CHRONIC ISCHAEMIC MYELOPATHY IN AORTIC ATHEROSCLEROSIS

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Introduction. The gradual onset of an ill-defined chronic paraparesis in an older individual with ultimate progression to severe paraplegia and sensory loss raises the possibility of a vascular origin, provided malignant disease has been excluded. To prove the diagnosis is difficult without autopsy but three such cases were diagnosed clinically by Skinhoj (1954). Even when the spinal cord is examined, apart from confirming necrotic areas, the appearance of the spinal arteries is usually normal. Thus Staemmler (1939) did not observe atheroma in the spinal cord in 700 unselected necropsies while Mannen (1963) reported an incidence of 2·6 per cent. for plaques of atheroma in the anterior spinal artery of 300 unselected geriatric cases. Why spinal vessels in contrast to those of the brain should be relatively immune to the effects of hypertension and atherosclerosis is not known (Elliott, 1964). Severe atheroma of the aorta has been frequently found in these cases. Thus Gruner and Lapresle (1962) recorded eight examples and Hughes (1965) mentioned three. Jellinger and Neumayer (1962) found completely unsystematised patchy cavitation in the cords of elderly patients presenting with a progressive atrophic paraparesis associated with severe aortic atheroma. Recently, Hughes and Brownell (1966) reviewed the literature and described five cases with scattered small focal areas of necrosis in the cord which were attributed to an ischaemic process arising from severe atheroma of the abdominal aorta.

To investigate the manner in which symptoms are produced by this association, it is imperative to carry out a comprehensive pathological examination of the radicular arteries supplying the spinal vessels and of the intercostal and lumbar arteries from which they originate, in addition to the aorta. As this extremely laborious dissection has been rarely undertaken the following case is reported in detail both from the clinical and pathological aspects.

CASE REPORT

A 59-year-old male (T. D.) became aware of progressive weakness first of the right and, a few days later, of the left lower limb early in March, 1966. The disability remained slight for about six weeks when he awoke with paralysis of both lower limbs and numbness up to the waist. The following morning he was unable to pass urine. He had suffered from a cough for the past 20 years since an attack of bronchitis but otherwise the previous medical and family histories were non-contributory. On 2 May 1966 he was admitted to hospital elsewhere and transferred to the neurological department on 26 May 1966.

On examination the cranial nerves and spine were intact. Some coarse fasciculation was observed over the shoulder girdles and arms, but the upper limbs were otherwise normal. There was flaccid paralysis of both lower limbs. The deep tendon reflexes were normal in the arms but depressed in the legs. The abdominal responses were absent and both plantars were extensor. Vibration sense was absent below the iliac crests and joint position sense was absent in the toes and defective in the ankles. Cutaneous sensation to pin prick, temperature and touch was impaired below the second dorsal segment including

the sacral area on both sides. Retention of urine had necessitated the use of an indwelling catheter and numerous deep pressure sores were present over the sacrum, buttocks and legs. General examination was unremarkable and the blood pressure was 190/90.

A chest radiograph revealed long-standing right basal pleural thickening. Radiographs of cervical and dorsal spines were normal, and a myelogram showed no abnormality between the lumbar sac and the foramen magnum. A full blood count was normal but the erythrocyte sedimentation rate (E.S.R.) was 50 mm./hr. The lumbar cerebrospinal fluid (C.S.F.) pressure and manometric observations were normal, and the fluid contained no white cells, seven red cells/c.mm., protein 35 mg./100 ml.; Lange no change. The Wassermann reaction (W.R.) was negative in the blood and C.S.F.

In view of the negative results of investigation, it was thought most likely that the patient was suffering from the effects of metastatic carcinoma, probably arising from the bronchus. Progressive deterioration ensued, complicated by both pulmonary and renal infections and by anaemia. Death occurred on 10 August 1966 about five months after the onset of symptoms.

