Thymectomy in Subacute Sclerosing Leucoencephalitis

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Subacute sclerosing leucoencephalitis is a well-known inflammatory affection of the central nervous system occurring predominantly during childhood and adolescence. Clinically, the initial phase of mental disturbances is followed by extrapyramidal signs associated with hyperkinesis. The E.E.G. is typical. In the cerebrospinal fluid gamma-G-globulins are raised and qualitatively altered. Subacute sclerosing leucoencephalitis is nearly always fatal, death occurring within a few months or some years after onset of the initial signs.

Sixty-nine patients with subacute sclerosing leucoencephalitis have been observed by us, six of whom are still alive. We think its incidence has increased in Czechoslovakia during the past 20 years, and we have therefore tried to find new methods of treatment. The present report deals with one patient with subacute sclerosing leucoencephalitis who was treated by thymectomy.

Case Report

Towards the end of his 13th year the patient showed a deterioration in his intellectual capacity, and his school results became unsatisfactory. There was a slow development of periodic choreiform hyperkineses of the muscles of the face and hands, particularly of the right one, together with a slight flexion of the trunk. In May 1965 he began to complain of deteriorating vision. He was no longer able to dress himself nor could he use common objects, such as a knife and fork. In September he had his first generalized epileptic fit.

On examination he could control his movements only with difficulty; he was negativistic and repeated sentences and words in a stereotyped way, and joked inappropriately. Hypertonia of the muscles and higher postural reflexes appeared, which were more marked in the right hand and foot, while there was also choreoathetosis, repeated at intervals of four to nine seconds. There was an inconstant Chaddock sign and fanning of the toes, more consistently on the right, but no patellar or ankle clonus was ever elicited. No sensory loss was found. Psychiatric findings suggested a hebephrenic syndrome arising out of leucoencephalitis. The E.E.G. picture showed periodic, high, diffuse delta waves typical of subacute sclerosing leucoencephalitis. In the cerebrospinal fluid there were 3 cells/cu. mm., predominantly lymphocytoid with reticulomonocytic elements; the total proteins were 45 mg./100 ml., the colloidal gold curve was 666543110; immunoelectrophoresis revealed a gamma-C-fraction and an increase in the anodic part of gamma-G-globulins. In the ventricular fluid 58 mg. of total protein per 100 ml. was found and the gold curve was 455543210.

The complement-fixation reaction (Běhounková, Kadlec, and Kolář, 1966), with 0.3 ml. of the patient's C.S.F. and a standardized antigen prepared from the brain of a patient with subacute sclerosing leucoencephalitis, was strongly positive (+ + +). The antigen used in the complement-fixation test was tested on 26 patients with subacute sclerosing leucoencephalitis, from 0.1 to 0.5 ml. of spinal fluid being used. With one exception the complement-fixation reaction in cerebrospinal fluid was positive at various degrees (+ to + + +) in these patients. The antigen as described here is not absolutely specific for subacute sclerosing leucoencephalitis, as it reacted to the spinal fluid of five patients out of a total of 288. These five all had inflammatory diseases of the brain.

The complement-fixation reaction is graded according to the amount of complement used in comparison with a control; + indicates use of 1 to 2 units, + + corresponds to 2 to 3 units, and if more than 3 units of complement are used the reaction is graded + + +. The antigen did not react with the serum of the control subjects, but with the sera of two out of 26 patients with subacute sclerosing leucoencephalitis, and then only with an intensity of +.

