated that there were no findings except for the usual postmortem change.

Summary of Urinary Output

	Urine Output	B.U.N.	Creatinine	Uric Acid
3/18/32 Admission	1000 cc.	-	-	-
3/19/32	225 cc.	-	-	-
3/20/32	200 cc.	-	-	-
3/21/32	0 cc.	81.0	3.19	-
3/22/32	0 cc.	95.1	-	6.34
3/23/32	5 cc.	112.0	2.00	8.4
3/24/32	0 cc.	147.0	-	-

Autopsy

The body is that of 28 year old, white female, well-developed and well-nourished, measures 145 cm. in length and weighs approximately 170 lbs. There is moderate edema about face but none over the rest of the body. Rigor is absent. Hypostasis is absent. There is no cyanosis or jaundice. The pupils are equal, each measuring 5 mm. in diameter. There is an incision, 14 cm. in length, paralleling the right costal margin. Moderate distension of the abdomen is present. Abrasions are present over right and left arms. There is a bloody, serous discharge from the vagina.

Peritoneal Cavity. There is 1500 cc. of slightly turbid fluid in the abdomen; no blood present. The Appendix is present and hangs free.

There is a slight excess fluid in both Pleural Cavities. The lungs are free. The Peri-cardial Sac is normal.

The Heart weighs 350 grams. The muscles, valves and lining appear normal. The Root of the Aorta is clear. The coronaries are normal.

TheRight Lung weighs 500 grams, Left 475 grams. There is very marked edema of both lungs and some atelectasis at the bases. No evidence of bronchopneumonia.

The Spleen weighs 225 grams, is somewhat soft, and more pulp than usual comes away when scraped with a knife.

The Liver weighs 2225 grams, is definitely swollen, and has a yellowish

tinge. There is no evidence of hemorrhage or necrosis.

The Gall-Bladder, Gastro-Intestinal Tract, Pancreas and Adrenals are normal.

Swollen, fatty, bloody

Each of the Kidneys weigh 225 grams. On the right side, the capsule has been stripped away and a biopsy has been taken at the time of operation. This biopsy is closed with omentum and there is no blood in the operative site. Both kidneys are uniformly swollen. On the left side, the capsule strips off easily leaving a smooth surface. The color of the external surface is pale yellow without evidence of hemorrhage. On cut surface, the cortex of the kidney appears somewhat thicker than usual. There is a sharp contrast in color between the cortex and pyramids. The cortices are uniform, pale yellow, fatty color without any blood markings; whereas the pyramids are blackish-brown color and no blood streaks or hemorrhage can be seen in them. The pelves of the kidneys and the ureters are normal.

No urine

The uterus is large and soft, extending about 4 cm. above the symphysis. On the posterior wall, there is a small cyst containing clear straw-colored fluid, measuring about 1.5 cm. in diameter. This cyst is just beneath the serous surface. The ovaries and tubes show no changes. The Bladder, vagina, uterus and adnexae are removed intact. The bladder and urethra are opened. There are a few hemorrhagic streaks under the mucosa. There is no tear of the mucosa or the wall of the bladder. The bladder is empty. The vagina is coated with shaggy blood clots. The cervix shows no tear. The inside of the uterus is covered with shaggy blood clots and desquamating lining. No adherent placenta or such can be recognized. No tears are present in the uterus.

The lining of the Aorta is clean and smooth.

There are no enlarged Lymph Nodes.

The Organs of the Head and Neck are not examined.

Diagnoses:

1. **Recent pregnancy.**
2. **Retained placenta (clinical).**
3. **Anuria (clinical).**
4. Moderate pleural and peritoneal effusion.
5. Edema of lungs and face.
6. Cloudy swelling and fatty liver.
7. Cloudy swelling and fatty kidneys.
8. Post-partum uterus.
9. Recent decapsulation of right kidney.
10. Abrasions.

Microscopic:

No glomerular lesion, normal vessels, degenerated tubular epithelium, blood in lumina, no necrosis of liver and kidneys.

Questions:

Was anuria due to glomerular lesion? There was no evidence of toxemia of pregnancy.

Was it due to retained placenta? Specific response (see literature) or reflex anuria.

Was it due to transfusion?

II. ABSTRACT

NECROTIC SEQUESTRATION OF THE KIDNEYS IN PREGNANCY.
(SYMMETRICAL CORTICAL NECROSIS)
Abstr. Koucky.

A clinical and anatomic-pathogenetic study.
Scriver, W. De M. and Oertel, H.
J. of Path. and Bact. 32:2, 1071-1094, '30.

Historical

1886, Jubel-Renoy, saw first case (following scarlet fever), 1898, Bradford and Lawrence reported 2nd case. 1906 to 1930, several authors reported cases. Largest series in 1920 by Jardine and Kennedy (6 cases). Authors present 3 cases, 1 of which recovered. Total 40 cases (including 3 author's) have been collected.

