HODGKIN'S DISEASE: AN UNUSUAL CASE WITH SPINAL SYMPTOMS

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We record this case because it displays certain less-known features of lymphadenoma which are of greater moment than a mere record of unusual manifestations of a protean disease.

Case History

The patient, a house-decorator aged 49, was in good health until October, 1942, when he noticed a swelling of the neck. Clinical examination in December revealed a mass of firm discrete glands in the left side of the neck and supraclavicular region and some smaller glands in the right axilla. No other abnormality was found clinically and the patient felt well. The red cell count, haemoglobin estimation, and total and differential white cell counts were normal. A large cervical gland was removed, and was reported on as a lymphadenoma by Dr. Fraser, pathologist to the Bristol Royal Infirmary. Radiotherapy was started in January, 1943, under the late Dr. Bryan Adams. (Details of radiotherapy are given in an Appendix.)

In March, 1943, a nodule the size of a walnut still remained in the left side of the neck, but this had disappeared by May, 1943, when no other abnormality could be detected. The patient was examined at three-monthly intervals and was well until August, 1946, when he complained of pains in the back and down the right leg. Clinical examination did not reveal any abnormality. Radiological examination did not show tumour involvement of the vertebrae, but osteoarthritic changes were noticed. No treatment was given. One month later the patient was seen again; he complained of having had lower abdominal pains, the character of which suggested girdle pains, and now had loss of power of the right leg and weakness of the left leg. On examination a mass in the right iliac fossa was found, with wasting of the right gluteus maximus and of the right hamstrings, weakness of both lower limbs, especially the right, spasticity, exaggerated tendon reflexes, and analgesia corresponding to a cord lesion at the level of the tenth dorsal segment. Sphincter control was normal. No further details are available.

Radiotherapy was then directed against the iliac mass and the spinal column between the eighth dorsal and the second lumbar vertebrae. On completion of the course the mass in the right iliac fossa had disappeared; the patient was free from pain, but loss of power in both legs was almost complete and he was now incontinent of urine and faeces. He was considered unfit for further radiotherapy and was removed to another hospital, where he was found by one of us to have the clinical picture of a complete transverse lesion of the spinal cord in the lower dorsal region. The cerebrospinal fluid was under normal pressure and showed a normal response to jugular compression. The protein, chloride, and cellular contents were normal, and the globulin and Lange tests were negative. Introduction of 2 ml. of lipiodol into the cisterna magna did not demonstrate spinal block.

In January, 1947, a suprapubic cystotomy was carried out and treatment was directed to keeping the patient comfortable. Large bed-sores and urinary infection developed and he died three months later—i.e., four and a half years after the onset of symptoms.

Post-mortem Examination

The body was extremely emaciated and dehydrated. There were large scars in the region of both knee-joints and marked talipes equinus. A large bed-sore took up the sacral area, buttocks, and lower half of the back; surrounding tissues were thickened and oedematous. No enlarged glands could be palpated and no glands could be found in the cervical, supraclavicular, axillary, or mediastinal regions, or in the abdomen.

A few small soft glands were present at the hila of the lungs and in the inguinal region; these were taken for examination. The structures of the mouth, neck, thorax, and abdomen showed no evidence of lymphadenoma: in particular the liver (2,035 g.) showed only a uniform nutmeg pattern, the spleen (130 g.) was small and presented a uniform pale-red pulp, and section of the ribs revealed a red marrow. Apart from the vertebral column the following were the only abnormalities found.

The lungs showed oedema and hypostatic broncho-pneumonia; the heart was flabby and the left ventricle was dilated. There was marked pyelonephritis and cystitis, with slight dilatation of the renal pelvis and ureters; the prostate contained abscesses. No mass was found in the right iliac fossa, but there were slight diffuse adhesions tacking down the caecum. The vertebral column and its integument showed no external abnormality or deformity. Section revealed a uniform sclerosis of the bodies of the seventh and eighth dorsal vertebrae, so that they were harder and paler than those of the other vertebrae, but none of the bodies showed any disorganization of architecture.

Removal of the spinal cord revealed no abnormality of the bony canal. The dura appeared normal and not even roughened on inspection with a hand-lens. The pia-arachnoid and nerve roots also appeared normal. The spinal cord showed slight evidence of flattening and softening in the upper lumbar and lower dorsal region. The cranium and the brain and its membranes showed no abnormality.

