ACUTE IDIOPATHIC PORPHYRIA PRESENTING AS A PROGRESSIVE PARESIS OF LANDRY TYPE

BY

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[WITH PHOTOGRAVURE PLATE]

Cases of acute porphyria, although rare, are probably more common than is generally believed. The association of acute abdominal symptoms, neurological abnormalities, and port-wine-coloured urine is characteristic, but one or other of the members of the triad may be absent, and in such cases the diagnosis becomes very difficult. The findings at necropsy are slight and depend upon the application of special techniques, so that cases unsuspected during life are rarely recognized on the post-mortem table. It is only by constant awareness, both in the ward and in the laboratories, that such cases will be recognized. In view of these facts the following case history is worth recording.

Case Report

A housewife aged 45 was admitted to the Chelsea Hospital for Women under the care of Mr. Frank Cook on June 17, 1948, complaining of amenorrhoea. She stated that for the past two to three years her periods had been painful and had on occasion been preceded and followed by a brown vaginal discharge. Her periods had been regular until two months before admission, when she had missed a period; she had, however, begun to menstruate one week before admission. Her past history was uneventful except for an attack of appendicitis in 1938.

On examination a tumour the size of an eighteen-weeks-pregnant uterus was felt in the lower part of the abdomen. No other abnormality was detected in any system.

A diagnosis of endometriosis was made, and she was operated upon on June 18, subtotal hysterectomy and bilateral salpingo-oophorectomy being performed. At operation a chocolate cyst of the ovary was found, and it was noted that the small intestine was at one point adherent to the posterior surface of the uterus.

Her post-operative progress was good, though she required occasional sedation with barbiturates, until July 2, 15 days after the operation, when she complained of marked malaise and weakness. Physical examination revealed nothing abnormal. The urine was examined and found to contain a few pus cells and Gram-positive cocci. She was given sulphadiazine, receiving a total of 30 g. over the next few days.

On July 5 she complained of numbness of the thighs and buttocks. She was noted to be dull mentally. On examination retention with overflow was found, the bladder being distended up to the umbilicus; there was marked weakness of the legs; the deep reflexes in the legs and the abdominal reflexes were absent, and the plantar responses were flexor. At this time the blood urea was 44 mg. per 100 ml. and the haemoglobin 86%. The Wassermann reaction was negative.

By July 7 the weakness of the legs had increased and she complained of weakness of the arms. A lumbar puncture was performed, clear colourless fluid at normal pressure being obtained. The C.S.F. contained no cells, and Pandy's test for increased globulin was negative. By July 9 the patient had complete areflexia in all limbs, and objective weakness of the arms was noted. On July 10 the diaphragm movements became paradoxical. The patient was then transferred to the Westminster Hospital.

On admission she was found to be mentally confused, speech was slurred, and her respirations were very rapid. Examination of the C.N.S. revealed the following signs: no pupillary reaction to accommodation; bilateral absence of corneal reflexes; left lower facial paralysis; a flaccid tetraparesis, most severe in the legs; weakness of the trunk muscles; complete absence of all deep reflexes; absent abdominal reflexes; and ill-defined areas of anaesthesia over both legs. Urine was sent to the laboratory for examination, as it was thought to be infected. *Streptococcus faecalis* was cultured. A specimen was sent to the Chemical Pathology Department; it was reported on as follows: "Urine almost normal in colour, but darkened on heating. Waldenström's test for porphobilinogen strongly positive. Total porphyrin 25 mg. per litre. The porphyrin was mainly ether-insoluble (uroporphyrin). Insufficient material for further identification."

On July 11 the patient was noted to be more dyspnoeic. The C.N.S. signs were unchanged, but examination of the chest revealed a poor air entry and scattered rales. A double-exposure x-ray film of the chest showed paradoxical movements of the diaphragm right and left. At 5 p.m. her respirations suddenly rose to 41 a minute and she died.

Post-mortem Examination.—This was performed by Dr. J. G. Humble on the day after death. Examination showed a curious purple-brown coloration of the heart muscle. Black pigment was scattered over the peritoneum. The trachea and large bronchi were full of mucus, and bilateral basal pulmonary oedema was found. The brain and spinal cord appeared congested, and there was a definite pressure cone. The right sciatic nerve seemed oedematous.

Microscopical Examination.—Sections of the right sciatic nerve stained with haematoxylin and eosin (Plate, Fig. 1) showed patches of lymphocytic infiltration, congestion of vessels, and perivascular collections of polymorphonuclear leucocytes and mononuclear cells. Sections of the lumbar and cervical cord stained with haematoxylin and eosin and with toluidine blue (Fig. 2) exhibited degenerative changes in the anterior horn cells, many of which showed central chromatolysis, some being reduced to mere ghosts. Sections of the cerebellar cortex showed severe degenerative changes in the Purkinje cells. Sections of the midbrain, basal ganglia, and cerebral cortex failed to reveal any abnormalities with the two staining methods used.