Clinical cases:

Case I.

Female, 34, had retroplacental hemorrhage in the 6th month of 15th pregnancy (12 normal pregnancies), 13th aborted at 3 months, 14th at 6

months. Last pregnancy unaccompanied by any signs of renal disease except flashes of light before eyes and attacks of dizziness. Six month fetus born one hour after induced labor. Placenta showed numerous white infarcts.

Day post-partum	Urine, Vol. cc.	Urea gm. per litre.	Blood, Creatinine mg. per 100 cc.	Blood pressure
1	60	-	-	-
2	11	0.528	2.47	160/110
3	1	-	-	160/100
4	0	1.25	4.28	145/100
5	0	1.54	4.0	135/95
6	0	-	-	140/90
7	0	-	-	135/85
8	0	1.71	6.60	-
9	0	-	-	-

Urine on admission showed large amount of albumin, a few granular casts and occasional red blood cells. After delivery, the urine contained albumin but no red blood cells.

The patient remained relatively bright and mentally clear; No convulsions or demonstrable edema. Vomiting did not occur. Death ensued as a gradual inanition without any classical uremic manifestations.

All various methods of therapy were tried without result.

Case II.

The clinical course was almost identical with Case I.

Day post-partum	Urine, Vol. cc.	Urea gm. per litre.	Blood Creatinine mg. per 100 cc.	Blood pressure.
1	450	-	-	-
2	1300	-	-	-
3	550	-	-	-
4	0	1.95	6.5	140/75
5	0	-	-	135/80
6	0	1.91	6.4	125/60
7	3	2.39	-	140/60
8	0	-	-	160/80
9	0	-	-	-

Case III.

Recovery. Patient had prenatal urine examination on several occasions when it was free of albumin and with average specific gravity of 1.018, blood pressure was constant at 110/60. Patient delivered at 4-1/2 months following a retroplacental hemorrhage. A transfusion of 350 c.c. was given following which the patient had a mild chill and the patient next day was definitely jaundiced and the Van den Bergh gave an indirect reading of eight units of bilirubin. No hemoglobinuria was observed.

The urine output in this case dropped to 160 c.c. on the second day. It rose to 540 c.c. on the 7th day, 1630 c.c. on the 9th day and was 3500 c.c. on the 11th day. The maximum urea was .40; N.P.N. rose to 104; creatinine to 6.0. The Mosenthal test on the 25th day showed 580 day urine ranging from 1.012 to 1.020 and 270 c.c. night urine of 1.018 specific gravity. MacLean urea concentration factor was 19.5. Urine showed traces of albumin up to the 30th day and was clear thereafter. Was this a transfusion reaction? Some recover.

Etiology

Infectious diseases (diphtheria, pulmonary tuberculosis, dysentery, pneumonia and peritonitis). Pregnancy - 29 cases, retroplacental hemorrhages 13 cases. Other Causes - prostatic cancer without obstruction.

Sex

5 males, 2 not stated (children), remainder females.

Comment

In only 1 case was a living child born. There may be absolutely no clinical signs or history to suggest a renal involvement or toxemia beforehand, but if there is, it is most commonly edema (15 cases). In 5 cases, there was a history of convulsions before anuria; in 5, after the establishment of the anuria. Vomiting is rare and occurs only as terminal symptom. Anuria is almost complete, coming on immediately postpartum to 5 days later and lasting in fatal cases from 2 to 13 days depending on completeness of the anuria.

All cases studied have shown albuminuria and majority red blood cells in urine. Only a few have had blood chemistry studies. Thirteen had blood pressure records, in 5 the systolic was over 150, in 5 below and 3 were at this level. Maximum was 200 systolic and no diastolic. On the whole, the blood pressure readings are so diversified that no clear conclusions can be drawn of their relation to the renal condition.

Anatomic-Pathogenetic Part.

Gross Changes

Weight 380 grams apiece. Present bulging, mottled, pale-yellow surface with irregular fine, dark reddish streaks and dots. On section, a bulging, pale yellow cortex is revealed which lacks any normal markings but is covered by reddish dots and streaks. It is well differentiated from a much darker but structurally well preserved medulla. Numerous "uremic ulcers" in the cecum and colon were found in one case.

Microscopic

It is possible to distinguish between the following cortical zones: First, larger irregular areas of advanced tissue dissolution showing structureless fused clumps; second, contiguous areas which are distinguished from the former by massive blood engorgement; and, third, patches and strands of non-necrotic but not normal kidney. This last is a subcapsular strip with characteristic changes of "nephritis" (epithelial crescents, glomerular exudate and periglomerular leucocytic infiltrations).