Histological Examination

Apart from moderate periportal fatty change the liver was normal, as was the spleen. The hilar and inguinal lymph glands showed a subacute inflammatory sinus catarrh. The sclerosis of the dorsal vertebrae was accounted for by a generalized increase of fibrillar connective tissue throughout the marrow, diminished vascularity, and hypoplasia of the cellular elements of the marrow so that they were represented by scanty small round cells. Other vertebrae examined revealed no abnormality. The spinal cord showed a transverse myelitis in the upper lumbar region, a segment of it having large patchy areas of demyelination irregularly scattered in all zones. Sections just above this level showed complete degeneration of the posterior ascending (sensory) columns, and sections below showed complete degeneration of the crossed and direct pyramidal tracts. No cellular lesion was found in the cord. These appearances are consistent with a transverse lesion produced by local external pressure.

The Original Biopsy

Dr. Fraser kindly gave us the original slide. The section was from a gland 1.2 cm. in diameter, and showed the classical features of Hodgkin's disease: there was complete replacement of the normal architecture by a pleomorphic cellular tissue containing the characteristic reticulum cells, some in giant form with or without double nuclei in mirror-image form, eosinophil leucocytes, lymphocytes, and plasma cells. The cellular tissue was broken up by a fibrillar stroma condensed into thicker bands in a few places.

Discussion

While the sceptic might be inclined to consider that the train of events originated with a mix-up in biopsy specimens and ended with a nervous disease complicated by deep x-ray therapy, the findings are not unknown. There are a number of accounts of cases of lymphadenoma with clinical remission from 10 to 36 years (Holmes and Schulz, 1946; Jackson and Parker, 1946). One must therefore conclude that, exceptionally with deep x-ray therapy, the disease may remain latent for long periods or completely disappear. Our case is remarkable in that we did not find evidence of the disease even in the form of a sclerotic process. It is considered that the sclerosed vertebrae are accounted for by the effects of radiotherapy, and if there was previous marrow involvement by lymphadenoma it was not sufficient to disturb the bony architecture. Robinson (1928) reports a similar finding in a case with spinal

symptoms treated with radiotherapy. The slight adhesions of the caecum are not uncommonly found at necropsy, and were not of a nature to indicate a healed lymphadenomatous lesion.

Spinal symptoms, though rare in lymphadenoma, are not unknown. The extensive literature has been reviewed by Allen and Mercer (1936). The clinical histories are similar to ours and are of paraplegia consistent with a transverse myelitis. Destruction of vertebrae by lymphadenoma tissue sufficient to cause collapse and compression fracture is rare, as also is pressure on the cord from lymphadenoma tissue extending direct from involved vertebrae. The commonest finding is a growth of lymphadenoma tissue in the epidural space adherent to the dura. Rarely this tissue has been found continuous through the intervertebral foramina with growth outside. The usual finding is an isolated epidural mass with no direct connexion with lymphadenoma tissue elsewhere, no bony lesion, and marked involvement of contiguous para-aortic lymph glands. A few cases with similar histories of paraplegia are, however, not immediately explicable on this basis. These cases have had either an epidural mass too small to cause the cord symptoms or no epidural mass at all. In all types gross demyelination is present at the appropriate cord level. Weil (1931) recorded epidural masses in 37 of 46 cases analysed, but in three there was only dural scarring. He interpreted this latter finding as indicating that lymphadenoma tissue capable of producing symptoms had previously existed. Those patients had received radiotherapy. Since in our case there was a transverse myelitis no different from what one finds in cases of compression fracture of a vertebra we consider that a similar explanation holds. This explanation is reinforced by the fact that in our case manifestations of lymphadenoma elsewhere had also completely disappeared.

In the type of case such as we have described Allen and Mercer dispute the belief that a dural lesion need necessarily have been present. They describe two cases with paraplegia, untreated by deep x-ray therapy, in which, though extensive lymphadenoma was present elsewhere, there was no lesion of the dura or of the spinal column. The spinal-cord lesion was an extensive oedema of the cord with slight congestion and round-cell infiltration. Recalling Gordon's results with intracerebral injection of lymphadenoma extracts in rabbits, they argue that the cord lesion is a similar type of viral or toxic reaction localized by the presence of extensive gland involvement with lymphadenoma in contiguous para-aortic glands; but their arguments could be equally well used to ascribe the cord lesion to lymphatic oedema secondary to the blockage of the paravertebral lymph circulation. Allen and Mercer's findings, however, indicate that a dural lesion need not always be the mechanism of cord lesions in lymphadenoma. Pathologists would be advised to bear this dispute in mind in future cases and to plan their investigations to allow of an examination of the paravertebral lymphatic plexus.