Autopsy Findings. The body was that of a thin wasted male with extensive pressure sores over the sacrum, lateral aspects of both thighs and left heel. The left pleural cavity was obliterated by old dense adhesions and there was a severe terminal bilateral bronchopneumonia. The heart was of normal size and appearance with minimal atheroma of the coronary arteries. The whole of the aorta was extremely atheromatous with many large erosions of the intimal surface on several of which fleshy fibrin thrombus had been deposited. The lower abdominal aorta was most severely affected but the ascending aorta, the arch adjacent to the left common carotid artery and the posterior aspect of the descending aorta round the origins of the lower intercostal and lumbar branches were similarly involved (fig. 1). The common carotid arteries were very atheromatous and the commencement of both internal carotid arteries was stenosed by fibrin thrombus deposited on large atheromatous plaques. The subclavian and vertebral arteries appeared healthy. The renal, coeliac and mesenteric arteries were widely patent and only slightly atheromatous. The viscera including the kidneys showed no gross abnormality and the urinary tract was free from infection.

FIG. 1

Severe diffuse atheroma of the lower thoracic and abdominal aorta with numerous erosions. $\times\frac{1}{3}$.

The brain (weight 1455 g.) showed bilateral frontal cortical atrophy with widened sulci and ex-vacuo dilatation of the ventricles. There was only patchy atheroma of the basal arteries mainly at their junctions. The spinal cord showed slight swelling in the upper thoracic region with congestion of the overlying pial vessels. The pia arachnoid was not thickened and there was no evidence of tumour infiltration or of any metastatic deposits either in the extradural tissue or in the vertebral bodies.

Microscopic Findings. Although no focal lesions were recognised in the brain on naked eye examination, several scattered minute areas of old softening were found in the cerebral cortex and basal ganglia in the routine sections. They consisted of areas of dense gliosis, wedge shaped in the cortex, in which an occasional lymphocyte and histiocyte could be recognised. No thrombosed vessels were seen in relation to these infarcts.

Sections from each segmental level of the cord were stained by Haematoxylin and Eosin, Nissl, Mallory's Phosphotungstic Acid Haematoxylin, Masson's trichrome combined with Verhoef's elastic tissue, Holmes' silver impregnation and Weigert's Myelin

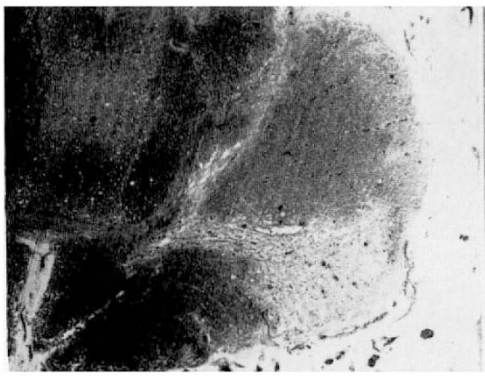


FIG 2

FIG. 3

Fig. 2.—Transverse section of right half of spinal cord at D2 showing necrotic area in antero-lateral column. Myelin. ×15.

Fig. 3.—Similar section at D3 showing necrotic area separated from the antero-lateral surface by a band of intact tissue. Myelin. ×15.

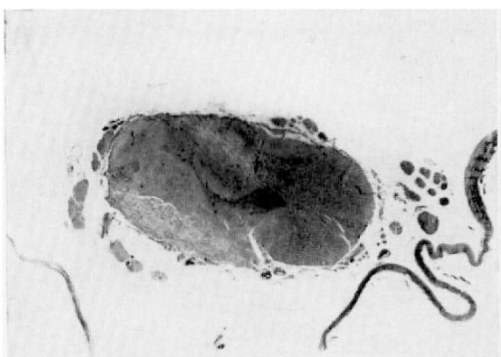


FIG. 4

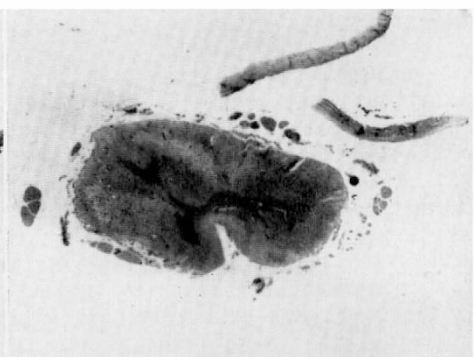


FIG. 5

Fig. 4.—Transverse section at D4 showing necrotic areas in right lateral and posterior columns. Myelin. ×7.

Fig. 5.—Transverse section at D5 showing crescentic area of necrosis extending across posterior columns into right lateral column. Myelin. ×7.