By scarlet red staining of gross sections, the fat distribution in the thrombosed blood vessels appears like fat-injected vessels in the cortex. The parenchyma is essentially free of fat.

Genesis:

The following differences from ordinary infarction are noted:

(1) Diffuseness and irregularity of the necrosis.

(2) Irritative changes (exudative and proliferative).

(3) Distribution of thrombosed vessels proceeds uniformly and evenly according to certain segmentary levels so that at least the majority of vessels of a certain level are obstructed.

The various pictures constitute the results of irritation of the arterial terminal segments, of different intensities.

Experiments demonstrate that the terminal vascular segments of a tissue respond to weak irritation by vasodilatation with increased stream; to medium stimulation by vasoconstriction with slowing of the stream while the proximal arteries remain constricted. Irritations may produce according to their concentration and time of action, in ascending scale: Hyperaemia, exudates, hemorrhages and finally complete blood stagnation with thrombosis. These findings present the reaction to irritation of varying intensity in different areas. The escape of the medulla has not been explained.

It is pointed out that the whole vascular system in pregnancy as well as in some infections shows decided upsets in its general irritability. It is suggested that serious circulatory breaks may possibly at least partly account for eclamptic symptoms. Relation of the retroplacental hemorrhages to vascular downfall is suggested.

The possibility of blood hyperlipemia is entertained to explain the concentration of fat in the thrombosed vessels.

Conclusions:

1. Two cases of anuria due to bilateral necrosis of the renal cortex confirmed by autopsy and a third clinical case of similar nature? which recovered are reported.

2. The outstanding clinical features are anuria, relative or total, marked azotemia, but frequently almost complete absence of uremic signs.

3. Necrotic sequestration of the kidney of pregnancy is the result of terminal arterial segmentary collapse (vasoparalysis).

4. The renal vascular disturbances seem to be related to a general abnormal state of vasomotor irritability of the pregnant state.

Comment:

Although this diagnosis was considered in our case, no necrosis was demonstrated (microscopically). The

gross description is the same, the clinical stories sound as if they could be the same, but typical necrosis is absent. Could this represent an earlier stage with death before necrosis had time to develop?

III. ABSTRACT

RENAL LESIONS IN THE TOXEMIAS OF PREGNANCY.
Bell, E. T., VIII, 1-42 (Jan.) '32.
Amer. J. of Path. Path. Koucky.

This paper is based upon a study of the kidneys from 20 cases of toxemia of pregnancy.

The clinical manifestations of the toxemias of pregnancy are so varied that it is difficult to arrange them in a logical classification. For the purposes of discussion, however, they may be divided into five groups: (1) typical eclampsia with convulsions; (2) eclampsia without convulsions; (3) preeclampsia; (4) hyperemesis gravidarum; and (5) pregnancy in association with preexisting renal disease.

1. Typical Eclampsia with Convulsions

The characteristic symptoms and signs in this disease are convulsions, hypertension, albuminuria, edema, headache, visual disturbances, nausea and vomiting, vertigo, restlessness, and, especially in fatal cases, coma. These symptoms are by no means all present in every instance, and apparently no single symptom is necessary to establish the diagnosis of eclampsia, but, by definition, typical eclampsia includes only those cases where convulsions are present.

The pathologist is justified in making a diagnosis of eclampsia if he finds hemorrhagic necroses in the liver in a case of pregnancy, but he cannot exclude eclampsia when no necrosis of the liver is found, since this lesion is occasionally absent.

Eclampsia is more frequent in primiparae than in multiparae. On the basis of the relative frequency of primiparous and multiparous births Buttner calculates that 1 instance of eclampsia occurs to every 220 to 270 primiparous, and to every 1100 to 1300 multiparous births. The greater tendency to eclampsia in primiparae is well established but entirely unexplained.

Eclampsia rarely develops before the fifth month of gestation.

It is to be noted that eclampsia develops in the vast majority of instances after the fetus and placenta have attained considerable size. It is estimated that the symptoms are relieved by emptying the uterus in over 50 per cent of the cases. The fact that, in at least 10 per cent, the symptoms first appear postpartum might be explained as a delayed action of the hypothetical toxin, since eclampsia rarely sets in later than 24 hours after labor.

In about 80% of cases of eclampsia preeclamptic symptoms are present before the onset of convulsions.

Eclampsia is about 10 times as frequent in those who have had a previous attack.

Convulsions are the characteristic feature of typical eclampsia, but the number of convulsions is very variable. Convulsions are not a necessary part of the eclamptic picture. (See "Eclampsia without Convulsions".

In many instances of eclampsia and preeclampsia, edema is inconspicuous or absent.

Albumin is found in the urine in practically all instances of eclampsia. Cases have also been reported in which no albumin was found at any time either before or after the convulsions.

Erythrocytes are often found in the urine in increased numbers.