Radiological investigation showed enlargement of the spleen, liver, and thymus (Fig. 1). In the serum the acid-phosphatase concentration was 7.7 units/100 ml., and the alkaline-phosphatase concentration 20.0 units/100 ml. The levels of fibrinogen, plasmin, plasmogen, and antiplasmin were within physiological limits. Brain biopsy showed a perivascular mononuclear infiltration, particularly around the veins, and a pericapillar increase in acid mucopolysaccharides (stained with alcian blue). Inclusion bodies were not found. Immunoelectrophoresis of brain tissue extract demonstrated as increase in gamma-G-globulins. By means of the transbronchial diagnostic pneumomediastinum with oxygen (Pěgřim, Říha, and Simeček, 1957), hyperplasia of the thymus was shown. Attempts

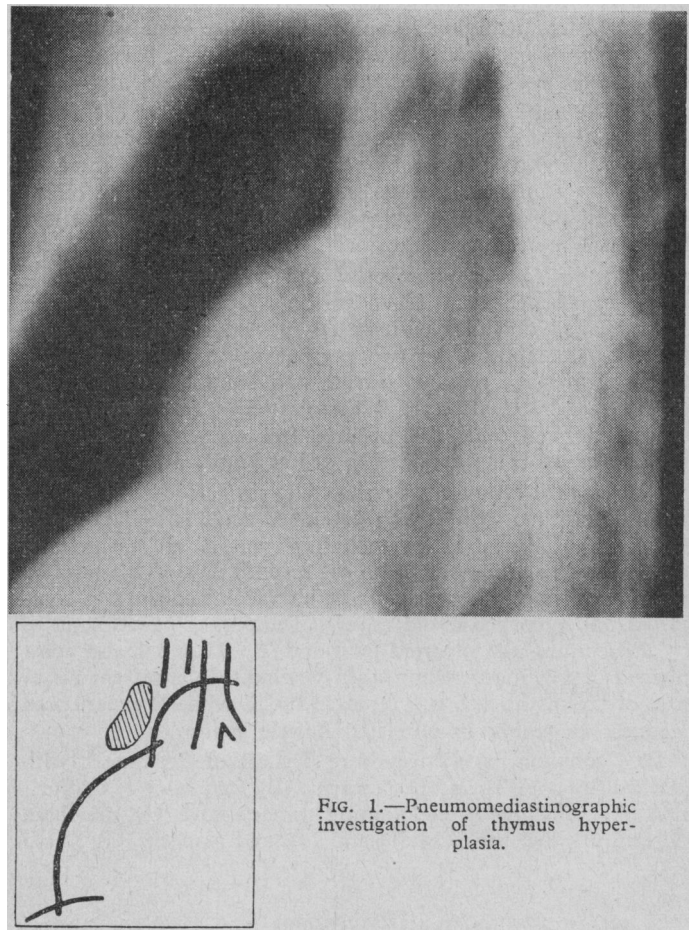

FIG. 1.—Pneumomediastinographic investigation of thymus hyperplasia.

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at virological isolation from the biopsied brain material and from the C.S.F. were persistently negative.

Despite corticosteroid treatment the symptoms steadily got worse. Because enlargement of the thymus had been found thymectomy was performed in November 1965 ; the thymus weighed 19.8 g. Histologically the thymus showed disappearance of the border between the cortex and the medulla of the thymus, hyperplasia of the reticular cells (Fig. 2), and numerous enlarged cystically altered Hassall's corpuscles (Fig. 3). Histochemically the substance in Hassall's corpuscles showed a positive reaction after staining by periodic-acid–Schiff. Alcian blue staining reaction was also positive.

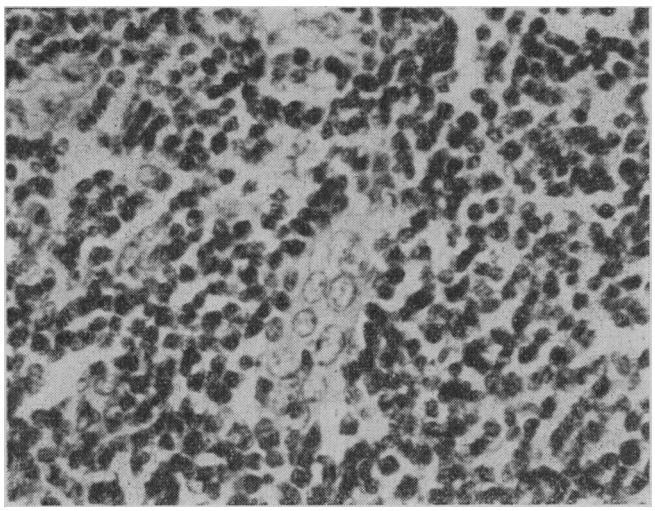


FIG. 2.—Collection of hyperplastic reticular cells. (H. and E. ×126.)

