THYROID ANTIBODIES IN CEREBROSPINAL FLUID

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We recently had the opportunity of examining the spinal fluid from a patient with neurosyphilis and coincident Hashimoto's disease. Antibody to thyroglobulin was detected in appreciable concentration and has since been found in the C.S.F. of four other patients with autoimmune thyroiditis.

Methods

Antibody to thyroid protein was estimated, using an adaptation of the tannic acid haemagglutination technique (Boyden, 1951; Boyden and Sorkin, 1955). Details of the method in which sheep erythrocytes treated with dilute tannic acid are coated with an extract of human thyroid gland have been described previously (Owen and Smart, 1958). Serial twofold dilutions of an original 1 in 5 dilution of C.S.F. were made in a suspension of the sensitized cells, the highest dilution showing maximal haemagglutination being taken as the titre. Possible non-specific agglutinins were eliminated by preliminary absorption with washed sheep erythrocytes.

Sera and C.S.F. specimens from four of the patients were also examined for the presence of complement-fixing antibody to thyroid substance. The method used in the case of serum was identical to that employed by Roitt and Doniach (1958) except that the strength was determined by screening of a 1 in 5 dilution of serum with two and four times the minimum haemolytic dose (M.H.D.) of complement (C') instead of at 1 in 5 and 1 in 20 dilutions of serum. For spinal fluid, 2 M.H.D. of C' were used with three strengths of C.S.F.—namely, 1 volume of 1 in 5 dilution, 1 volume of undiluted C.S.F., and 2 volumes of undiluted C.S.F.

Clinical Data

Case 1.—Woman aged 54. Four-year history of shooting pains in the legs, together with swelling of the neck and loss of energy. Examination revealed tabes dorsalis. She had a moderately hard nodular goitre but showed no clinical evidence of disturbed thyroid function. Drill biopsy of the thyroid revealed Hashimoto's disease. ^{131}I uptake was normal. Serum: Wassermann and Kahn positive; cholesterol, 280 mg./100 ml.; proteins, electrophoresis, and flocculation tests normal. C.S.F.: Wassermann positive; 110 lymphocytes and 5 polymorphs per c.mm.; protein 160 mg./100 ml.; Lange 5554221000; sugar and chlorides normal.

Case 2.—Woman aged 60. Sixteen months' history of lassitude, intolerance of cold, and inability to concentrate. Examination revealed long-standing rheumatoid arthritis, large firm goitre, and marked hypothyroidism; no neurological abnormality. Drill biopsy of the thyroid showed Hashimoto's disease. ^{131}I uptake less than 5% in 24 hours. Serum: cholesterol, 515 mg./100 ml.; protein, 9.3 g./100 ml. (albumin 3.8 g./100 ml., globulin 5.5 g./100 ml.); electrophoresis showed marked increase in gamma-globulin; flocculation tests abnormal (zinc sulphate 16 units, thymol turbidity 7 units, thymol flocculation +++, cephalin cholesterol +++). C.S.F.: Wassermann negative; protein 121 mg./100 ml.; Lange 1110000000; sugar and chlorides normal.

Case 3.—Woman aged 47. Three months' history of swelling of neck. Known case of pernicious anaemia. Examination showed a small firm goitre; no signs of altered thyroid function; no neurological abnormality. ^{131}I uptake normal. Serum: Wassermann negative; cholesterol, 228 mg./100 ml.; protein, 7 g./100 ml. (albumin 3.4 g./100 ml., globulin 3.6 g./100 ml.); electrophoresis showed raised gamma-globulin; flocculation tests abnormal (zinc sulphate 32 units, thymol turbidity 9 units, thymol flocculation +, cephalin cholesterol ++). C.S.F.: Wassermann negative; protein, 39 mg./100 ml.; Lange, 1110000000; sugar and chlorides normal.

Case 4.—Man aged 69. Non-goitrous myxoedema, bilateral exophthalmos, no neurological abnormality. Malabsorption syndrome confirmed by usual investigations. ^{131}I uptake 5.7% at 24 hours. Serum: Wassermann negative; cholesterol, 175 mg./100 ml.; proteins, 5.5 g./100 ml. (albumin 3 g., globulin 2.5 g.); electrophoresis showed raised gamma-globulin; flocculation tests normal. C.S.F.: Wassermann negative; protein, 56 mg./100 ml.; Lange, 1110000000; sugar and chlorides normal.

Case 5.—Man aged 45. Ten weeks' history of muscular pain, swelling, and tenderness; intolerance of cold and gain in weight. Examination revealed a myxoedematous condition; small hard goitre; firm swollen muscles. ^{131}I uptake less than 5% at 24 hours. Serum: Wassermann negative; cholesterol, 436 mg./100 ml.; proteins, 9.6 g./100 ml. (albumin 5.4 g., globulin 4.2 g.); electrophoresis showed raised gamma-globulin; flocculation tests abnormal (zinc sulphate 24 units, thymol turbidity 15 units, thymol flocculation ++, cephalin cholesterol 0). C.S.F.: Wassermann negative; protein, 120 mg./100 ml.; Lange, 1110000000; sugar and chlorides normal.

Concentration of Thyroid Antibody by Tannic Acid Haemagglutination Method*

Case No.	In Serum	In C.S.F.
1	21 units	10 units
2	16 ,,	7 ,,
3	21 ,,	7 ,,
4	14 ,,	7 ,,
5	25 ,,	13 ,,

* In logarithmic units corresponding to number (n) of serial twofold dilutions of original 1 in 5 dilution of serum or C.S.F. Titre reciprocal = 5×2^n.