Hypertension is an almost constant symptom of eclampsia. Hypertension precedes the convulsions in a vast majority of instances, but not invariably.

The retention of water and sodium chloride in eclampsia is well known. The glomerular lesions are sufficiently marked to account for some renal insufficiency.

Author reports 14 cases of typical eclampsia.

Anatomical Changes in Eclampsia

The Liver

Degenerative lesions of some type are found in the liver almost constantly. The characteristic gross lesions are irregular areas of hemorrhage

associated with necrosis or atrophy of the liver cords (hemorrhagic necrosis) and small areas of anemic necrosis.

The Kidneys

The kidneys are affected in practically all cases of eclampsia. The macroscopic changes are constant and easily recognized. The kidneys are usually slightly enlarged and their external surfaces are smooth. On section the cortices are pale and cloudy and occasionally a yellowish tinge is noted. There is some variation in the intensity of the cloudy swelling in different instances. The macroscopic changes are therefore not pathognomonic of eclampsia, the same lesion being found in a large number of toxic and infectious processes.

On microscopic examination the tubules show the changes characteristic of cloudy swelling. The cells of the secreting tubules are usually somewhat swollen and often they contain small fat droplets. In the lumina of the tubules, casts and precipitated albumin are usually observed. Fahr emphasizes the importance of hemoglobin in the casts. In the more severe injuries there may be some evidence of necrosis and degeneration of some of the tubular epithelium. The tubular lesion is likewise not peculiar to eclampsia. It is the typical effect of toxins or toxic substances in the circulating blood, but it may also result from anemia caused by spasm of the renal arteries.

The Glomerular Lesions

When the azo-carmine stain is applied to the glomerulus in eclampsia, it is easily seen that the thickening of the capillary wall is due, almost entirely, to a massive thickening of the capillary basement membrane. The glomerular epithelial cells are only slightly altered. Occasionally they contain fine droplets of fat or hyaline granules, but they show no evidence of proliferation. As a rule the endothelial nuclei are slightly increased in number. The narrowing of the lumina of the capillaries is evidently due, usually, to thickening of the capillary basement membrane. The capillaries are rarely completely obstructed, but in some tufts their thickened walls are in contact and they seem to be totally occluded. Capillaries of this type appear hyaline in hematoxylin-eosin preparations.

2. Eclampsia without Convulsions

This group includes fatal toxemias, usually with some preeclamptic symptoms, but without convulsions. The diagnosis is established by the finding of typical necrosis of the liver at postmortem.

Ordinarily there is not much justification for this subgroup of eclampsia. Cases are frequently reported in which only one convulsion occurred; and others are reported where muscular twitchings but not true convulsions were present. The following protocol records a case which differs clinically in no way from typical eclampsia, except in the absence of convulsions.

3. Preeclampsia

Preeclampsia is characterized by the presence of the symptoms and signs which usually precede the eclamptic convulsion. The most important of these are hypertension, albuminuria, visual disturbances, edema, headache, nausea and vomiting, vertigo, and so on.

The clinical phenomena indicate that the same type of lesion is present in preeclampsia as in typical eclampsia, although it is presumably less severe. Heynemann described a case of preeclampsia in which death was due to premature separation of the placenta. The characteristic changes were present in the liver and kidneys. Even the typical glomerular lesions were found. Heynemann states that 6 similar cases have been reported. This would seem to establish the essential identity of eclampsia and preeclampsia. (Two cases might well be classified as preeclampsia rather than as eclampsia without convulsions.

4. Hyperemesis Gravidarum

In general this form of toxemia is different from eclampsia, but cases occur which show some of the features of eclampsia, and raise a doubt whether these two forms of toxemia are entirely distinct entities.

5. Pregnancy in Association with Preexisting Renal Disease.

Eight cases have come under the author's observation in which it is reasonably sure that chronic renal disease was present prior to pregnancy.

There is usually a marked aggravation of the nephritic symptoms. The distinction from gestation eclampsia is difficult when the function of the kidneys prior to pregnancy is unknown. All the symptoms of eclampsia, namely - hypertension, albuminuria, edema, headache, visual disturbances, vomiting, convulsions and coma - may occur in nephritis uncomplicated by pregnancy. However, if a definite impairment of renal function is demonstrable, the diagnosis of preexisting chronic nephritis may be established.

Summary

In fatal cases of eclampsia a characteristic glomerular lesion is found.

The glomeruli show a marked narrowing of all their capillaries, caused usually by an increase in thickness of the capillary basement membrane, but sometimes by an increase of endothelial cells.

One case is reported in which the lesions resulting from an attack of eclampsia seven years before are described. These consist of focal hyaline areas in the glomeruli with partial or complete glomerular obliteration and varying degrees of tubular atrophy. It is shown that a peculiar form of chronic renal disease may result from the eclamptic kidney.