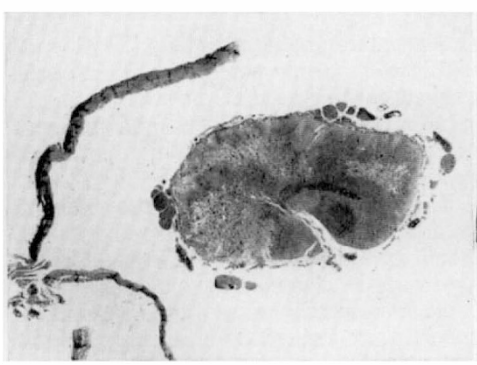


FIG. 6

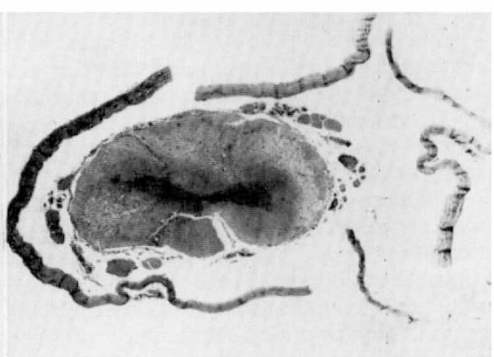


FIG. 7

Fig. 6.—Transverse section at D6 showing areas of necrosis in posterior and lateral columns. Myelin. ×7.

Fig. 7.—Transverse section of D7 showing crescentic area of infarction extending round the spinal cord. Myelin. ×7.

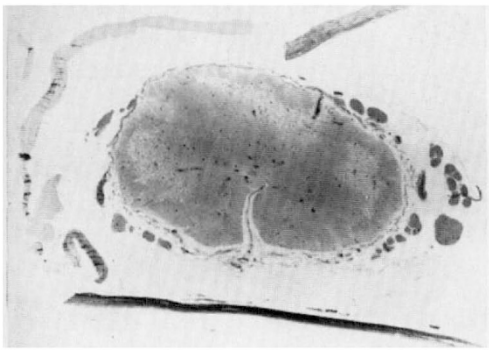


FIG. 8

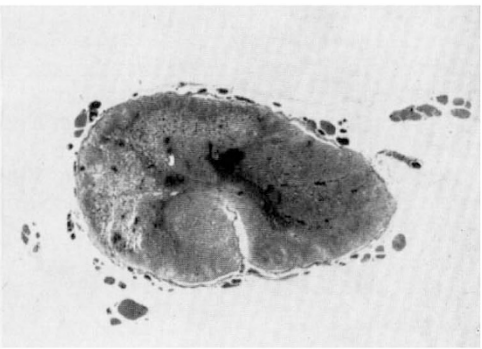


FIG. 9

Fig. 8.—Transverse section at D8 showing necrotic areas in lateral and posterior columns. Mallory's P.T.A.H. ×7.

Fig. 9.—Transverse section at D9 showing crescentic area of infarction, extending across the left posterior horn. Myelin. ×7.