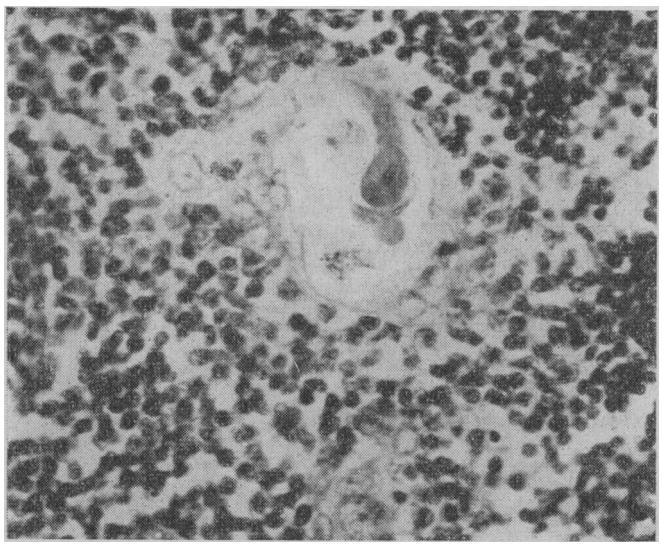
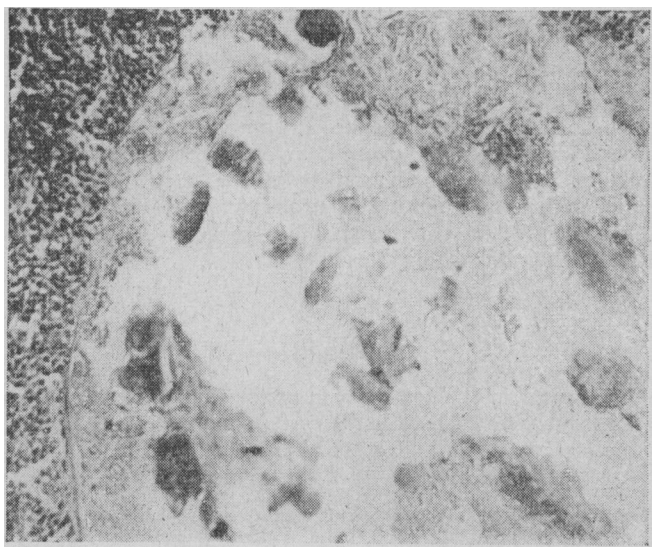


FIG. 3.—Above, Hassall's corpuscle with atypical arrangement of reticular cells. (H. and E. ×106.) Below, Cystically changed Hassall's corpuscle. (H. and E. ×63.)



Within two weeks of thymectomy the patient's hebephrenic syndrome had improved, and this improvement has been maintained, together with a diminution in the extrapyramidal signs. After four months a repeat examination of the C.S.F. was carried out. This showed a concentration of 40 mg./100 ml. (with 22% of gamma-globulin) and a gold curve of 223321000. Autoantibodies were still present in the C.S.F. The E.E.G. picture still showed typical pseudorhythmic R-complexes. Agar-gel electrophoresis of the serum showed two abnormal fractions of gamma-G-globulins of slow electrophoretic mobility. The acid-phosphatase concentration fell to 5.9 units/100 ml.

The duration of subacute sclerosing leucoencephalitis from the onset of the first clinical signs of the disease has so far been more than two and a half years.