In one case of hyperemesis gravidarum glomerular lesions were found which correspond entirely to those of typical eclampsia. In three other cases the glomeruli were normal. A fatty liver without necroses is characteristic of this form of toxemia.

When a woman with chronic renal disease becomes pregnant, there is usually an aggravation of all the nephritic symptoms. The condition cannot be distinguished from preeclampsia and eclampsia unless the condition of the kidneys prior to pregnancy is known, or unless there is a definite impairment of renal function. Chronic nephritics show no special tendency to develop gestation eclampsia.

Comment:

Our case does not show an "eclamptic" glomerular lesion and toxemia is an unlikely diagnosis.

IV. ABSTRACT

REACTIONS FOLLOWING TRANSFUSION OF BLOOD, WITH URINARY SUPPRESION AND UREMIA.

Bordley, J., III, Arch. Int. Med. 47:288-317 (Feb.) 1931.
Path. Koucky.

For more than 250 years those who have attempted to restore health by the transference of blood from a normal to a diseased person have been keenly aware of certain attending dangers. As early as 1667, Jean Baptiste Denys described in vivid style the outstanding features of the so-called hemolytic transfusion reaction, which until recently served as an inexplicable and insuperable barrier to the transfusion of blood. An understanding of the nature of the incompatibilities that are responsible for these frequently fatal reactions came only after the studies of Landsteiner on hemagglutination in 1901; a simple method for determining compatibility grew out of the classifications of Jansky (1907) and Moss (1910). As a result of these discoveries, transfusion of blood became a popular therapeutic procedure at about the time of the World War; today, provided one has taken the necessary precautions in preliminary grouping and cross-agglutination tests, it is a procedure relatively free from danger. Nevertheless, transfusion reactions still occur, and although some of them are undoubtedly due to carelessness in the preliminary steps, it has been learned that certain reactions, most of them mild but others severe and fatal, cannot be clearly explained on the basis of the obvious incompatibilities discovered by Jansky and Moss.

Three broad types of reaction are set forth: the "incompatible,"

the "citrate" and the "allergic." The names would imply that the classification is etiologic, but the etiology cannot be well established except for the first of the three.

This classification of transfusion reactions is inadequate in one important respect: It does not tell the complete story of the reacting recipient. One is left to wonder what happens to the person who receives blood that is not suited to his circulation and who, newertheless, does not die immediately.

The subject of delayed reactions following transfusion is not entirely new; a number of clinical and pathologic details have been outlined in case reports by various authors. Just where these prolonged or delayed reactions fall into the common classifications it is difficult to say. From the available data one is led to believe that most of them, perhaps all, are due to the use of demonstrably incompatible blood.

Author reports 3 cases and reviews 14 from the literature.

Summary of Clinical Data.

The Patient

The series is made up of 17 patients, most of them relatively young adults. Anemia of some kind was present in all of them, but the cause of the anemia, its severity and the general condition of the patient at the time of transfusion seem to have had little influence on the occurrence of a reaction or its ultimate outcome. Reactions occurred so frequently in young persons who had been well until the onset of a sudden and severe hemorrhage that it would seem reasonable to exclude chronic illnesses, such as nephritis, heart disease, etc., from an important role in the causation of the response.

The Donor

In not a single case is there complete and satisfying evidence to prove that the blood of the donor was compatible with that of the recipient. Definite incompatibility was established in six cases. In two others there was probable incompatibility since transfusion was performed as an emergency measure without previous tests. One patient seems to have presented an example of a queer change in blood group and was probably given incompatible blood. In one, cross-agglutination was not tested. In 5 cases the statement is made that there was no cross-agglutination, but in none of these was the blood group of the donor determined; in only one was the recipient's group known. In one case, the recipient and donor were of the same blood group (group not stated) and there was no cross-agglutination. In one, the recipient and donor were both of group II and there was no cross-agglutination. In none of the 7 cases in which cross-agglutination was found satisfactory was there a retest of the agglutination reactions after transfusion, and the latter step, according to our experience in one case and Lindau's experience in one case, would seem to be of considerable importance.

The Transfusion

The methods used in preparing and injecting the blood seem to have been of little importance; citrate was used in about half of the cases. On the other hand, the amount of blood injected was a significant factor in determining the final outcome. A definite statement of the amount transfused was made in 15 of the 17 cases; 10 of these patients died and five recovered. In the five who recovered, the average amount injected was 314 cc., whereas the 10 who died received an average amount of 564 cc. No patient receiving less than 350 cc. died, and no one receiving more than 540 cc. recovered. The patient who survived after a transfusion of 540 cc. ran the most severe course of the recovered patients and until the 12th day seemed on the verge of death.