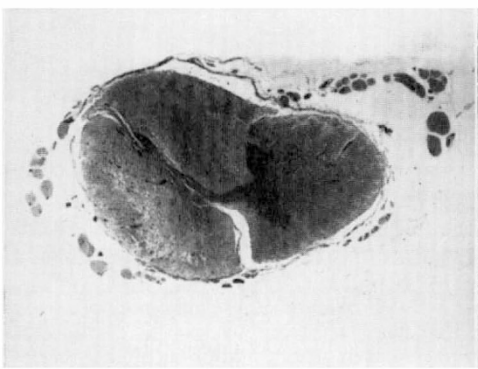


FIG. 10

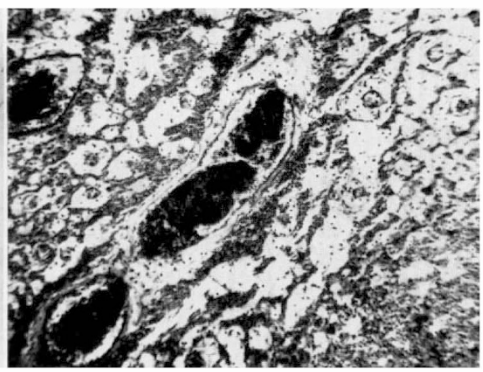
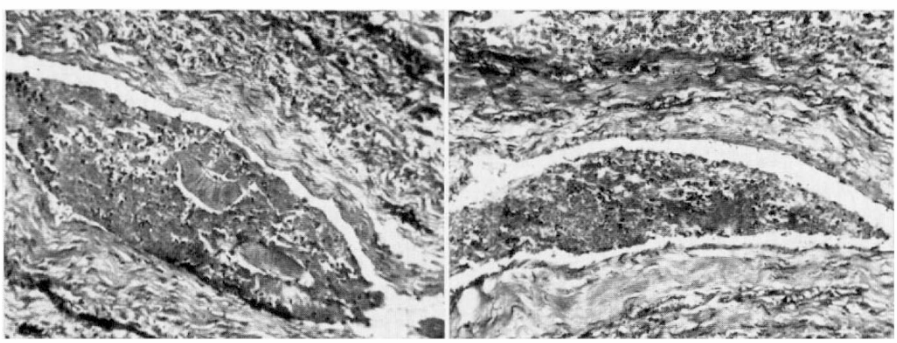


FIG. 11

Fig. 10.—Transverse section of D10 showing area of necrosis in left lateral column. Myelin. ×7.

Fig. 11.—Section of necrotic area of spinal cord at D6 showing fibrinous embolic material in small intramedullary arteries. Numerous histiocytic nuclei can be seen in the vacuoles in the surrounding tissue. H. & E. ×102.



A B

FIG. 12

Longitudinal sections of (A) lower intercostal artery and (B) lumbar artery showing masses of atheromatous material lying free in the lumen. H. & E. ×150.

method. In the cervical and first thoracic segments there was ascending degeneration in the posterior and antero-lateral columns. At D2 there was a wedge-shaped area of necrosis in the right antero-lateral column of white matter extending from the surface into the superficial part of the anterior horn (fig. 2). At D3 the area was separated from the antero-lateral surface by a thin band of intact tissue (fig. 3). At D4 the area was much larger extending dorsally in the lateral column and there was a transversely elongated area

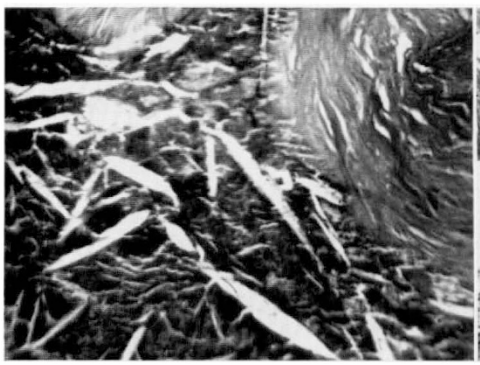


FIG. 13

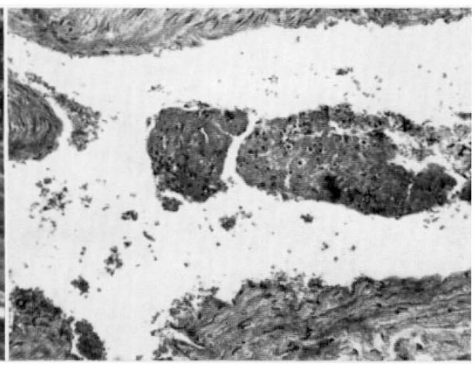


FIG. 14

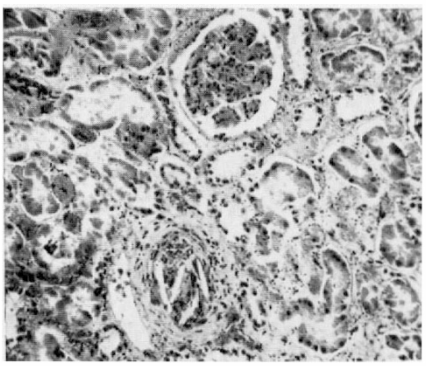


FIG. 15

Fig. 13.—Grumous material containing cholesterol crystal clefts on the surface of eroded atheromatous area of abdominal aorta. H. & E. ×152.

Fig. 14.—Section of radicular branch of upper lumbar artery showing a few small cholesterol crystal clefts in atheromatous embolic material in lumen. H. & E. ×150.