Results and Discussion

The relative concentrations of antibody in serum and C.S.F. are shown in the accompanying Table. The ratio between the two averages 10 logarithmic units or approximately 1,000 to 1. This is similar to that between serum and C.S.F. gamma-globulin (Tiselius, 1937; Gries *et al.*, 1953), and would be consistent with the hypothesis that C.S.F. antibody is derived direct from that in blood.

It is interesting to note that in two of the three patients shown to have complement-fixing antibody in the serum (Case 1+++, Case 3+++, Case 5±) this antibody could also be detected in the spinal fluid (Cases 1 and 5) despite the relatively low sensitivity of the method.

In the three patients without neurological disease who were myxoedematous at the time of examination, the total C.S.F. protein was found to be raised—markedly in Cases 2 and 5 and slightly in Case 4. This has been reported previously in untreated hypothyroidism and found to disappear with adequate

thyroid replacement therapy (Thompson *et al.*, 1929). The "paretic" Lange curve in the C.S.F. of Case 2, however, requires further explanation. It suggests a relative increase in C.S.F. gamma-globulin due to the combination of hypothyroidism and hyperglobulinaemia (found in many cases of autoimmune thyroiditis, including non-goitrous myxoedema). Such an increase was demonstrated electrophoretically in myxoedema by Bronsky *et al.* (1958).

Summary

Antibody to thyroglobulin was detected in the spinal fluid of five patients with autoimmune thyroiditis. In two out of three patients who had complement-fixing antibody in the serum, this antibody could also be detected in the C.S.F. In three patients who were hypothyroid the total C.S.F. protein was raised.

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SIMULTANEOUS OCCURRENCE OF INTRACRANIAL ANEURYSM AND ARTERIOVENOUS MALFORMATION

REPORT OF CASE SUCCESSFULLY TREATED

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Both cerebral aneurysms and arteriovenous malformations are well-recognized causes of spontaneous subarachnoid haemorrhage. However, the simultaneous occurrence of both lesions is a great rarity, and up to 1959 only 14 examples had appeared in the literature (Boyd-Wilson, 1959). Recently a 49-year-old woman was investigated at Killearn Neurosurgical Unit for subarachnoid haemorrhage; she was found to have an aneurysm arising from the right posterior inferior cerebellar artery and also an arteriovenous malformation situated in the posterior upper surface of the right cerebellar hemisphere.

Because of the paucity of such cases in the literature, and especially as both lesions were successfully treated, this case is reported with a brief review of the previous literature.

Case Report

A 49-year-old widow was admitted to Knightswood Hospital on December 26, 1959. For the previous five years she had suffered from headaches, which were occipito-vertical and often unilateral, though either side might be affected. At first the headaches were very severe in the afternoons after hard work, but recently they had been occurring in the early mornings. On the day of her admission she had wakened with headache, which she regarded at first as her usual attack of migraine. On bending down to wash her face, however, the headache became intense. She then noticed stiffness of her neck and heard peculiar noises inside her head; a little later she started vomiting and had diarrhoea.

On admission she complained of severe occipital headache, blurring of vision, and occasional double vision.

On examination she was found to be grossly obese. The blood-pressure was 180/110 and the apex beat was displaced 1 in. (2.5 cm.) outside the midclavicular line. The aortic second sound was accentuated. She was irritable and mildly confused. There was definite nuchal rigidity, with Kernig's sign. No localizing signs, however, were discovered: the deep tendon reflexes were brisk, but both plantar reflexes were flexor. A lumbar puncture disclosed a heavily blood-stained fluid at a pressure of 350 mm. of water. Gradually over the next few days the headache became less severe, but she occasionally felt dizzy and continued to see double. Three weeks later, on January 18, 1960, she suddenly became comatose; after lumbar puncture the cerebrospinal fluid was found to be uniformly blood-stained and under increased pressure. By the next day she had recovered consciousness, but was mildly confused and disorientated: the left plantar reflex was noted to be extensor.

These findings necessitated her transfer for further investigation at Killearn Neurosurgical Unit on January 22. On examination there, in contrast to her condition four days previously, she was alert and fully orientated. The nuchal rigidity persisted. Ophthalmoscopic examination revealed marked papilloedema with subhyaloid haemorrhages and attenuated arteries. With some defect of fixation the visual fields showed a left homonymous cut, complete on the right and involving the lower quadrant on the left. On deviation of the eyes to the left a few nystagmoid movements were observed in the initial phase of the deviation. Other cranial-nerve functions were normal. Muscular tone and power were undisturbed and sensation was intact throughout. Both plantar reflexes were flexor and the deep reflexes were symmetrical. No bruit was audible over the orbits or over the parieto-occipital areas.

Bilateral carotid angiography on January 22 showed no deformity apart from some spasm of the terminal portions of both internal carotid arteries. Four days later (January 26) a right vertebral angiogram revealed a small aneurysm arising from the right posterior inferior cerebellar artery, and an arteriovenous malformation probably situated on the upper surface of the right cerebellar hemisphere (see Figs. 1 and 2).

On January 28—a month after the first haemorrhage—exploration of the right posterior fossa was carried out by Mr. A. Paterson. The right posterior inferior cerebellar artery was identified, and was noted to be very tortuous and sclerotic. The artery was followed distally in an anterior direction around the anterior aspect of the tonsil and then posteriorly on to the hemisphere where it broke into two small branches. No aneurysm could be found and eventually the posterior inferior cerebellar artery was clipped a considerable distance from its origin. The impression at the time was that the clip was distal to the aneurysm. The upper dural flap was then raised until the upper surface of the cerebellum could be seen, and close