CERVICAL VERTEBRAL DEFORMITY IN VON RECKLINGHAUSEN'S DISEASE OF THE NERVOUS SYSTEM

A Review with Necropsy Findings

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The pathological changes of bone in von Recklinghausen's disease of the nervous system include bone infiltration, surface erosion by the adjacent tumour, congenital defect, the effects of neurotrophic or vascular influence, growth disturbance from epiphyseal involvement, osteomalacia from renal tubular defects, and bone softening from disuse.

Brooks and Lehman (1924) were probably the first to draw attention to local bone changes in neurofibromatosis. They ascribed the bone changes to neurofibroma, but none of their biopsies gave evidence of actual bone infiltration. The observations of Whiston (1953) and Friedman (1944), however, leave no doubt that neurofibromatous involvement of bone does occur. Whiston's patient, a twenty-two-year-old woman with a three-year history of pain and swelling of the wrist, showed radiographic evidence of cystic change in the carpal bones. Biopsy revealed erosion of bone by neurofibromatous tissue. She had multiple skin tumours and café-au-lait spots. Friedman's Case 4 concerned a thirty-one-year-old man who had shown multiple neurofibromatosis since childhood: the femur was thickened and there were cyst-like spaces, biopsy showing neurofibromatous involvement of the marrow.

Sometimes, although there is no infiltration of bone the pressure of adjacent tumours may give rise to bone deformity: for example, widening of the intervertebral foramen by dumb-bell tumours; widening of the internal auditory meatus by acoustic tumours; and erosion of ribs in intercostal neurofibromatosis which may resemble the notching seen in coarctation of the aorta.

There is often no such ready explanation for the bone changes that are observed, and many of these are to be ascribed to developmental failure, which is easy to accept in association with a disease which is the manifestation of a familial anlage defect.

Usually the involvement of bone and of soft tissue is in the same site (Mackenzie 1950). It is especially common for bone hypertrophy to be related to a local plexiform neurofibroma. Possibly local mechanical factors other than true infiltration of bone may be responsible. There may be a neurotrophic influence causing bone change. Parkes Weber (1930) suggested that neurofibromatous involvement of the periosteum caused periosteal hyperaemia and consequent overgrowth of bone. Bone and soft-tissue gigantism was regarded by Inglis (1956) as an associated local disturbance of a developmental type. We have found that, in patients having pronounced skin pigmentation or pigmented moles together with major bone deformities, both lesions are often in the same segment.

Growth at the epiphyses before they have fused may be influenced by changes in vascularity secondary to a local tumour, or by actual destruction from infiltration by neurofibromatous tissue with resultant lengthening or shortening of the limb.

Another mechanism whereby skeletal changes may arise was suggested by the observation of Gould (1918) that some patients with von Recklinghausen's disease have changes in the bone histologically identical with those of osteomalacia. This was surveyed by Saville (1955) who reviewed case reports of osteomalacia with von Recklinghausen's disease and noted a

FIG. 1
Case 1—The cervical vertebral deformity.

FIG. 2
Case 2—The cervical vertebral deformity.

FIG. 3
Case 3—The cervical vertebral deformity.

FIG. 4
Case 4—The cervical vertebral deformity.

frequency that was probably too great to be a chance finding. This would appear to be a variant of resistant rickets from associated congenital defect of the renal tubules, and not a manifestation of neurofibromatosis itself.

Finally it should be noted that major manifestations of neurofibromatosis may give rise to disuse of a part with secondary rarefaction of bone.

FREQUENCY OF BONE CHANGE IN VON RECKLINGHAUSEN'S DISEASE

The determination of an accurate figure for the frequency of bone change in neurofibromatosis would need a complete skeletal survey in every patient, and there would still be difficulty from uncertainty in the definition of von Recklinghausen's disease of the nervous system. Although earlier workers gave an incidence of 7 per cent, Holt and Wright (1948) found that 29 per cent of their cases displayed abnormality of bone. In a more recent study (Heard 1960) changes in bone were present in 45 per cent of a group of seventy-nine patients.

Vertebral bone changes in von Recklinghausen's disease—There seems no doubt that vertebral changes are the most common: Miller (1936) reported an incidence of 43 per cent; Heard (1960) reported 47 per cent. The usual vertebral abnormality is a low thoracic kypho-scoliosis. Scoliosis in neurofibromatosis is said to have been described first by Weiss (1921), who gave credit for the original observation to Engman, a dermatologist. The cause of scoliosis in this disease is not known with certainty, but the possible explanations are: 1) that the scoliosis is part of a generalised mesoblastic disturbance; vertebral anomalies are common among the congenital defects accompanying neurofibromatosis; 2) neurofibromatous infiltration; 3) pressure erosion by local tumour; 4) bone softening due to osteomalacia; 5) porosis due to muscular weakness. In fact, the histological study of changes in bone in neurofibromatosis is incomplete, no doubt because the disease is usually benign and protracted in its course. Inglis (1950), at necropsy on a thirty-four-year-old man with kyphosis and a collapsed vertebra with generalised neurofibromatosis, found no evidence of neurofibromatous tissue at the site of the collapse, nor in neighbouring nerves.

CERVICAL VERTEBRAL ABNORMALITIES IN VON RECKLINGHAUSEN'S DISEASE

Case 1—A twenty-three-year-old woman suffered from generalised neurofibromatosis. Thoracotomy had revealed extensive plexiform neurofibroma in the lower cervical and upper thoracic nerve roots. There was cervical kyphosis (Fig. 1) which may have arisen from erosion of bone by adjacent mid-cervical neurofibroma but this was not proved. Ten years later she developed paraplegia from intraspinal tumours at the level of T.1 and T.2.