Control Examination.—Seventeen months after thymectomy the patient is free of seizures and hyperkinesias. Pyramidal signs are lacking. This improvement of the neurologic syndrome is unfortunately not matched by a similar alleviation of the psychologic impairment. The patient is imbecile, though he can take care of his needs, and recognizes relatives and physicians. He is still on prednisone and antiepileptics.

Discussion

Enlargement of the thymus was also seen in three other patients out of nine with subacute sclerosing leucoencephalitis examined by pneumomediastinum produced by the transbronchial route with oxygen. Fig. 4 shows thymic hyperplasia in a 15-year-old boy with subacute sclerosing leucoencephalitis. In the course of prolonged treatment with corticosteroids,

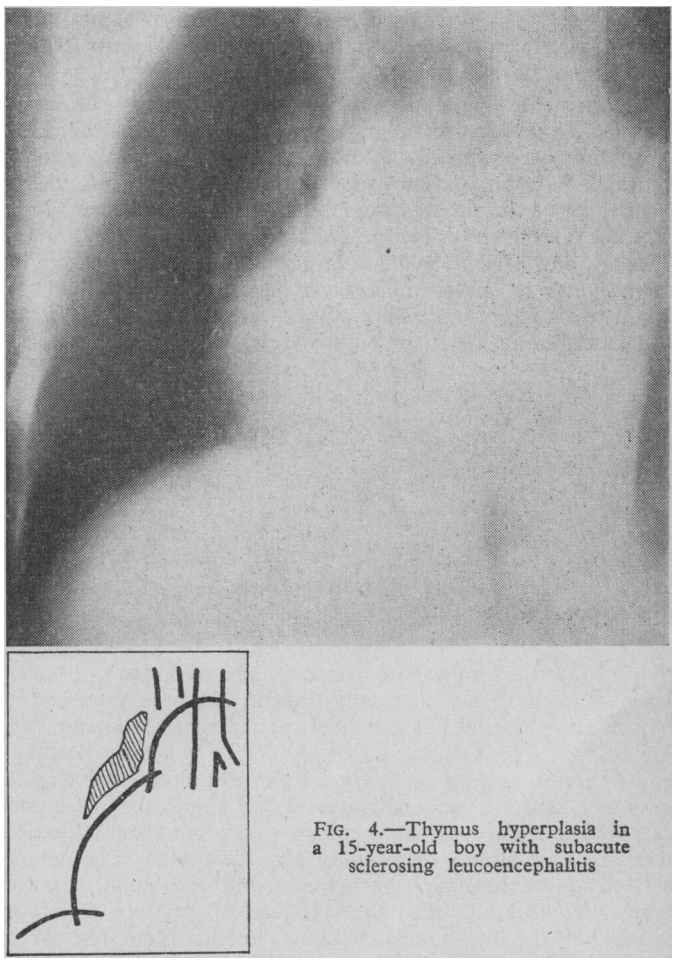


FIG. 4.—Thymus hyperplasia in a 15-year-old boy with subacute sclerosing leucoencephalitis

the clinical picture showed apparent stabilization of the abnormal neurological signs in these patients, and the 15-year-old boy has so far lived for more than four years since the onset of the illness.

Subacute sclerosing leucoencephalitis is accompanied by an increase and a qualitative change in the cerebrospinal fluid gamma-G-globulins (Kolář, 1966a) and by appearance of autoantibodies against the brain-tissue antigen in the C.S.F. of subacute sclerosing leucoencephalitis patients (Běhounková *et al.*, 1966). The symptoms and laboratory manifestations of subacute sclerosing leucoencephalitis may have a remittent course. Other manifestations of the disease include splenomegaly, hepatomegaly, and pathological changes, mainly in the cathodic part of the serum gamma-G-globulins (Kolář, 1966c ; Kolář, Obručník, Fárková, Dvořák, and Musil, 1967).