Comments

This woman had no relevant past history. At no time previously had she reacted adversely to any drug; the only drugs given after operation were potassium citrate, sulphadiazine, and an occasional dose of phenobarbitone. Her illness apparently lasted, from first to last, only 10 days. The spread of symptoms and signs was from below up (Landry type). A double-exposure x-ray film taken the day she died showed paradoxical movements of both sides of the diaphragm and a small area of collapse in the right lower lobe. Had not examination of the urine revealed uroporphyrin the diagnosis might have been completely missed, even at necropsy. The triad of abdominal symptoms, neurological signs, and highly coloured urine so suggestive of porphyria may not always be present; only one or two of these findings may be forthcoming, as in this case.

The peculiar clouding of consciousness and confusion noted in our patient have often been observed before—for example, Case 2 of Mason *et al.* (1933), and Abrahams *et al.* (1947). The ascending (Landry) type of paralysis has been known to occur in acute porphyria for many years (Courville and Mason, 1931; Kinnear Wilson, 1940). Occasionally there may be a recovery from an acute attack, with death in a second acute attack (Denny-Brown and Sciarra, 1945; Davies, 1949).

The microscopical lesions in the C.N.S. are those that have been described by previous writers (Denny-Brown and Sciarra; Mason *et al.*). With the exception of the changes

in the Purkinje cells, they fit well with the clinical signs and provide an explanation for the respiratory failure which was the immediate cause of the patient's death.

It is impossible to be certain whether this case should be regarded as one of acute idiopathic porphyria or whether it was toxic in origin, as we were unable to obtain enough urine for the porphyrin to be typed. Of the drugs which she received, the sulphadiazine would have been the most likely cause of her condition; Dobriner and Rhoads (1940) mention both clinical and experimental evidence that sulphonamides may cause increased excretion of porphyrins, and sulphadimidine (sulphamezathine) was one of the drugs administered in the fatal case reported by Abrahams *et al.* The difficulty remains that in all reported cases of toxic porphyria the predominant excretion product has been coproporphyrin.

In our case symptoms, though slight at first, preceded sulphadiazine administration. The balance of evidence therefore seems to us to be in favour of this being an acute idiopathic porphyria rather than a toxic one. The urinary findings and the rapidly progressive neurological picture would also make this the more likely diagnosis.

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REFERENCES

- Abrahams, A., Gavey, C. J., and MacLagan, N. F. (1947). *British Medical Journal*, 2, 327.
 Courville, C. B., and Mason, V. R. (1931). *Arch. Neurol. Psychiat., Chicago*, 25, 848.
 Davies, D. (1949). *British Medical Journal*, 1, 846.
 Denny-Brown, D., and Sciarra, D. (1945). *Brain*, 68, 1.
 Dobriner, K., and Rhoads, C. P. (1940). *Physiol. Rev.*, 20, 416.
 Mason, V. R., Courville, C., and Ziskind, E. (1933). *Medicine*, 12, 355.
 Wilson, S. A. Kinnear (1940). *Neurology*, p. 303. Arnold, London.

CONVULSIONS IN CHILDHOOD

BY

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The article by Nathan and Ransford (1949) prompts me to record six cases of convulsions in children between the ages of 5 and 11 years. These were observed between 18 and 25 years ago and their subsequent medical history has been recorded. I attended the mothers of Cases 4, 5, and 6 at their confinements. The observations were made during an investigation of the cortico-thalamic reactions to visceral tensions, which may represent only a small group of a type of epileptic convulsion—the viscerocortical. The neurological syndrome, however, with which these cases appear to be associated has since become the basis of certain obstetrical procedures. These observations were made before electroencephalography came into use, and there was then no knowledge of cortical electrical potentials and the variations of their rhythmic patterns.

Case 1

A boy aged 10 suddenly and for no apparent reason fell to the floor in a typical epileptic fit. The fits recurred every 15 minutes for an hour and lasted two to three minutes. He had bitten his tongue and become incontinent. When I saw him he had just recovered from a fit, was lying on a bed, restless, unconscious, but frowning and mouthing his lips over closed teeth as if trying to free them of an unpleasant taste. There was no history of constipation. He was not cutting any teeth. He had had a large tea—it being Christmas Day. A few minutes after

the fit he became conscious and I decided to empty his stomach. This was effectively done. The resulting vomit was enormous. After an hour's rest he was perfectly normal and had no memory of what had happened, except that he had been sick.