Robb-Smith (1947) has reported briefly some interesting results since he instigated an attempt to produce a rational classification of the progressive lymphadenopathies. From classical lymphadenoma (verum) he differentiates, among others, lympho-reticular medullary reticulosis—a progressive lymphadenopathy in which the morbid lymphoid tissue consists of a proliferation of lymphocytes and abnormal reticulum cells as in lymphadenoma but lacking the essential fibro-myeloid element (fibrillar tissue, leucocytes) of the latter. Previously lympho-reticular reticulosis would have been included as a disease in the "Hodgkin group," which indeed Pullinger (1932) describes and illustrates. According to Robb-Smith (1947) the disease has a better prognosis than lymphadenoma verum, and he states that it is "a

slowly progressing disorder commonly presenting with lymph-node enlargement at a single site, most commonly cervical, and after this has been treated by surgery or radiotherapy there will be a symptom-free interval of several years and then a recurrence at a different site. There is a liability for paraplegia to develop in the later stage due to dural involvement, and sarcomatous transformation may take place after a course of ten to fifteen years." Our case, with primary involvement of cervical and axillary glands, their disappearance, and a symptom-free interval of three and a half years, followed by recurrence in the right iliac fossa and development of spinal symptoms, is similar to his account. Whilst this behaviour may be truer for lympho-reticular reticulosis it can be said that occasionally lymphadenoma verum may behave similarly, as our case showed the classical histology of lymphadenoma. Robb-Smith's account reinforces our argument that, despite the negative findings at the necropsy, our case is encompassed by the protean natural history of Hodgkin's disease, and we hope that this account will encourage the clinician to search for the earliest signs of cord involvement so that treatment may be directed at an amenable stage.

Summary

A case is described of lymphadenoma verum involving cervical and axillary glands which resolved after radiotherapy. Three and a half years later glands in the right iliac fossa became involved and symptoms of paraplegia developed consistent with a transverse myelitis. Radiotherapy was directed to the spine and the iliac region. Post-mortem examination six months later revealed no trace of lymphadenoma anywhere and nothing to account for a transverse myelitis of the upper lumbar zone.

Attention is drawn to the literature of lymphadenoma with spinal involvement, in which symptoms of transverse myelitis are commonly accounted for by dural masses of lymphadenoma tissue. More rarely, no dural or bony lesion may be found to account for the cord involvement, though there is marked involvement of contiguous para-aortic lymph glands. In this circumstance the theories of possible pathogenesis of the spinal lesion are briefly referred to. The unique train of events in our case is shown to be consistent with the known vagaries of lymphadenoma.

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REFERENCES

- Allen, I. M., and Mercer, J. O. (1936). *J. Neurol. Psychopath.*, **17**, 1.
Holmes, G. W., and Schulz, M. D. (1946). *New Engl. J. Med.*, **235**, 789.
Jackson, H., and Parker, F. (1946). *Ibid.*, **234**, 103.
Pullinger, B. D. (1932). *Report of the Rose Research on Lymphadenoma*, p. 119 and Fig. 70. Bristol.
Robb-Smith, A. H. T. (1947). In *Recent Advances in Clinical Pathology*, Edited by S. C. Dyke, p. 350. London.
Robinson, G. A. (1928). *J. Amer. med. Ass.*, **91**, 1548.
Weil, A. (1931). *Arch. Neurol. Psychiat.*, **26**, 1009.

APPENDIX

Details of X-ray Therapy

Factors.—200 kV.; 15 mA.; 50 cm. focal skin distance; 1 mm. Al + 1 mm. Cu filtration; 30 r/minute intensity. (All incident doses are without back scatter.)

Jan. 14 to Feb. 19, 1943.—(1) Left supraclavicular area: Field (15×15 sq. cm.); 9 applications, each 150 r incident. (2) Right axilla: Field (15×15 sq. cm.); 7 applications, each 150 r incident.

Sept. 18, 1946.—Pelvis (4 fields) (anterior 20×15 sq. cm., posterior 20×15 sq. cm., right lateral 20×10 sq. cm., left lateral 20×10 sq. cm.); 19 applications to each field, each 100 r incident, giving total dose in pelvis 3,325 r.

Oct. 15 to 23, and Oct. 31 to Nov. 6, 1946.—Spine, L5-D8; 2 fields, left and right posterior oblique, each 18×7 sq. cm.; 13 applications to each field, each 200 r incident, giving total dose of 4,375 r on area of spine treated.