Immediate Reaction

A severe immediate transfusion reaction occurred in all but 7 of the cases. Two of these 7 were under anesthesia during the injection of the blood, and in them it is difficult to attach much importance of the absence of this reaction. In at least 6 of the 10 cases in which immediate reactions occurred, symptoms were first noted during the injection of blood, and in 3 of these the symptoms were of such severity that an injection was cut short. The manifestations

vary somewhat from case to case, but as a rule the characteristic features are a sense of great discomfort, signs of collapse, vomiting, chill and a sharp rising temperature. The more acute symptoms rarely last more than a few hours, and as they subside hemoglobinuria is generally noted; it was observed in 10 of the 15 cases in which it was specifically looked for and it is possible that it was present in an 11th instance in which the urine was described as "red". The first urine voided after the transfusion practically always contained albumin. Dating from the immediate reaction, there was suppression of urine in every one of the 17 cases.

The Interval

In all instances, with the subsidence of the immediate reaction, the patients seemed to improve. This interval of improvement lasted from 1 day or 2, to about a week, during which the patients were brighter and appeared to have derived distinct benefit from the transfusion. In 6 cases there was jaundice of a mild grade which disappeared after a day or so. There was no tendency for the hemoglobin and red blood corpuscles to decline; generally they showed an elevation over the pre-transfusion level. Leucocytosis was noted in several cases. During the interval of improvement, the outstanding untoward feature was continued oliguria which, in a number of cases, was associated with persistent nausea and vomiting.

The Delayed Reaction

This was generally ushered in by symptoms of the central nervous system, of which agitation or drowsiness was the commonest. The symptoms began from a day or two to a week after the transfusion and progressed to a peak which was reached from the 8th to the 12th day. In the patients who recovered and from the 4th to the 18th day in the fatal cases. The outstanding observations were those usually associated with severe impairment of renal function, and belong to the syndrome commonly called uremia. In all cases in which the chemistry of the blood was studied there was considerable retention of non-protein nitrogen, and in one case, the carbon-dioxide combined power of the plasma fell to 18.7% by volume. The phthalein excretion in the 2 cases in which it was studied was remarkably reduced. Edema was noted in 5 cases, and was extreme in 1. The blood pressure was definitely increased in 3cases, but in several other cases in which it was followed, there was no significant rise. Convulsions were observed in 4 cases and coma was noted in 5 cases. It is interesting that 2 of the 5 patients who became comatose recovered. In 3 cases, there was definite purpuric phenomena at the peak of the reaction, and in a 4th case, frequent epistaxes were noted. In case 1 the purpura was associated with a fall in the platelet count.

The Outcome

Six patients recovered and 11 died. In the patients who recovered, the peak of the reaction was reached from the 8th to the 12th day. In the fatal cases death occurred between the 4th and 18th day, with 10 days as the average duration of life after transfusion. All 11 deaths occurrred with uremic manifestations. Recovery was associated with considerable diuresis beginning at the peak of the reaction. Only in 1 case did recovery seem to result from any radical form of treatment; in this instance, decapsulation of the kidneys was performed. In several other cases, spontaneous recovery was as dramatic as the result in this case. We cannot be sure that the decapsulation of the kidneys was responsible for the happy outcome.

Summary

1. A delayed or prolonged reaction following transfusion is described in 17 cases. These cases, 3 are reported for the first time, and 14 have been gathered from the literature.

2. The reaction generally runs a peculiar and highly characteristic course which presents the following features; (a) immediately after transfusion, there is a sharp febrile reaction, followed frequently by a hemoglobinuria and invariably by suppression of urine; (b) there is an interval of several days during

which there is symptomatic improvement but continued oliguria; (c) after this interval the characteristic features of the delayed reaction develop rapidly. They usually begin with agitation or drowsiness, which is replaced by outspoken evidences of uremia. Convulsions and coma may supervene.

3. The outcome is frequently fatal; 11 of the 17 patients died. Recovery is associated with the diuresis; death occurs in uremia.

4. At autopsy the kidneys are swollen, the tubular epithelial cells contain droplets of a peculiar pigmented material and show advanced degenerative changes; the tubular lumina are filled with various cells, blood pigment and debris. Small necroses are generally found in the liver.

5. The events may be summarized as follows: A subject receives an injection of incompatible blood, his kidneys are severely damaged and in due course of time uremia sets in. Several possible explanations of these events are discussed.

6. The delayed reaction is not rare; beside the 17 cases discussed in detail, a number of cases in the literature are cited.

Comment:

Was this the cause of our patient's death even if the bloods were "compatible"? It seems so? A definite example follows for comparison. The gross and microscopic lesions are the same in both cases.

V. CASE REPORT

CARCINOMA OF THE STOMACH. POST-TRANSFUSION UREMIA.

Path. Pearson.

The case is that of a white male, 51 years of age, admitted to the University Hospitals 10-7-31 and died 11-2-31 (26days).