Fig. 15.—Section of kidney showing cholesterol emboli in a small artery adjacent to glomerulus. H. & E. ×150.

of necrosis in the posterior columns (fig. 4). This latter area became much more prominent at D5, extending into both posterior horns to link up on the right side with an elongated area in the lateral column (fig. 5). At D6 there were three discrete foci of necrosis involving a large wedge-shaped area in the right antero-lateral column, a transversely elongated area situated in the posterior columns and right posterior horn, and a small wedge-shaped area in the dorsal part of the left lateral column (fig. 6). At D7 the area in the right antero-lateral column had become much smaller, whilst extending across the posterior columns, left posterior horn and left lateral column was a large crescentic area of necrosis separated from the surface by a thick band of intact white matter (fig. 7). This crescentic shaped lesion also involved D8 (fig. 8) and extended into the D9 segment on the left side (fig. 9) becoming smaller and eventually confined to the left lateral column at D10 (fig. 10). Below this level the cord was intact apart from descending degeneration in the dorsal half of the lateral columns. The infarcted areas had a similar appearance consisting of pale staining vacuolated necrotic tissue in which were numerous histiocytes

and scanty lymphocytes. In only one small intramedullary artery in the necrotic area on the right side at D6 was fibrinous embolic material seen in the lumen of the vessel (fig. 11). The anterior and posterior spinal arteries and their branches seen in all these sections were patent, healthy and free from atheroma.

The aorta was removed at autopsy together with the paravertebral tissues. Several of the pairs of intercostal and lumbar arteries were dissected out from their origins in the aorta and sectioned serially some transversely and others longitudinally. Although many of these vessels originated in parts of the aorta severely eroded by atheroma so that it was difficult to see their openings with the naked-eye, the sections surprisingly showed the lumen to be widely patent and the atheromatous process either did not extend into the vessel or, if it did, it was minimal. In all the sections examined, however, embolic atheromatous material was seen lying free in the lumen or occasionally loosely attached to the wall (fig. 12). Most of this material was eosinophilic and structureless staining positive with P.A.S. and Luxol Fast Blue and resembling in its appearance the soft grumous material lying on the surface of the eroded areas in the aorta (fig. 13). A few small cholesterol crystal clefts were seen in the embolic material (fig. 14).

Although the kidneys appeared healthy, microscopically there were several minute wedge-shaped cortical infarcts and small arteries in relation to these contained cholesterol emboli (fig. 15).

DISCUSSION

The insidious onset of paraparesis in a middle aged man with a chronic cough, followed after six weeks by flaccid paralysis of the lower limbs and a sensory level over the trunk, suggested metastatic carcinoma. However, no primary carcinoma was detected, plain radiographs and myelography excluded spinal compression and the normality of the C.S.F. pointed away from subacute necrotic myelitis. There was no clinical evidence of significant hypertension, atheroma or cardiac disease, but an aortogram would have revealed the severe aortic disease and might have shown a reduction in the number of segmental vessels. The striking absence of spasticity, despite the presence of severe weakness, might at first have been attributable to spinal shock, but this feature remained throughout the course of the illness. It suggested the presence of a lesion extending over many segments of the spinal cord that had interrupted reflex arcs concerned with muscle stretch.

At autopsy, the intense atheroma of the aorta suggested that it had blocked the openings of the lumbar and intercostal arteries or had extended into these branches. However, microscopy showed that this was not so and the walls of these small vessels together with the anterior and posterior spinal arteries were healthy. Instead, numerous atheromatous emboli were found in the lumina of the lumbar and intercostal arteries. The spinal cord contained many small areas of infarction between D2 and D10. At the upper and lower limits these were wedge-shaped and confined to the antero-lateral columns. Over the remainder of the affected cord, areas of infarction were crescentic and lay in the watershed territory between tissues supplied by the central branches of the anterior spinal artery and the penetrating branches of the peripheral circumferential pial vessels, extending between the posterior and anterior spinal arteries (Hassler, 1966). As both these spinal arteries originate from the radicular arteries, especially in the thoraco-lumbar region (Adamkiewicz, 1882), atheromatous emboli would tend to be held up at the proximal origin and at the distal bifurcations of the radicular arteries causing ischaemic myelopathy. That emboli may migrate distally has been demonstrated in the cerebral circulation of animals by Denny-Brown and Meyer (1957) and radio-

graphically in man by Dalal *et al.* (1965). Only one small intramedullary vessel was found to contain embolic material in the present case but it is likely that showers of emboli had occurred, causing intermittent ischaemia. Evidence of extra-spinal embolism was detected in the brain and kidney.

