SUB ACUTE COMBINED DEGENERATION

The incidence in a series of 110 cases of Pernicious Anaemia

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The frequency of occurrence of subacute combined degeneration of the spinal cord in patients with pernicious anaemia has long been a subject for discussion. Widely divergent figures, ranging from 20 to 80 per cent.,^{1,2} have been quoted at different times. As a whole, it would appear that the older writers regarded it as more common than would be accepted by most people today, but no recent surveys seem to have been published. We thought it a matter of interest to investigate the point in a series of cases of pernicious anaemia seen at the General Hospital, Birmingham.

Material

The records of all patients admitted to hospital with pernicious anaemia in the seven-year period from 1948 to 1954 have been examined. In all they comprise 110 cases, of which 80 were female and 30 male; this preponderance of the female sex is presumably the result of biased sampling since it is not an expected characteristic of the disease. The average age at onset of symptoms of disease was 56 and 59 years respectively for males and females with ranges in each case from 38 to 69 and from 27 to 81. The diagnosis of pernicious anaemia was chiefly based upon the presence of macrocytosis (mean corpuscular volume over 94 c.μ.), histamine-fast achlorhydria, bone-marrow studies (where available) in which most showed megaloblastosis and/or other features of liver factor deficiency such as giant metamyelocytes, macropolycytes and multi-segmented megakaryocytes, and upon the observation of an adequate reticulocyte response to therapy. In a number of cases the newer diagnostic techniques have also been relied upon for ancillary information; for example, assay of the serum B₁₂ level and the decrease in serum iron content following B₁₂ therapy.

Whilst there is little difficulty in constructing exact criteria for the laboratory diagnosis of pernicious anaemia, the diagnostic classification of

its neurological complications is a rather more complex problem.

It is well known that the peripheral nerves as well as the spinal cord may suffer simultaneous damage, and it is impossible (short of full autopsy examination) to determine the contribution which each makes to symptomatology, since one may mask the other clinically. We have assumed that cases presenting with distal paraesthesiae, and purely peripheral motor and sensory signs with absent limb jerks, hypotonia, and muscle tenderness are examples of peripheral neuropathy without spinal cord lesion. On the other hand, patients with signs of pyramidal tract disorder (as witnessed by muscular weakness, increased tone, exalted tendon reflexes, absent superficial abdominal reflexes, and extensor plantar responses), and/or signs of posterior column involvement (shown by defect of position and vibration sense, and disturbance of co-ordination and balance), we have taken to be cases of pure subacute combined degeneration of the cord. Since cord dysfunction is the more important factor from the therapeutic and prognostic point of view, we have regarded mixed cases showing features of both categories (myelopathy and neuropathy) as belonging essentially in the subacute combined degeneration group.

One of the difficulties which arises in the assessment of neurological signs in elderly people is a progressive senile degeneration of the nervous system. Howell (1949)³ made a comprehensive study of 200 Chelsea pensioners between the ages of 65-90 years. He found that the motor power was good or fair in 91 per cent., and the plantar responses were flexor in 95 per cent. of cases. However, tendon jerks showed greater abnormality and in over half of the cases over 70 years the ankle jerks were absent, the percentage with absent knee and ankle jerks increasing rapidly with age. Sensory disturbance proved even more difficult to assess, but joint position sense was normal in 98 per cent. Vibration sense was

present in 87 per cent. at the knees and in 56 per cent. at the ankle in the age-group 60-75 years. The neurological findings in our patients over 60 years were specially scrutinized, and where possible those considered to be due to senility were excluded.

TABLE I

Type of Neurological Disorders	Males	Females	Total	Per cent.
S.C.D. { Myelopathy 40% { Myelopathy and Neuro- pathy ..	7	24	31	28
Neuropathy ..	0	13	13	12
Pernicious anaemia ..	3	10	13	12
alone ..	20	33	53	48
Totals ..	30	80	110	100

110 cases of pernicious anaemia:
With neurological signs .. 57
Without neurological signs .. 53

As will be seen from Table I neurological signs were present in 57 of our 110 cases. In 13 (12 per cent.) the picture was one of uncomplicated neuropathy, whilst in the remaining 44 there was unmistakable evidence of cord damage of postero-lateral column type, either pure (31 cases (28 per cent.)), or mixed with peripheral nerve lesions (13 cases (12 per cent.)). Thus 40 per cent. of our series of 110 cases of pernicious anaemia had definite evidence of subacute combined degeneration of the cord. No correlation was apparent between the severity of the anaemia and the presence of neurological signs of any sort. In fact six patients with S.C.D. had red blood cell counts of 4.5 million or over.

Examination of the age of onset of symptoms showed that the majority (36 of a total of 53) with pernicious anaemia alone were over 55, and that those with neurological signs were again more numerous over this age (37 of a total of 57). These figures suggest that the incidence of neurological complications is no higher in the young

than in the old. Lastly, an attempt was made to correlate the length of history of illness with the appearance of neuropathy or myelopathy. Statistical analysis showed no significant difference between the group with pernicious anaemia and those with nervous semeiology.

The efficacy of therapy in those with neurological signs could not be assessed, for during the period under study there was a great influx of new liver preparations, and vitamin B₁₂ became available during the latter years. However, only one case of S.C.D. relapsed after reaching maximal improvement. This patient had stopped liver therapy for six months and at the end of this period both the anaemia and the S.C.D. had progressed markedly.

This series shows a preponderance of female (80) over male (30) cases. No satisfactory explanation could be found for this bias of case selection, but it is of interest that this trend is a constant feature of the analysis of all case-records of the United Birmingham Hospitals, 1950-55 (Waterhouse personal communication).

Summary

A survey of 110 cases of pernicious anaemia is presented. Subacute combined degeneration of the cord was present in 40 per cent. All cases of senile neurological degeneration were excluded. The signs of S.C.D. were not related to length of symptoms of B₁₂ deficiency, the age of the patient or the degree of anaemia. This high figure stresses the need for careful neurological examination in the diagnosis and follow-up of pernicious anaemia.

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