Sudden onset - pain

6- -31 - Drank a glass of beer and immediately had a burning sensation in epigastrium. From then on whon his stomach was empty, he had a gnawing sensation in epigastrium which was relieved by food (ulcerated lesion?).

Mass

7- -31 - Pain became more severe and constant and was not relieved by food. Progressive weakness and hard mass in the epigastrium developed.

Obstruction

8-15-31 - Vomited after eating. Stomach felt full at times, and he had to induce vomiting for relief of pain. Constipation developed.

Bleeding

9- -31 - Stools became tarry. Lost 28 pounds in weight since June. Appetite is good but is afraid to eat foot because it gave him gas pains.

Nausea

10-2-31 - Began to feel nauseated.

Hospital

10-7-31 - Admitted to University Hospitals. Physical examination reveals a white male, 51 years of age, poorly nourished and pale but well-developed. Hard mass in abdomen which is easily palpable in epigastrium and to left. Mass moves with respiration and is tender to touch. Laboratory: Hb. 34%, rbc's 1,740,000, wbc's 5,150, pmn's 78%, L 15%, M 7%, slight polychromatophilia and anisocytosis. Progress: Put on liquid diet (Sippy), cream and milk, 3 oz. every hour.

Transfusion - X-ray of Chest

10-8-31 - Complains of pain in abdomen. Transfusion of 500 cc. of citrated blood. Pulse and temperature normal. X-ray of chest, diaphragm , mediastinum, heart and pleura are normal. Lungs show no evidence of disease. Conclusion: Negative chest. Urine - specific gravity 1.024, few wbc's and rbc's. Stool - dark, no gross blood, benzidene strongly positive. Gastric content - no free Hcl, benzidene strongly positive.

Second transfusion

10-10-31 - Mineral oil, dram i, 3 times daily. Given 500 cc. of citrated blood by the indirect method. No reaction. Hb. 38%.

X-ray of Stomach

10-14-31 - Mineral oil, dram i, 2+ daily. Sodium bicarbonate gr. x, 3 times daily. Complains of burning in epigastrium. Gastro-intestinal study - there is a very large filling defect involving the distal half of the stomach. This corresponds to palpable mass. Considerable dilatation of the stomach is present due to the obstruction. There is only a thin stream of barium leaving the stomach along the lesser curvature. The infiltration does not extend very far up along the lesser curvature which would suggest that it is operable. At 6 hours, there was almost complete retention of the barium meal in the stomach and the head of the meal was in the terminal ileum. Conclusion: Large obstructive carcinoma of the stomach.

10-16-31 - Gastric lavage, 2 times daily. Gastric lavage, 350 cc. retention of dark brown, thick flukd. Complains of nausea. Urine - specific gravity 1.020. Stool - dark brown, soft, benzidene strongly positive.

Third Transfusion - Reaction

10-19-31 - Patient feels fairly comfortable. Gastric lavage, 300 cc. retention. Surgical note: Transfused. Donor and patient, Group IV, and no agglutination. 100 cc. given. Complains of pain in back. Dyspneic, cold and clammy. Transfusion discontinued. 0.5 cc. adrenalin given. Pulse weak and thready. Complains of pain in stomach. Feels nauseated. Vomits. Returned to bed having violent chills. Blood pressure 100/70. Another 0.5 cc. adrenalin given. Still having violent chills. Hot water bottles applied. 0.5 cc. adrenalin repeated. One-half hour later felt comfortable. Pulse improved. 4 :45 P.M. - intravenous of 500 cc. saline with acacia started. Ephedrine hydrochloride gr. 3/4 (H). Coughed up about 200 cc. of blood. Intravenous 2000 cc. saline given. Gr. 1/6 (H) Morphine sulphate.

Better - Oliguria

10-20-31 - Slept fairly well. Pulse about same. Takes fluid well. Liquid stool of red-brown color. Proctoclysis discontinued. 400 cc. bloody emesis. Pulse to 154. Temperature 99.4 Output 200 cc., intake 1600 cc.

Worse

10-23-31 - epigastric pain. Codeine sulphate gr. i. Emesis of 600 cc. light brown fluid. Dizzy and nauseated most of time. Intravenous 3000 cc. 10% glucose. Codeine sulphate gr. i. Pulse 72, temperature to 99. No urinary output today. Intake 1600 cc. Intake today, 3050 cc. Donors of previous transfusion regrouped and found to be group ii instead of group iv. Hb. 52%.

Uremia

10-25-31 - Small emeses at times. Feels nauseated. 4000 cc. subcutaneous saline given. Gastric lavage. Nasal tube inserted. Urinary output 150 cc. Intake 2150 cc. Emesis of 350 cc. Adrenalin M x. given, 3 times. Gastric lavage, 50 cc. retention. 2000 cc. 10% glucose given. Very frequent emeses. Pulse 116. Temperature 101. Urinary output 400 cc., total intake 240 cc. N.P.N. - 99.8. Icteric index 6 units.

