COMMENT

It is assumed that the symptoms referred to in the left leg were the result of a sudden arterial occlusion that occurred during the epileptic convulsions. There are two possible explanations to account for the obstruction. The first is that the convulsions led to the displacement of an atheromatous plaque somewhere in the arterial tree which passed distally and lodged in the left posterior tibial artery. The alternative explanation is that the severe and prolonged contractions of the leg muscles damaged the intimal lining of the artery, with resulting thrombosis. In spite of the absence of objective evidence of peripheral arteriosclerosis, it seems more likely that the symptoms were due to arterial obstruction by a dislodged atheromatous plaque, possibly from the aorta.

I am grateful to Dr. C. Worster-Drought for permission to publish this report and for his advice in its preparation.

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Toxic Hepatitis and P.A.S.

To date, three isolated instances of toxic hepatitis occurring during the course of treatment with *para*-aminosalicylic acid (P.A.S.) have been recorded (Cuthbert, 1950; Hurrell, 1950; Landsborough, 1951). The Medical Research Council Report (1950), which deals with the results of combined streptomycin and P.A.S. therapy, makes no reference to this complication; it therefore seems opportune to present a further case in detail.

CASE REPORT

A 2-para aged 31 was admitted to hospital on September 28, 1950, suffering from active bilateral pulmonary tuberculosis complicated by laryngitis. She had received treatment for pulmonary tuberculosis in a sanatorium in 1945, and remained well until 1950, when pregnancy supervened; she was confined in July of that year. At the time of admission to hospital active lesions involved the upper and mid-zones of both lungs, and there was advanced tuberculous infiltration with ulceration of the vocal cords and epiglottis.

Routine treatment was prescribed, and streptomycin dihydrochloride, 1 g. in divided daily doses, and sodium P.A.S., 15 g. daily, were given from October 3 until November 8. On October 31 the patient developed a rise in temperature, with rigor and sickness, and eight days later a generalized scarlatiniform erythema with gross oedema of the face was observed. Streptomycin and P.A.S. (total dosage 540 g.) were then stopped, and mepyramine hydrogen maleate ("anthisan"), 1 g. thrice daily, was administered. This was discontinued in favour of diphenhydramine hydrochloride ("benadryl"), 300 mg. a day, as from November 15.

On November 16 the temperature was 103° F. (39.4° C.), and she continued to be febrile for a further period of 18 days, fever being accompanied by rigor, sickness and diarrhoea, and albuminuria. Jaundice developed on November 18, became pronounced within a few days, and was accompanied by mental confusion and hallucinations.

A blood examination on November 17 showed: leucocytes, 12,500 (polymorphs 40%, lymphocytes 50%, monocytes 7.5%, basophils 2.5%). The plasma bilirubin content was 6.5 mg. per 100 ml.; blood urea, 30 mg. per 100 ml.; prothrombin time, 41 seconds (control 19 seconds); blood level of P.A.S., 0.52 mg. per 100 ml. Blood culture was sterile and W.R. negative.

Despite the evidence of hepatic dysfunction, streptomycin was restarted and was continued without further interruption until January 13, 1951 (total 94 g.), but P.A.S. was not again given, since, in the opinion of one of us (A. G. F.), it had been the probable cause of both the toxic erythema and the hepatitis. Lead acetate lotion was applied to the face and ung. oleum eucalypti to the remainder of the body.

Blood examination on November 22 showed: serum proteins, 5.75 g.% (albumin 1.6 g., globulin 4.15 g.); alkaline phosphatase, 39.5 units; bilirubin, 12.5 mg. per 100 ml.; thymol turbidity, 9 units. On November 25 jaundice was still present and the liver was moderately enlarged and palpable below the costal margin. One week later the generalized erythema had almost completely faded, and a fine branny desquamation was observed. The jaundice was subsiding, and the patient seemed to have improved, her mental attitude being much brighter. By December 8 both jaundice and erythema had cleared; the local treatment was now discontinued, and benadryl was gradually withdrawn.

Blood examination on December 6 showed: serum proteins, 6.25 g.% (albumin 3.6 g., globulin 2.65 g.); serum bilirubin, 1.8 mg. per 100 ml.; alkaline phosphatase, 16.4 units; thymol turbidity, 7 units; and on December 27 serum proteins 8 g.% (albumin 4.4 g., globulin 3.6 g.); alkaline phosphatase, 18.3 units; bilirubin, 0.6 mg. per 100 ml.; thymol turbidity, 8 units.

At the time of discharge from hospital, on June 1, the patient's general condition was satisfactory; she felt well and had gained weight. Radiological examination showed the pulmonary lesions in the upper zones to have become inactive; sputum had been tubercle-negative on three consecutive monthly examinations, and the tuberculous laryngitis was found to have healed. Over a month later she was still apyrexial and symptomless, and there had been no recurrence of rash; sputum was tubercle-negative, and the x-ray appearance of the lungs was unchanged.

DISCUSSION

The pathogenesis of this hepatic dysfunction is still obscure, and in consequence the evidence that P.A.S. caused a toxic hepatitis can only be presumptive. Nevertheless, a search for other possible causal factors, including contact infection, was unsuccessful.

Features peculiar to this patient, which differ from previous reports and are worth special mention, include:

(1) The widespread scarlatiniform character of the rash, associated with fever and collapse. Hitherto the sensitization rashes noted and described in association with P.A.S. therapy have most often been of morbilliform type, and there seems to be some evidence that untoward cutaneous reactions to P.A.S. are due to its salicyl radical (Horne, 1949; Kierland and Carr, 1949). Eruptions due to ingestion of salicylates are usually either scarlatiniform or morbilliform erythematous.

(2) Despite the gravity of her tuberculosis and the serious nature of the hepatitis she not only survived but was much improved on discharge from hospital, the tuberculous lesions having apparently healed. Of the other cases previously reported one died and two recovered.

(3) The total dosage of P.A.S. given was 540 g., dosage until the onset of symptoms being 435 g. (Cuthbertson gave 800 g., Hurrell 163 g., and Landsborough 270 g. until the onset of symptoms, total dosage 465 g.). It would appear that reaction is due to individual idiosyncrasy rather than to overdosage with P.A.S.

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