FAMINE ŒDEMA AND ITS TREATMENT WITH MERCURIAL DIURETICS

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In the Bengal famine of 1943-44 in the affected population and among the patients in the hospitals and camps for sick destitutes occurred many cases of generalized œdema, and among these patients many deaths occurred, the terminal event usually being œdema of the lungs.

In some of these patients, the œdema was caused by some definite disease present, for example severe anæmia, chronic malaria, severe hookworm infection, advanced kala-azar, etc., and a few definite cases of acute nephritis were encountered. In many of the cases, however, the condition was apparently nutritional in origin and corresponded closely to what has been described in the literature of famine as famine œdema. It is not the object of the present note to discuss in detail the nature, ætiology, signs and symptoms of this condition, since we are concerned here mainly with treatment, but we will give a brief outline of the clinical picture.

The condition may be seen at any age and in either sex with prolonged semi-starvation and exposure, possibly complicated by attacks of malaria, dysentery or diarrhœa. Œdema of the subcutaneous tissue begins to appear. It always appears first in the most dependent parts, the feet and legs, and it may spread to the arms and hands, to the abdomen with the occurrence of marked ascites. Œdema of the genital organs is frequently marked. Œdema of the face is slight or absent except at a late stage. This differentiates it markedly from the œdema of nephritis, and also, of course, the absence of the characteristic changes in the urine.

Ascites is often a marked feature, and this seems to be accentuated by the occurrence in many of the patients of enlargement of the liver with some evidence of cirrhosis and portal obstruction. This condition of the liver seen in famine cases cannot be discussed here. It has been a very striking feature in many cases, and tends to support the recently-developing idea that a dietetic or nutritional factor may be concerned in the causation of cirrhosis. With the development of marked ascites, fluid is found in the pleural cavities and there then develops œdema of the lungs which is often a terminal event.

The effect of posture on the distribution of œdema is marked; the fluid shifts according to which side the patient lies on.

In these cases, the absence of enlargement of the heart and the absence of tachycardia and also of any evidence of peripheral neuritis differentiate the condition clearly from the 'wet' form of beriberi.

Hypoproteinæmia has been a common finding, but in some cases this has been slight, and the chief change was not in the total plasma protein but in the albumin-globulin ratio. Total protein as low as 3.5 grammes per cent has, however, been recorded. Anæmia is usually present, but it is not of such a severe degree as to explain the œdema. Owing to the massive œdema present, the emaciation of the patient may be completely masked, although the thinness of the face contrasts markedly with the swelling of the dependent parts of the body.

A feature in that of many of these cases has been the history of recurring attacks of diarrhœa. During an attack of diarrhœa, the œdema diminishes, and when the diarrhœa ceases, or is controlled by treatment, the œdema increases, but weakness is progressive throughout. These attacks of diarrhœa differed rather markedly from the nutritional diarrhœa described by Aykroyd and Gopalan (1945), but this matter cannot be discussed further here.

We would, however, note that, although it was unusual to isolate any pathogenic organism in these cases of diarrhœa, the diarrhœa often responded excellently to the administration of drugs of the sulpha group, particularly sulphaguanidine or sulphathiazole. As stated above, however, the control of the diarrhœa in this way was frequently followed by an increase in the œdema.

In cases of famine œdema, the urine output is persistently low, a trace of albumin is frequently present, but definite evidence of nephritis in the form of red blood cells, casts, granular or even hyaline, is absent.

The blood pressure seen in these cases varies rather considerably. During and after attacks of diarrhœa, the blood pressure is frequently low, sometimes very low, but in the presence of a generalized œdema the blood pressure is often normal, and may even be slightly on the high side. It appears to us that the patients with a high blood pressure responded better to the treatment mentioned below.

Treatment of the condition.—The rational form of treatment of the condition appears to be by diet, preferably a high protein diet, to remedy hypoproteinæmia which appears to underlie the condition. In less marked cases, all that is needed is rest and good diet; and with this treatment the œdema in some cases will disappear within a few days, although it tends to recur when the patient gets about. In severe cases in our series control of the condition by hospitalization and diet has been difficult or impossible. The administration of a good diet rich in protein will frequently bring on profuse diarrhœa with rapid deterioration of the patient's condition although the œdema may get less.

Other forms of treatment suggested have been the intravenous injection of suitable protein solutions such as protein hydrolysate. This appears to have beneficial results in some cases, particularly those with low blood pressure, but the evidence of the value of protein administration is not conclusive. Moreover, in patients with general anasarca and œdema of the lungs, one hesitates to give large amounts of fluid intravenously.

A number of cases were treated with vitamins, multi-vitamin tablets, and also individual vitamins, particularly vitamin B_1. The response to this treatment was never marked, and often very slight or absent. Another form of treatment which might be beneficial is the giving of intravenous transfusions of blood serum, blood plasma reconstituted from dried serum, or dried plasma but in more concentrated form than usual, perhaps only half the usual amount of distilled water being added. So far, we have had no opportunity of trying this form of treatment which would seem to be, in many ways, ideal.