Edema

10-29-31 - Repeated emeses of greenish material. Hypodermoclysis 2000 cc. normal saline. 200 cc. 25% glucose, intravensusly. Body is somewhat edematous. P.S.P. - total of 0% in 3 hours. N.P.N. - 151.3 mg. Pulse 100, temperature 99. Urinary output 575 cc., intake 2000 cc.

10-30-31 - Breathing is slow but not labored. Seems weaker. Repeated emeses of particles of necrotic tissue? Edematous around eyes and ankles. Intravenous of 2000 cc. 10% glucose given by hyperdomyclysis. Pulse 100.6, temperature to 99, and respirations 18.

Pulmonary edema

11-1-31 - Emesis which contains fresh blood. Intravenous 1000 cc. 10% glucose given. Morphine sulphate gr. 1/6 (H). Very restless and dyspneic. Breathing is noisy. Considerable fluid in the lungs. Expectoration of small amount of bright red blood. Medical note: Hasbeen vomiting a good deal today. Fluids begun. Still unable to eat. Refuses practically everything. There are a few rales in the bases of the lungs. Temperature 98.4. Respirations show some

Increase in rate. 10.00 A.M. - Congestion of both lungs and moist rales heard over entire area of both lungs. Respirations are rapid. Pulse irregular and rapid. Very nervous. Pulse 125 , temperature 98.2, respirations 36. No urinary output. Intake 1800 cc.

Exitus
11-2-31 - Respirations are somewhat rapid and irregular. Purulent discharge from nostrils. Morphine sulphate gr. 1/6 (H). 7:30 A.M. - respirations 45. Arms and feet edematous. 8:45 A.M. - Morphine sulphate gr. 1/6 (H). Respirations labored. Pulse 123 and regular. 11:15 A.M. - patient expired.

AUTOPSY:

The body is that of a well-developed but poorly nourished, white male 51 years of age, measuring 173 cm. in length and weighing approximately 130 lbs. Rigor is present.

Edema
Hypostasis is purplish and posterior. There is edema of both ankles and slight edema of the hands. Body is very pale. No cyanosis or jaundice. Pupils measure 4 mm. each and are regular. Multiple puncture wounds in both antecubital spaces.

Ascites
About 400 cc. of clear, straw-colored fluid in Peritoneal Cavity. The peritoneum is glistening and free. The Appendix is subcecal and free.

Hydrotherax
Each Pleural Cavity contains about 500 cc. of clear, straw-colored fluid. The Pericardial Sac contains a moderate amount of fluid.

The Heart weighs 350 grams. The valve edges are free and normal. The chambers are normal. There is no evidence of any disease in heart itself. The Roof of the Aorta shows a minimal amount of sclerosis. The coronaries show a slight amount of sclerosis.

Edema
The Right Lung weighs 1100 grams, the Left 950 grams. Both lungs are very edematous all over, more marked at the bases. Upon cutting these across and with the least amount of pressure, a large amount of fluid exudes from lungs. The lungs are examined for any evidence of infection but none is found. There are no tumor masses present.

The Spleen weighs 100 grams. The capsule is grayish and wrinkled. On cut surface, the pulp is very soft and red.
Cloudy

The Liver weighs 1745 grams, and shows a moderate amount of cloudy swelling. This is sectioned very carefully to see if there is any evidence of tumor metastasis to liver but none can be found.

The Gall-Bladder and Ducts are normal.

The stomach is next examined and on external examination, a mass can be palpated in prepyloric region. Posterior surface of stomach adherent to transverse colon. On anterior surface near pylorus, there is very small perforation which undoubtedly is postmortem. Stomach is opened and there is large, ulcerating perforating type of carcinoma which is situated in pre-pyloric region and involves about the lower third of stomach. Small perforation near anterior and prepyloric region of stomach which is postmortem. Mass which is attached to transverse colon is also on point of perforation. Nodes along lesser curvature of stomach all involved and those around head of pancreas are involved.

The Pancreas and Adrenals are normal.

The Kidneys (each) weigh 250 grams and are rather soft and swollen in appearance. On cut section capsules strip very easily revealing smooth surfaces which appear whitish in places. On cut section, kidneys are very soft and whitish.

Medullae are congested.
The Bladder and ureters are normal.

Diagnoses:

1. Carcinoma of stomach (ulcer).
2. Metastasis to glands of lesser curvature.
3. Metastasis to glands around head of pancreas.
4. Edema of lungs (marked)
5. Bilateral hydrothorax.
6. Ascites
7. Anuria (clinical) with uremia.
8. Cloudy swelling of liver & kidneys.
9. Peripheral edema.
10. Puncture wounds.