A CASE OF PERIARTERITIS NODOSA OF THE CENTRAL NERVOUS SYSTEM.

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This is a clinical and pathological report on an unusual case of periarteritis nodosa in which the disease was confined chiefly to the brain and spinal cord. The diffuseness, variability and intermittency of the neurological signs and symptoms over a period of two years, in the absence of many of the more usual somatic manifestations of periarteritis nodosa, was responsible for the nature of the disorder not being diagnosed before death. Mental symptoms were prominent throughout the last year of illness. T.A.B. pyrexic therapy coincided with a marked remission in physical and mental symptoms, whilst arsenical therapy appeared to precipitate the terminal exacerbation of symptoms.

Case History.

C. H—, a man born in 1892, had a medical history of chronic catarrh of the upper respiratory tract, development of deafness in the left ear in 1937, and jaundice in 1940. It is not certain whether or not sulpha drugs were given for any of these conditions. During 1944, in his 51st year, he began to experience occasional attacks of stabbing pain in the left side of his face, accompanied by pyrexia. In February, 1946, he developed an atypical left trigeminal neuralgia after an attack of influenza with pyrexia. This was relieved by injection of the Gasserian ganglion with alcohol, but was soon followed by a new set of symptoms. He developed an intermittent temperature of up to 100° F., with stabbing pains in the back of the neck followed some weeks later, in early March, 1946, by vomiting and giddiness. He was examined by a neurologist, who found rotary nystagmus on looking to the right and analgesia over the first and second divisions of the left fifth cranial nerve. The C.S.F. showed 110 cells per c.mm. (polymorphs 24 per cent., lymphocytes 76 per cent.) and 80 mgm. of protein per 100 c.c. There was inability to distinguish heat and cold over the skin of the right leg with a relative analgesia and anaesthesia below the level of the ninth dorsal segment on the right side.

By May, 1946, the patient was complaining of diplopia, due to a partial palsy of the right third cranial nerve, with weakness of the right hand and right lower limb and attacks of painful cramp. The C.S.F. showed 70 cells per c.mm. (16 per cent. polymorphs, 84 per cent. lymphocytes), and 100 mgm. protein per 100 c.c. The Kahn and Wassermann tests were negative. In June he was given a course of penicillin which made no impression upon his physical condition. From September to December, 1946, he had occasional rises of temperature to 100° F. with giddiness and unsteady gait, and by December was beginning to complain of insomnia, depression and difficulty in concentration. He was very restless and unduly agitated over money matters. At this stage neurological examination revealed: right pupil slightly larger than the left one; left-sided ptosis, anaesthesia
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over the first and second trigeminal areas on the left side; slight weakness of left facial movement, tongue protrusion slightly to the right, marked slurring, dysarthria and a diminution in muscle tone and weakness in the right arm and leg. There was impairment of postural sensation on the right side with extreme tenderness on pressure over the cervical nerve roots. The tendon reflexes in the right arm were brisk and in the left arm absent. The left abdominal reflexes were unobtainable, but the right ones were present. The knee and ankle jerks were brisk, the right plantar reflex extensor. Sensory testing was unsatisfactory because of his drowsy condition. About a month later his mental state began to deteriorate more rapidly and he became confused, disorientated and deluded; speech became incoherent and his conduct mildly manic. The C.S.F. was under normal pressure but contained an excess of lymphocytes.

On admission to Holloway Sanatorium on 12, March 1947, he was restless and unpredictable in his conduct, getting out of bed and refusing all food. His conversation was almost unintelligible and he could not give coherent replies to even the simplest questions. There was generalized muscular weakness and complete inability to fend for himself. He had gradually become bedridden and dirty in his habits. The erythrocyte sedimentation rate was 25 mm. in one hour, haemoglobin 92 per cent. (Haldane), and total red cell count 4·15 millions per c.m.m., total white cell count 7,200 per c.m.m. (polymorphs 69 per cent., eosinophils 1 per cent.). The Kahn reaction was negative, the blood pressure 150/100. The urine contained no abnormal constituents. The C.S.F. was not under increased pressure, but contained 52 lymphocytes per c.m.m., a total protein of 60 mgm. per 100 c.c. and gave a Lange curve of 112 10000.0.

A purely descriptive diagnosis of "confusional syndrome with extensive neurological complications" was made. The condition was thought by the consulting neurologist to be an unusual form of relapsing encephalomyelitis due to a virus or torula organism.

