Case of Tuberous Sclerosis and Haemorrhagic Retinopathy (with Fundus Photographs)

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Tuberous sclerosis is a genetically determined disorder (Duke-Elder, 1940) characterized by mental deficiency, epilepsy, skin fibromata, and maldevelopment. Patients may not always present with the complete form of the disorder. It is said that the disease is usually fatal, the majority of patients dying before the age of 24. The patient in the following case is 38.

Case Report

The patient, who was born in 1928, was said to have been well up to 1945, when she began to develop fainting attacks or fits. In August of that year she attended Ayr County Hospital, where it was noted that she was nervous and that her fits seemed to be related to menstruation. A provisional diagnosis of petit mal was made and $\frac{1}{2}$ gr. (32 mg.) of phenobarbitone was ordered. Subsequently the use of thyroid was also advised. The late Dr. J. N. Tennent also saw her repeatedly at this time. He reported normal vision and no refractive error, but "considerable swelling of the right optic disc; rather cystic-like on nasal side." The fields of vision showed a possible defect in the right upper nasal quadrant. X-ray film of the skull, however, showed possible enlargement of sella, though this was not confirmed on repeat. Six weeks after the initial observation it was thought that *both* optic discs were swollen, the right more pronounced, and in April 1946 Dr. Tennent noted a "tapioca grain appearance" of the right disc. In September 1949 stabilization of the fits on phenytoin sodium and phenobarbitone was carried out, and in October she was admitted to Ballochmyle Hospital for investigation. The abnormal findings were confined to the electroencephalogram, which was carried out at Killearn Hospital. The report stated: "Gross dysrhythmia with low voltage from all leads. This indicates marked cerebral dysrhythmia—attacks epileptic." Several fits occurred under observation, and a psychiatrist reported "major and minor fits preceded menses," and, the following week, "Intelligence below average but not defective. No gross emotional disorder." On his advice she was given phenytoin 400 mg. daily in divided doses, benzedrine 5 mg. at midday, and phenobarbitone 1 gr. (65 mg.) morning and night. These reduced but did not eliminate the fits.

In March 1956 she had a nocturnal fit, after which she was completely aphasic for 10 days. In May she complained of defective vision and was referred to the medical outpatient department of Heathfield Hospital. The complaint appeared to be glare; there was a history of several attacks of status epilepticus, and for the first time a facial rash was mentioned. There was no abnormality in the fundi, but an iron-deficiency anaemia was found and treatment with primidone suggested, because of the mixture of petit and grand mal, in addition to iron therapy.

At review the anaemia had improved but the patient failed to come into hospital for fuller investigation.

In 1961 she developed a persistent cough, and from January 1964 she felt weak and unwell and developed gradually increasing oedema. She was admitted to the medical ward at Heathfield Hospital on 24 February 1964.

On examination the positive findings were marked clubbing of fingers and oedema of hands and feet, slow speech, and rather poor intelligence. X-ray film of chest showed an area of consolidation in the right lower lobe and recent bronchopneumonia was suggested. Sputum culture showed pneumococci. X-ray examination of the skull revealed no abnormal calcification in the cerebral hemispheres. The blood picture showed severe anaemia, and a sternal marrow puncture was therefore performed. The latter showed appearances compatible with the diagnosis of megaloblastic anaemia, and treatment initially by blood transfusion and then iron by mouth with injections of folic acid was given. By 14 July 1964 her haemoglobin had risen (from 4.1 to 15.4 g./100 ml.). Phenytoin was continued.

Fundus examination on 25 February revealed haemorrhages and exudates in the left eye with drusen of the optic nerve head and one exudate. It was suggested that this indicated a vascular retinopathy and tuberous sclerosis. This diagnosis was later confirmed (Figs. 1 and 3).

On 20 November 1964 (Fig. 2) all haemorrhages and exudates had cleared, though the drusen in the other eye naturally remained unchanged (Fig. 3). Her visual acuity with correction was 6/5 right and left when last seen on 13 October 1966.

Discussion

It is tempting to conclude from the wording of J. N. Tennent's report in 1946 that he had in mind the actual diagnosis made in 1964. His detailed description of the appearance of the discs shows that there was no great change in them

FIG. 1.—Left fundus on 28 February 1964, showing numerous retinal haemorrhages, mainly in the nerve fibre layer, and some "exudates."

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over this long time, though the number of drusen (R—14, all nasal; L—2 nasal, 1 superior temporal) may have increased (see Reese, 1940).

The term "drusen" is a confusing one. There are several conditions in which this term is used (Duke-Elder, 1940), but as applied to the optic disc the word was first employed in German literature as *Drusenbildungen* ("granular formations," apparently a mineralogical term (Fuchs, 1951)). Parsons anglicized the word to drusen in an excellent comprehensive review of the subject (Morton and Parsons, 1903), but up to the time of his paper only two cases had been diagnosed ophthalmoscopically before pathological examination.

Nodules occur in the retina in tuberous sclerosis (Van der Hoeve, 1920, 1923), including the disc, but the specific type known as drusen of the optic disc was not connected with this disease until Reese made the suggestion in 1940.

The megaloblastic anaemia was presumably the result of a folic acid block from the diphenylhydantoin (see Goodman and Gilman, 1965). This type of megaloblastic anaemia is uncommon (Williams, 1963). It appears to require long-continued use of the drugs (Badenoch, 1954; Berlyne *et al.*, 1955)—as was the case here.

FIG. 2.—Left fundus on 20 November 1964, showing complete clearing of the haemorrhages. One drusen can be seen at the upper temporal margin of the disc.

As can be seen from the fundus photographs, with treatment of the anaemia the haemorrhages in the left eye cleared rapidly, with restoration of the visual acuity (Figs. 1 and 2).

FIG. 3.—Right fundus on 20 November 1964, showing numerous drusen on the nasal side of the disc.

Summary

A case is described of probable tuberous sclerosis, or Bourneville's disease, in a woman who presented at the age of 16 with major and minor epileptic seizures. She also showed adenoma sebaceum and drusen of the optic disc, low intelligence, temper tantrums, and hysteria. The fits were partially controlled by phenytoin, benzedrine, and phenobarbitone from the age of 21, but subsequently she developed megaloblastic anaemia which required treatment with folic acid.

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