Case 2—A twenty-four-year-old woman with neurofibromatosis had progressive transverse myelitis at the level of the third cervical vertebra for one year. There were no histological studies. Figure 2 shows the cervical vertebral deformity.

Case 3—A twenty-six-year-old woman presented with headaches and a convulsive disorder. She had numerous café-au-lait spots and soft pedunculated neurofibromas on the back. There were no symptoms or signs referable to the cervical spine, the condition of which is shown in Figure 3.

Case 4—A thirty-five-year-old woman, who had multiple subcutaneous nodules and café-au-lait patches and a family history of von Recklinghausen's disease, had a large pigmented tumour over the back of the neck and shoulder. The condition of the cervical spine is shown in Figure 4. She also displayed well marked "scolloping" of the lower lumbar and upper sacral vertebrae, a condition recognised to occur in neurofibromatosis quite apart from any accompaniment by intraspinal tumours (Heard and Payne 1962).

FIG. 5

FIG. 6

Case 5. Figure 5—Patient at the age of four years. (From Holt and Wright 1948, *Radiology*, 51, 647.)
Figure 6—The cervical vertebral deformity.

FIG. 7

FIG. 8

Case 5. Figure 7—The spinal cord, with a malignant tumour involving the left cervical nerve roots and a small neurofibroma of a right cervical nerve root (necropsy specimen). Figure 8—Radiograph of hemisection of the cervical vertebrae taken at necropsy. Inset is a reconstruction of the specimen to demonstrate the histological findings. Black, vertebrae; stippled, intervertebral disc; cross-hatch, neurofibroma; broken line, soft-tissue outline of the specimen. There is neoplastic destruction, to a greater or lesser degree, of all the vertebrae. One of the intervertebral discs has been completely replaced. The small wedge-shaped vertebra (C.6) is shown histologically in Figure 10.

FIG. 9

FIG. 10

Case 5. Figure 9—Neoplastic destruction by erosion of the anterior surface of a vertebra and an intervertebral disc. The neoplasm shows the characteristic dimorphous picture of a neurofibroma, nerve-like bundles set amidst a diffuse fibromatous proliferation. The periosteum and perichondrium are not recognised as such; they are replaced by, or transformed into, neoplasm. (Haematoxylin and eosin, $\times 9$.) Figure 10—From top to bottom: neurofibroma, vertebra and intervertebral disc. This section was taken through the centre of an almost completely destroyed vertebra. It is represented by the small wedge-shaped piece of bone on the radiograph (Fig. 8) and reconstruction (inset to Fig. 8). (Haematoxylin and eosin, $\times 16$.)

Case 5—This patient, who died when he was twenty-five years old, had no family history of von Recklinghausen's disease. He had many superficial skin tumours and café-au-lait spots. His condition at the age of four years is shown in Figure 5. The grossly deformed and useless left arm was amputated when he was eight years old. Later tumours were removed from the vicinity of the left shoulder and of the left ear. Otherwise he was in fairly good general health until 1956, two years before his death, when he had difficulty in walking. In December 1957, while pushing his car, he suffered sudden weakness of the lower limbs with impaired sensation below the nipples. There had been spasm in the legs but no bladder or bowel disturbance. He was admitted to the University of Michigan Medical Center in January 1958. There was spastic paraplegia with a sensory level at T.4; and a large mass at the root of the neck on the left side. There was very marked deformity of the cervical vertebrae (Fig. 6). He refused proper investigation or treatment. In March 1958 he was readmitted. There had been continued improvement in the paraplegia but the mass in the left side of the neck had enlarged and he had difficulty in swallowing and in breathing. He died from sudden respiratory obstruction.

Necropsy—There was a large encapsulated tumour in the left supraclavicular region weighing 1,600 grammes. The tumour involved the upper left intercostal nerves and displaced the trachea and oesophagus to the right (Fig. 7). There were several other tumours in the intercostal spaces involving the intercostal nerves, the largest measuring six centimetres by two centimetres. Another tumour arising in association with the vagus nerve measured five centimetres by two centimetres. The spinal cord appeared to be normal except that at the site of abrupt angulation in the mid-cervical region it was flattened and taut. On several

nerve roots, and within the subarachnoid space, there were small tumours, the largest measuring two centimetres by half a centimetre: none appeared to compress the cord. The paraplegia was attributed to stretching and angulation of the cord by the vertebral deformity. (Paraplegia in von Recklinghausen's disease must not be ascribed too readily to compression by tumour: an extreme gibbus was responsible in more than half of twenty cases described by Miller in 1936.) Among the bony deformities there was hypoplasia of the upper left ribs with a "pigeon-chest" deformity.

Histological examination—Sections from the large tumour at the root of the neck showed neurofibrosarcoma.

Bone specimen—A vertical hemisection of the cervical vertebrae at the site of gross angulation was removed for study. (The spines and laminae had previously been removed.) A radiograph of the specimen is illustrated in Figure 8 and shows that the kyphosis is due to almost complete disintegration of the sixth cervical vertebra.

Histological examination showed benign neurofibromatous tissue eroding and infiltrating the vertebrae. Figure 8 (inset) is a reconstruction demonstrating the extent of the tumour tissue and its relationship to the vertebrae. Figures 9 and 10 illustrate the histological detail.

SUMMARY

1. The bone changes in von Recklinghausen's disease of the nervous system are reviewed and the gross deformities that are sometimes encountered in the cervical region are illustrated.
2. A case is described in which, at necropsy, histological study of affected vertebrae revealed actual neurofibromatous erosion and infiltration.

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