In this hospital, it was thought worth while to try the effect of mercurial diuretics in patients with general anasarca and œdema of the lungs. It was not expected that the treatment would have any permanent beneficial effect, but it was thought that it might tide the patient over the crisis when œdema of the lungs was present or threatened. The number of cases treated in this way in this hospital has not been very large, about 20, but in some cases the immediate results have been very striking, and moreover, to our surprise, the benefit in many of the cases seems to be permanent. It should be stated, moreover, that this treatment had been applied only to cases in which other modes of treatment had failed to produce any benefit.

The best way to indicate the type of results which have been seen in these cases is to quote some case reports.

Case 1.—A boy, aged 12, admitted from a famine orphanage with a report from the medical officer to state that he had been in the orphanage with good food and care for six months during which time he has had alternating attacks of diarrhœa and generalized œdema. Attempts to increase the diet caused a recurrence of diarrhœa; cutting down the diet reduced the diarrhœa but increased the œdema.

On admission, the patient was very emaciated and weak, was suffering from diarrhœa and had some œdema. The liver was large and hard and the veins on the abdominal wall were dilated. Some ascites was present; weight 34 pounds; serum protein 4.9 gm. per cent; albumin and globulin equal; blood pressure 70 and 50. Urine output was low, and the urine showed only a trace of albumin.

The diarrhœa was controlled by sulphaguanidine, but the œdema rapidly increased with an increase in body weight of 5 or 6 lb. in a few days. Accordingly the patient was given ammonium chloride by mouth and ½ c.cm. of neptal (May & Baker) by injection. That day, 68 oz. urine were passed, and the œdema became less. Two days afterwards, the diarrhœa started again, and once more sulphaguanidine was given which controlled it, but the œdema, ascites, etc., returned. This time ¾ c.cm. of neptal was given. The diuresis was not marked, only 40 oz., but from that time the urine output has continued at a reasonable level. Within a few days of these two injections of neptal, the œdema disappeared and also the ascites, and the general condition improved rapidly. It was found possible to increase his diet, and neither the diarrhœa nor the œdema recurred. After two months in hospital, his weight has increased by 22 lb. in spite of the disappearance of the œdema, the blood pressure rising to 90 and 60. The liver though still palpable is smaller. The plasma protein value is now 7.4 gm. per 100 c.cm., and the patient is about to be discharged practically normal. Some enlargement of the liver and dilatation of the veins on the abdominal wall are, however, detected.

Case 2.—Male, aged 30, with a history of prolonged semi-starvation, weakness and attacks of diarrhœa. The emaciated condition of the patient is hidden by a generalized œdema and ascites, the œdema being very marked in the dependent parts. The chest showed moist sounds, and the condition suggested some œdema of the lungs. Blood pressure was 130 and 90. Hæmic murmurs in the heart; serum protein 6 gm. per cent, globulin 3.2, albumin 2.8. Urine output is low with a trace of albumin. Marked diarrhœa is present.

For several days after admission, the patient was given no special treatment except rest and diet. The diarrhœa and œdema persisted unchanged. The diarrhœa was treated with sulphaguanidine and was controlled, but the œdema persisted and increased. In the first two weeks in the hospital, his weight increased from 89 to 98 pounds owing to an increase in the œdema. He was then treated with ammonium chloride and salyrgan (Bayer). After the injection of ½ c.cm. a diuresis of 80 oz. occurred, then the urine output fell again. Four days later, an injection of 1 c.cm. was followed by a diuresis of 100 oz. followed by a fall in the urine output. A week later, a third injection of 2 c.cm. produced less marked immediate diuresis, but the urine output from then on remained at a reasonable level. With this treatment, within 14 days the patient's weight came down from 98 and 74 lb. owing to the disappearance of the œdema. Then it was possible to increase his diet without producing diarrhœa. The patient was discharged from the hospital about a fortnight later, still weak and emaciated, but with no diarrhœa and no œdema.

Case 3.—Male, aged 30, with a history of semi-starvation and diarrhœa, showing a generalized œdema and marked ascites with moist sounds present in the chest. Blood pressure 105 and 80, urine output low, with a trace of albumin. Plasma protein 6.4 gm. per cent, globulin 4.1, albumin 2.3. The patient's emaciated condition was masked by the œdema. After 7 days' hospitalization and diet, no improvement was seen; his weight was reduced by only 2 lb. He was then put on neptal treatment, four injections being given during the next two weeks. During this time, his weight fell from 110 to 87 lb., a fall of 23 lb. After the fourth injection, the urine output remained good and his weight was further reduced a little. During the next few weeks, his diet was increased with an increase of several pounds in weight and no recurrence of diarrhœa, or œdema, and he was discharged in good general condition, plasma protein being 7.6 gm. per cent, albumin and globulin being equal, 3.8 gm. per cent.