As there was no obvious specific form of treatment a course of non-specific protein therapy (Parfitt, 1938) was started on March 24, 1947, four million T.A.B. vaccine bacilli being given intravenously on the first occasion and the dose doubled at each subsequent injection. Treatment was given twice a week for two months, producing pyrexias in the earlier stages up to 103° F. By the end of this period the patient's mental condition showed a definite improvement; he was cleaner in his habits, had greater emotional control and, although ataxic, was up and about, fully dressed, and enjoyed the radio and reading. He was orientated for time and place, recognized and conversed with his relations and made enquiries about their welfare. A further C.S.F. examination revealed that the cells had dropped to 3 lymphocytes per c.m.m., the total protein to 40 mgm. per 100 c.c. and the Lange curve to 00000.000. The duration of this period of improvement was about five weeks.

On 2 June, 1947, his treatment was changed, after eight days interval, to bi-weekly injections of neo-arsphenamine. This was done because T.A.B. vaccine was now failing to produce any appreciable pyrexia. Three weeks later he developed an itchy urticarial rash on both arms. This coincided with the beginning of rapid general physical and mental relapse and progressive deterioration. After two weeks' respite all injections were stopped on 4 July, 1947. By that date the total protein in his C.S.F. had risen to 90 mgm. per 100 c.c., the colloidal gold test was still entirely negative, and his condition was becoming extremely grave. On 30 July, 1947, his wife decided to take him home, and he died five months later, on 25 November, 1947, aged 55, after several "fits," followed by paralysis and coma, which his home doctor considered were due to sudden obliteration of large cerebral arteries.

PATHOLOGICAL REPORT.

At autopsy no abnormality, and in particular no infarct, was observed in any of the general organs or in the uncut brain and spinal cord, but examination after fixation revealed small nodules, just visible to the naked eye, along the course of several medium-sized arteries, particularly the anterior spinal artery. Only the brain, spinal cord, pituitary and spleen were preserved for further investigation.

Coronal sectioning of the brain showed both lateral ventricles slightly dilated and cystic softening in the anterior limb and genu of each internal capsule (Fig. 1). There was no evidence of petechial, or larger, haemorrhages.
Histological investigation revealed striking changes in medium-sized and small arteries especially at the base of the brain and around the spinal cord. In the interpeduncular fossa of the midbrain the posterior perforating arteries were surrounded by a mass of necrotic tissue (Fig. 2). This was made up of nuclear debris and contained no caseation, no giant cells and (on repeated examination) no tubercle bacilli. Many of the arteries displayed severe necrosis of the media and infiltration of the whole wall of the vessel by lymphocytes and fibroblasts, but no eosinophils or giant cells. The elastica interna was split and broken in places. The intima was necrosed to a lesser degree than the media and was occasionally proliferated, causing reduction in the lumen of some of the affected vessels, but seldom to the extent of complete obliteration. The adventitia was heavily prolif erated and infiltrated by lymphocytes (Fig. 3). Evidence of old recanalized thrombosis of the lumen was observed within the most conspicuous nodule on the anterior spinal artery. One aneurysmal dilatation was noted close to the origin of the left middle cerebral artery. Not all the arteries in an affected region displayed these changes, for instance, around the periphery of any given level of the cord. Another feature was that as the same vessel was followed upwards or downwards in serial sections the pathological changes came and went.

The subarachnoid space contained collections of lymphocytes and plasma cells, especially over the base of the brain and around the cord. The cerebral cortex displayed no noteworthy histological abnormality beyond chromatolysis of about one-third of the Betz cells (presumably due to retrograde degeneration from the softening in the internal capsules). The basal ganglia, internal capsule and thalamus, on the other hand, exhibited softenings (white infarcts) of various sizes and ages, roughly symmetrical in the two hemispheres. The ganglionic arteries in and around these regions showed all stages of occlusion and cuffing with lymphocytes and plasma cells. Similar but more irregular areas of softening were scattered throughout the medulla and the tegmentum of the midbrain and pons. Both temporopontine tracts were heavily gliosed. The Purkinje cells of the cerebellum displayed homogenizing necrosis over wide areas. Within the cord pathological small arteries and early softening were apparent especially in the lateral white columns at lower thoracic levels and the fasciculi involved were degenerating. Some of the vasa nervorum of both anterior and posterior nerve roots showed the periarteritic changes, especially at lumbar levels. Vessels of
FIG. 2.—Posterior ganglionic arteries in the interpeduncular fossa, showing inflammatory changes typical of periarteritis nodosa (H. and E. × 65).

FIG. 3.—Higher power view of a section of the anterior spinal artery, showing the destruction of media, the proliferation of adventitia and intima, and the infiltration by lymphocytes. (H. and E. × 250.)
the pituitary and of the spleen showed no such changes. There were no amyloid
changes in the spleen.

DIscussion.