Aortic disease can result in ischaemic or necrotic damage to the spinal cord in several ways. Aneurysmal dilatation or more commonly a dissecting aneurysm can compress the origin of the intercostal or lumbar arteries. Thus Thompson (1965) collected seven cases from the literature and added one of his own. Blackwood (1958) reviewed 3737 post mortem reports from the National Hospital, Queen Square, London and found only nine cases of vascular disorder affecting the spinal cord of which one had a dissecting aneurysm. Other cases have been reported by Hill and Vasquez (1962) and Kepes (1965). Less commonly embolism and thrombosis in the aorta may cause spinal cord dysfunction (Hunt and Cornwall, 1925; Hirsch, 1954; Cook, 1959) whilst infarction is especially liable to occur when the upper abdominal portion is involved (Dragescu and Petrescu, 1929; Corbin, 1961; Rudar *et al.*, 1962). Similar effects can be produced if the lower thoracic or upper abdominal aorta is occluded during surgical procedures (Adams and van Geertruyden, 1956) or damaged as a result of a physical trauma (Hughes, 1964). Atherosclerosis of the aorta can thus interfere with the blood supply to the cord by narrowing or occluding the intercostal or lumbar arteries, either at their origins or by extending into them, by initiating dilatation, dissection or thrombosis, or by giving rise to fibrin or atheromatous emboli.

The concept that atheromatous material may become embolic was first suggested by Panum (1862), who quoted the gross necropsy findings in the case of the Danish sculptor, Thorwaldsen, and ascribed the sudden death to rupture of an atheromatous plaque in a coronary artery with occlusion of that vessel. No microscopic confirmation was recorded. Further mention of the possibility of atheromatous emboli was made by Allbutt (1915) and Le Count (1918). Benson (1926) reviewed the literature on aortic atheroma giving rise to emboli and concluded it was more common than hitherto had been realised. Flory (1945) reported both the occurrence of these emboli in small and medium sized arteries of the kidney, spleen, pancreas and thyroid in human cases and the experimental production of similar lesions in arteries of the lungs of rabbits after the intravenous injection of atheromatous material. A similar correlative study of the process in the human and in the experimental animal was carried out by Snyder and Shapiro (1961).

Meyer (1947) first reported atheromatous emboli in the cerebral circulation. Zak and Elias (1949) in describing three cases mentioned the possibility of cerebral damage being caused by this type of embolisation. They also found emboli in the marrow of the vertebrae in one. In the cases reported by Winter (1957), Schornagel (1958), Sayre and Campbell (1959), David *et al.* (1963) and Sturgill and Netsky (1963) emboli were present in the cerebral arteries whilst three of the five brains examined by Handler (1956) showed encephalomalacia. Atheromatous embolisation was suggested as a factor in the aetiology of acute pancreatitis by Probstein *et al.* (1957) but the disseminated nature of the lesions in the abdominal viscera and lower extremities was stressed by Fisher *et al.* (1960). Gore and Collins (1960) found that in 59 cases of spontaneous atheromatous embolization the brain was involved in 10. In the series of 38 patients described by Thurlbeck and Castleman (1957) 15·8 per cent. had kidney emboli which were also a feature of the reports by Margolin *et al.* (1957) and by Kaplan *et al.* (1962). Gangrene of the

lower extremities resulted in the case reported by Hoye *et al.* (1959) whilst occlusion of the coronary artery by embolic atheromatous material was found by Wenger and Bauer (1958).

The syndromes produced by atheromatous embolism were reviewed by Eliot *et al.* (1964) and by Retan and Miller (1966). When non-vital structures were involved the embolism was sub-clinical. A single large embolus would produce a major clinical event suggesting disease of one particular organ whereas multiple small emboli would produce a multiple system disease masquerading as polyarteritis nodosa (Richards *et al.*, 1965).

This brief summary of the literature reveals that almost every organ of the body, especially the abdominal viscera, and the lower limbs can be affected by atheromatous emboli from the aorta. The interest and thoroughness of the investigator appear to be important factors in determining where such lesions are found. Mention of the spinal cord, apart from a few exceptions, is curiously lacking. Périer *et al.* (1960) described two examples of necrosis of the spinal cord in the territory supplied by the posterior spinal arteries. In the first the state of the aorta was not mentioned, but in the second, a man of 65, obstruction of the posterior spinal arteries by emboli of atheromatous material from a thoracic aortic aneurysm was demonstrated. Soloway and Aronson (1964) reported on 16 cases of atheromatous emboli to the central nervous system. In two of these, emboli were observed in vessels supplying the spinal cord though there was no associated myelomalacia. However, only three routine sections of the cord were examined.