Examination of biopsy or necropsy brain tissue from patients with subacute sclerosing leucoencephalitis has shown mainly perivenous collection of mononuclear cells which probably contain glycolipoprotein complexes, since these fluoresce when examined by ultraviolet light. Moreover, the presence of abnormal gamma-G-globulins in these specimens from patients with subacute sclerosing leucoencephalitis has also been shown (Kolář, Dencker, Obručník, Černá, and Skatula, 1966).

The perivascular mononuclear infiltrates in the brain, persisting for months to years, the increase and the qualitative changes of gamma-G-globulins in brain tissue, the participation of the extraneural reticuloendothelial system in the development of subacute sclerosing leucoencephalitis, together with the presence of antibodies against a brain-tissue extract used as antigen in the cerebrospinal fluid, all suggest a neuroimmunopathological basis for this disease. This process seems to be not completely analogous with the immunological events leading to experimental allergic encephalomyelitis.

Involvement of the thymus in the development of autoimmune processes, particularly those in which delayed hypersensitivity is concerned, is now generally accepted (Good, Finstad, Peterson, Kellum, and Surtherland, 1965 ; Loghem, 1965). Nevertheless, thymectomy, especially in older subjects, does not prevent the appearance of autoantibodies (Kerr, Duran, Thomas, and Wright, 1965). So far the therapeutic effects of thymectomy in myasthenia gravis have not necessarily been found to be beneficial. Some improvement after thymectomy was described in a patient with systemic lupus erythematosus (Mackay, Goldstein, and McConchie, 1963), but this could be attributed to prednisolone therapy.

The improvement in the neuropsychiatric symptoms in our patient with subacute sclerosing leucoencephalitis is noteworthy, though it can hardly be ascribed to the corticosteroid therapy, which was given in small doses. Nevertheless, a spontaneous remission of the subacute sclerosing leucoencephalitis, which was accompanied also by a fall in the cerebrospinal fluid gamma-G-globulins, cannot be excluded in this case.

Thymic hyperplasia in patients with subacute sclerosing leucoencephalitis suggests that the "central" lymphoid tissue may play a part in the development of the disease. Possibly the thymus influences the development of subacute sclerosing leucoencephalitis unfavourably by supporting the autoimmune histotoxic process, but the right moment to recommend thymectomy in patients with subacute sclerosing leucoencephalitis will be determined only by careful study of further cases of the disease.

Summary

Enlargement of the thymus may be found in some patients in the course of subacute sclerosing leucoencephalitis. We describe a case of subacute sclerosing leucoencephalitis treated by thymectomy in which considerable improvement resulted.

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Renal Colic

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Since 1958 an "immediate" intravenous pyelogram (I.V.P.), taken while the pain is actually present, has been used in the routine investigation of cases of suspected renal colic admitted to the Pontefract General Infirmary. This is a busy hospital, and it has often been necessary for the consultants to delegate to junior staff the responsibility for the initial diagnosis and supervision of the *x*-ray films, which were often taken by junior radiographers during the evening and the night. The details of the *x*-ray examination have varied, but in general we have taken a control film, and films 10 and 30 minutes after the injection of the intravenous medium. Further films were taken until the ureter was outlined ; this may not happen until as long as 24 hours, but the rate of appearance of the nephrogram can be a guide to the timing of the later films.

While a typical attack of renal colic can be recognized confidently, in the atypical attack an immediate intravenous pyelogram showing delayed excretion, a nephrogram, and slow filling of the kidney drainage system compared with the normal side provides impressive confirmation of the obstruction to the kidney and permits the use of strong analgesics. The further management of the case depends on the demonstration of the cause of the obstruction.

Results

The results in the 146 cases in which immediate I.V.P. was carried out were: stones in 84 cases, abnormal *x*-ray films in 27, normal *x*-ray films in 31, and other diseases in 4.

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