There would seem no reasonable doubt that the condition is one of uncom-
plicated periarteritis nodosa. The primary (arterial) and secondary (infarctual)
pathological appearances are typical of periarteritis nodosa in every detail
(Kernohan and Woltman, 1938; Malamud and Foster, 1942; Miller and Daley,
1946). Syphilis and tuberculosis can be excluded on serological and bacterio-
logical as well as histological grounds. Thromboangiitis obliterans affecting
the brain (Davis and Perret, 1946/7) cannot be confused pathologically, although
it may produce a similar mental picture (Perk, 1947). Temporal arteritis
appears to be confined to individuals over the age of 55, has a good prognosis
apart from its effects on vision, and is generally characterized by multinuclear
giant cells within the necrotic media (Cooke et al., 1946; Crosby and Wads-
worth, 1948; Miller, 1949). On the clinical side, the initial symptoms, the
fluctuating location of lesions, their remittances, the mild pyrexia especially
during exacerbations, and the over-all gradual deterioration, are typical general
features of periarteritis nodosa. There were, however, no manifestations
related to the organs most commonly affected by the disease; no nephritic
syndrome, no tachycardia disproportionate to temperature, no polymorphic
leucocytosis or eosinophilia, no skin or muscle nodules. This accords with the
macroscopic autopsy findings.

A persistent low luetic form of Lange colloidal gold curve in the C.S.F., in
the absence of any other serological reaction related to syphilis, was recorded
in the personal case described by Malamud and Foster; persistent high total
protein and lymphocyte cell-count in the C.S.F. had previously been com-
mented upon in the literature.

Involvement of the central nervous system, previously variously estimated
to have occurred in from 8 per cent. to 20 per cent. of cases of periarteritis
nodosa described in the literature, was found early in the symptomatology in
7 of 16 fatal cases investigated by Parker and Kernohan (1949). Four of these
seven had cerebral involvement; two had been diagnosed as cases of multiple
cerebral abscess, one as a rapidly growing glioma and the fourth as a case of
cerebral arteriosclerosis.

The aetiology of periarteritis nodosa was for long obscure. Kernohan and
Woltman and Malamud and Foster emphasized the inflammatory appearances of
arterial lesions. Considerable experimental evidence has been accumulated
since the pioneering work of Rich and Gregory (1942) to indicate that allergy
plays a big part in the aetiology. Owing to the frequency with which specific
bacterial infections, as well as nonspecific minor respiratory infections, ante-
cede the illness, the antigen has been suspected to be bacterial in origin. Miller
and Daley, however, after a well balanced review of the clinical and exper-
imental evidence, like many other recent investigators, favour the view that
the condition represents a non-specific hypersensitive reaction of anaphylactic
type to a variety of antigens. They consider that there is much evidence that
the changes in the blood vessels differ only in degree from the less severe acute
arteritis seen in acute rheumatism. These changes Miller (1949) conceives
of as due to the repeated whealing of chronic recurrent urticaria of the blood vessels leading ultimately to multiple focal necrosis of their walls. Among other clinical evidence in support of allergic pathogenesis is Rosenak and Maschmeyer’s (1945) and Black-Schaffer’s (1945) description of cases of periarteritis nodosa apparently determined by a hypersensitivity to sulpha drugs; and Miller and Nelson’s (1945) and Turner and Paterson’s (1946) reports, each of one case, of periarteritis nodosa where the onset seemed clearly attributable to the exhibition of antisyphilitic arsenical drugs. In this connection it is of interest that arsenic has been employed as a form of treatment for periarteritis nodosa (Kernohan and Woltman).

Whether in the present case arsenical (or sulpha) drugs had been administered to the patient before the onset of his neurological illness is not known, but certainly the neo-arsphenamine injections 18 months later seemed to accelerate his physical and mental deterioration. The writers can find no record that pyrexial therapy has ever before been reported to appear to benefit periarteritis nodosa of the central nervous system.

SUMMARY.

The clinical and pathological findings are described in a fatal case of periarteritis nodosa confined largely to the central nervous system and associated throughout the last year of life with conspicuous mental symptoms. The diffuse, variable, intermitting, almost purely neurological signs and symptoms defied correct clinical diagnosis throughout an illness of two years’ duration. The cerebrospinal fluid displayed an abnormal amount of total proteins, increased lymphocytes and a low luetic type of colloidal gold curve. A striking remission in the physical, serological and mental state of the patient coincided with a two months’ course of pyretotherapy by means of T.A.B. vaccine, whereas a very sudden relapse and progressive deterioration coincided with the occurrence of urticaria during a course of injections of neo-arsphenamine.

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