Chronic myelopathy is seldom recognised clinically as a consequence of aortic atheroma (Wells, 1966) but these two reports together with the examples collected by Corbin (1961) and by Gruner and Lapresle (1962) suggest the association may be more frequent. Garland *et al.* (1966) also raised the possibility of an embolic causation of the necrosis of the spinal cord in their cases where aortic disease was encountered but they were unable to prove this. They stressed the importance of examining thoroughly the full extent of the blood vessels supplying the spinal cord from the aorta in addition to the spinal arteries and their branches in the lepto-meninges.

Severe atheroma of the aorta, especially in its abdominal part above the bifurcation, is a common condition whereas spinal atheromatous embolism is apparently relatively rare. Several reasons may account for this discrepancy. Firstly, as Otken (1959) and Schornagel (1961) have suggested, the smaller emboli may be without clinical significance. Then, as has been observed by Luessenhop *et al.* (1962) in the brain, emboli may migrate through the vasculature in a soltatory fashion and larger lepto-meningeal arteries may dilate in response to emboli contained therein. Further, the long and tedious examination of the spinal cord and the tracing of its blood supply from the aorta which is required to prove the embolic process has deterred many from comprehensive autopsy study. The other factors concern difficulties in recognising the embolic material which may be eosinophilic, grumous and structureless resembling fibrin. It may not contain definite cholesterol crystal clefts or they may be most conspicuous. The foreign body giant cell reaction to these crystals may disappear after a few days and the reaction which persists is an intense inflammatory reaction in the vessel wall and extending into the surrounding tissue, in which eosinophils may be prominent (Zak and Elias, 1949; Otken, 1959). In the spinal cord this panarteritis could be easily misinterpreted as a form of myelitis.

Thus if atheromatous embolisation of the spinal cord can occur in cases of severe aortic atheroma, it ought to be more commonly found and may well account for the slowly progressive paraplegic syndromes found in older patients, in whom it should be suspected. Thus it might have been a factor in some of the cases reported by Jellinger and Neumayer (1966) where the spinal tributaries of the severely atheromatous aorta were free from thrombosis or occlusion. It could also provide an explanation for the spinal cord symptoms in patients with aortic occlusion where the block is well below the level of the renal arteries or near the terminal bifurcation, as in Case 10 of Henson and Parsons (1967), and therefore too low to account for the myelopathy. As the partial blocking of the orifices of the intercostal and lumbar arteries by eroding aortic atheroma may lower the blood pressure in the spinal arterial bed (Jellinger, 1967), the ischaemic damage would be considerably augmented by embolic material. Such emboli will tend to affect the watershed territory between the main radicular arteries, as in the thoracic segments, and between the anterior and posterior spinal arteries in any of these segments. Unilateral or, more likely, bilateral motor or sensory symptoms in the lower limbs may thus ensue. According to whether the site of embolic impaction is in a vessel close to the cord or more proximally situated as at the origin of radicular arteries, either wedge-shaped or arcuate areas of necrosis in the thoracic cord will be produced. Their finding, especially when multiple and associated, in the presence of healthy spinal arteries and an atheromatous aorta is very suggestive of an embolic causation of the myelopathy.

Summary

A clinico-pathological study of a man of 59 who slowly developed weakness of the legs progressing to complete paraplegia is described.

Multiple small areas of necrosis were found in the thoracic cord associated with extensive aortic atherosclerosis. The infarcts were either wedge-shaped in the lateral columns or crescentic in the watershed territory between anterior and posterior spinal arteries, and would account for both the motor and sensory symptoms.

The damage to the spinal cord was due to emboli of grumous material containing some cholesterol crystals originating in the severe eroding atheroma of the aorta. The intercostal, lumbar, radicular and spinal arteries were free from atheroma.

The literature on atheromatous embolism is reviewed and the various ways in which aortic disease can affect the spinal cord are discussed.

It is concluded that owing to the frequency of aortic atheroma compared with the infrequent finding of atheroma of spinal arteries, this mechanism may be a prominent factor in the production of chronic ischaemic myelopathy.

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