The response in all cases of famine œdema was not equally good. As stated above, in patients with a low blood pressure and inanition, the response was often relatively poor, although if the general condition and the blood pressure improved the response also improved. In patients with serious infections, for example kala-azar and tuberculosis of the lungs, the response may be poor, and also in very severe

anæmias; even in kala-azar, however, this treatment has proved useful.

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A CASE OF HYPERGLYCÆMIA SHOWING AN UNUSUAL RESPONSE TO THYROID THERAPY*

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MRS. X, a doctor aged 42, was admitted to hospital on 29th March, 1943, for the treatment of hyperglycæmia. A few days previously, a Medical Board had rejected her as unfit for military service owing to the presence of sugar in the urine and palpable spleen and liver.

History. General.—The patient stated that she was thin and under-developed in early adult life and that while a medical student her age was taken to be fourteen; she was treated with thyroid. She had an abundant growth of thick hair while at college, but it had gradually fallen and become thinner in quality. Her skin always tended to be greasy. She married at the age of 30, and her weight increased gradually afterwards up to 11 stones 2 lbs. She had mild attacks of asthma in 1929 and several similar attacks up to 1939. She had rheumatic fever in 1937. She worked in Burma as a doctor until evacuated in May 1941.

Gynæcological.—Catamenia at 11½ years; periods regular and rather profuse; no conceptions. Menopause with high fever at 33 years following a plague inoculation. Treatment with multi-glandular pills with pituitary extract for early menopause produced severe headaches.

Family.—Her sisters were all thin like her and grew fat after childbirth. Two brothers suffer from urticaria.

Physical examination.—She was rather obese, weight 9 stones 6 lbs., height 5 feet 2 inches; alert and active; skin slightly coarse, and complexion blotchy; pulse 80; blood pressure 126/80; spleen not palpable; liver could not be palpated owing to a thick abdominal wall. Except for a prolonged expiration heard all over the chest, other systems were found normal.

Laboratory examination.—Blood examinations revealed no abnormality in the blood picture or in the counts. The blood cholesterol was 267 mgm. per cent. Eye examination showed no abnormality. Stool examination showed no ova or amœbæ.

A sugar tolerance curve done on 26th March, 1943, showed a fasting blood sugar of 394 mgm. and a maximum rise to 588 mgm. two hours after giving glucose; the patient was on extra high carbohydrate diet for two weeks before this. On the 3rd April, 1943, the fasting blood sugar was 428 mgm.

Treatment.—The patient was kept on a reduced diet of 1,517 calories for about a week, and as there was no improvement, thyroid ½ grain twice daily for 12 days and 1 grain twice daily for 8 days was given and the diet was further reduced by about 200 calories. With this treatment, the weight came down by 3 lbs. and the fasting blood sugar from 428 to 160 mgm.; the B.M.R. rose from — 13.6 to — 9.4.

Thyroid was now stopped, but the same diet was continued for about three weeks. At the end of the first week the fasting blood sugar rose to 176 mgm. Thyroid was again started ½ grain twice daily, and the weight and fasting blood sugar came down within two weeks. Ordinary hospital diet of 2,311 calories was now resumed and thyroid continued; a week after this regime there was a rise in the fasting blood sugar. 'Panmelitus' 2 tablets twice daily was given for a week but the fasting blood sugar continued to rise. The diet was then reduced to 1,632 calories and insulin was given 40 units daily for 2 days and 8 units daily for another 2 days. There was no reduction in the fasting blood sugar.

The patient was discharged from hospital on 10th June, 1943, and advised to continue thyroid ½ grain twice daily for 3 months with a diet of roughly 1,600 calories and no carbohydrate restrictions. At the end of this period, her weight was 8 stones 11½ lbs. and the fasting blood sugar came down to 130 mgm. Thyroid was then stopped; 15 days later the weight was less by 2 lbs. but the fasting blood sugar rose to 137 mgm.

Urine examination throughout her stay in hospital and afterwards was negative for sugar except once when there was just a trace.

Discussion.—The interest in this case lies in: (1) The apparently symptomless high blood sugar levels and the high renal threshold. Though clinically the case was not a well-defined case of hypothyroidism the patient seemed to do well on thyroid. Her complexion and skin improved. She felt generally better and thought that her memory had improved; her former employer remarked that he had never seen her look fitter. This fact along with her history of under-development in adolescence, sterility, and early menopause, and the tendency to obesity, suggests that this is a case of hyperglycæmia due to endocrinal imbalance, not falling within any of the recognized types.

(2) The hyperglycæmia failed to respond to diet alone. The fasting blood sugar on 3rd April, 1943, was 428 whereas with thyroid therapy

*Paper condensed by editor.