He is now 35 years of age, has never had a recurrence of these attacks, was an exceptionally brilliant student at school, and was an outstanding athlete. He is a member of a family whose names are well known in the athletic and industrial world.

Case 2

A boy aged 6 had a series of epileptic fits for no apparent reason. They occurred every five minutes and had been going on for over an hour when I saw him. He was well nourished and a good specimen of a curly-haired boy. His history was that he had not felt well that day. He was lying on the bed in a fit when I saw him, with his head thrown back, his back hollowed, his legs rigid, and his arms in tonic spasm extended in front of his abdomen. His breathing was stertorous, his face cyanosed, his teeth tightly clenched, and strabismus showed through widely opened eyelids. There followed a series of clonic contractions from which he relaxed with a groan. He had not bitten his tongue, but there was the puckered frown upon his forehead and mouthing similar to Case 1. Not having felt well, he had had only a few mouthfuls of bread and milk during the day. There were no history of injury, no pyrexia, and no evidence of the onset of an acute inflammatory condition.

Examination of the abdomen however, revealed a distended descending colon and sigmoid lying like a large rope stretching almost from the splenic area to the pelvis. He was at once given a rectal injection of 2½ oz. (70 ml.) of equal parts of glycerin and oil. A mass of scybala and constipated faeces was passed, being followed after a few moments by a large and well-formed evacuation of the bowel which in mass was out of all proportion to the size of the child.

This fine boy was killed in action as an officer of the Guards Brigade at the age of 25. He had never had any recurrence of his convulsion, but had grown up a scholar and athlete. His father had been an athlete of considerable accomplishment.

Case 3

A boy aged 11 was sent into hospital with a history that he had epileptic fits. His doctor had never known him to be ill previously. He came of a good artisan stock and had several brothers and sisters. There was no history of illness in the family, epilepsy or allergy. Twenty-four hours before admission to hospital he had his first fit, which was followed by one approximately every hour. When he was admitted he was unconscious. His temperature was over 100° F. (37.8° C.) and he was considered to be suffering from acute infective encephalitis.

When I first saw him he was lying unconscious in bed with his head thrown back. A gentle effort to bring it forward precipitated a fit which lasted about two minutes. When the clonic movements ceased he lay frowning and mouthing as did the two previous cases.

Sir Henry Head pointed out to me, when I was his house-physician, that if convulsions were accompanied by mouthing a "visceral accompaniment" should be suspected. Between attacks this boy had complained of acute abdominal pain and put his hands over the lower abdomen. He lay fully stretched out upon the bed. Abdominal examination revealed a firm lump, apparently in his caecum. There was no tenderness or peritonism. His white cell count showed an eosinophilia with no rise of polymorphonuclear leucocytes. Assuming from these observations that his might be a case of ascaris toxæmia with visceral irritation, I gave him santonin followed by castor oil, which he was able to swallow. I refrained from doing an immediate lumbar puncture. Eight hours later he was sitting up in bed looking perfectly well, having no memory of what had happened. A jar was produced containing four large roundworms. In 24 hours the treatment was repeated and another bunch of large roundworms was expelled. At the end of three days he was sent home perfectly well.

C. H. STUART-HARRIS, ZENA FRANKS, AND D. TYRRELL: DEATHS FROM INFLUENZA

FIG. 1.—Trachea from Case 4. Most of epithelium desquamated and replaced by exudate of leucocytes and fibrin.

FIG. 2.—Trachea from Case 2. More advanced change than Fig. 1. Epithelium replaced by a necrotic slough.

FIG. 3.—Bronchiole from Case 2. Necrosis of entire wall; dark areas of necrotic epithelium are massed cocci.

FIG. 4.—Lung from Case 2. Edge of area of haemorrhagic infarction with extensive oedema in rest of lung.

FIG. 5.—High-power view of lung of Case 2. Intense congestion and masses of cocci; little leucocytic reaction.

F. DUDLEY HART AND P. COLLARD:
ACUTE IDIOPATHIC PORPHYRIA

FIG. 1.—Right sciatic nerve, showing lymphocytic infiltration with perivascular leucocytes and mononuclear cells.

P. H. BUXTON AND A. WILLCOX: ENDOTHELIOMA OF THE PLEURA

FIG. 1.—Radiograph of chest, December, 1947, showing rounded shadows on the left side.

FIG. 2.—Biopsy specimen showing the spindle-shaped cells in whorled arrangements. ($\times 260$.)

FIG. 2.—Section of lumbar cord showing chromatolysis in anterior horn cells.