often been surprisingly mild and have been disproportionate to the degree of cerebral disturbance seen during life.

It is suggested that, to some extent, the severity of the illness may be assessed by observing the mode of onset, the depth and duration of unconsciousness, the frequency of convulsions, and the persistence of signs indicating focal damage of the brain.

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REFERENCES

- Baker, A. B. (1935). *Amer. J. Path.*, **11**, 185.
 Barrett, A. M., Gairdner, D., and McFarlan, A. M. (1952). *British Medical Journal*, **1**, 1317.
 Brewis, E. G., and Neubauer, C. (1948). *Ibid.*, **2**, 416.
 Campbell, A. M. G., Guy, J., and Walter, W. G. (1952). *Arch. Dis. Childh.*, **27**, 507.
 Dawson, J. R. (1933). *Amer. J. Path.*, **9**, 7.
 — (1934). *Arch. Neurol. Psych., Chicago*, **31**, 685.
 Foley, J., and Williams, D. (1953). *Quart. J. Med.*, **22**, 157.
 Greenfield, J. G. (1950). *Brain*, **73**, 141.
 Hurst, E. W. (1941). *Med. J. Aust.*, **2**, 1.
 Jennings, G. H., Hamilton-Paterson, J. L., and MacCallum, F. O. (1949). *British Medical Journal*, **2**, 210.
 Kelleher, W. H., Bratton, A. B., and MacCallum, F. O. (1949). *Ibid.*, **2**, 213.
 McAlpine, D., Buxton, P. H., Kremer, M., and Cowen, D. J. (1947). *Ibid.*, **2**, 1019.

EXTRAMEDULLARY PLASMOCYTOMA

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Plasma-cell tumours may occur in bone and in soft tissues. Multiple myeloma is the most common manifestation, and its clinical and pathological features are well known. The solitary plasmocytoma of bone and extramedullary plasma-cell tumours are less common, while the interrelationship of the three conditions is still not finally proved. This case of extramedullary plasmocytoma is recorded because of its rarity, its unusual clinical presentation, and its interest as a case for differential diagnosis.

Case History

A man aged 55, who had lived in Jamaica all his life, was admitted to the Royal Infirmary, Sheffield, in August, 1952. In March, 1950, he had noticed a swelling on the left side of his neck. The following day he had a pyrexia of 102° F. (38.9° C.), and was treated by his doctor with penicillin injections. After a week the temperature subsided, but the swelling in his neck remained. The temperature rose again for several days in May, 1950. A radiograph of his chest and a full blood count at this time revealed only a "slight anaemia." His doctor diagnosed tuberculous glands of the neck. Thereafter, at intervals of six weeks, he had pyrexia, occasionally as high as 104° F. (40° C.), which persisted for several days before subsiding. In April, 1952, a lymph-node biopsy was reported on as Hodgkin's disease.

On examination three enlarged lymph nodes were present in the left anterior triangle of the neck. The largest of the three was approximately 2 cm. in diameter. They were freely mobile and painless. Examination of the oral cavity was normal and there was no evidence of dental caries.

The nose, nasopharynx, pharynx, and larynx were examined by an otolaryngologist and pronounced normal. A complete clinical examination revealed no other abnormality.

Investigations.—X-ray examination of the chest, skull, lumbar spine, long bones, and accessory air sinuses revealed nothing abnormal. The Wassermann and Kahn reactions were negative. Agglutination reactions: *Brucella abortus* and *Brucella melitensis* less than 1/10. The urine was examined on many occasions: albumin was constantly present, but tests for Bence Jones proteose were repeatedly negative. Plasma protein: serum protein, 8.3 g. per 100 ml. (albumin 4 g., globulin 4.3 g.). Haematology: haemoglobin, 82%; red cells, 4,000,000; leucocytes, 7,000 (band cells 3%, lymphocytes 24%, polymorphs 64%, monocytes 6%, eosinophils 3%). The white-cell morphology appeared to be within normal limits. Platelets 620,000 per c.mm. (Lempert). Bone marrow (left ilium): The abnormal features included the presence of some macronormoblasts and an occasional megaloid cell. Abnormal nests of plasmocytes and their precursors were seen—in all, 5.6% of 500 cells. There was megakaryocytic hyperplasia.

Biopsy of the cervical lymph node on August 29 was reported on by Professor Willis as follows: "The extremely heavy infiltration of this lymph node by plasma cells is, I think, rather more than might be accounted for by any inflammatory disease, and my diagnosis is plasmocytoma. Whether this may be due to a primary growth in the upper respiratory passages or to skeletal myelomatosis can only be decided by other investigations, especially x-ray studies of the bone. The high plasma protein level favours myelomatosis. Bence Jones proteosuria should be carefully watched for."

The patient's general condition remained good and no further pyrexia occurred. As the radiological examination of the bones, the clinical state of the patient, and the other investigations were against a diagnosis of multiple myeloma, the lesion in the neck was treated with x-irradiation as a case of primary extramedullary plasmocytoma. Satisfactory regression of the remaining enlarged glands took place.

Since his return to Jamaica he has remained in good health. No Bence Jones proteosuria has been demonstrated. Radiological findings (skull, thorax, vertebral column, pelvis, long bones of upper and lower extremities) were normal in May, 1953.

Discussion

Solitary plasmocytoma is an established clinical condition. Although any part of the skeleton may be the site of such a lesion there appears to be a special predilection for the innominate bone and the long bones of the lower limbs. Amongst recorded cases are those of Rogers (1930), Chesterman (1936, 1948), Leedham-Green *et al.* (1938), Willis (1941), and Lumb (1948).

Willis (1941) considers that in order to establish a diagnosis of solitary plasmocytoma the following criteria must be fulfilled: microscopical proof that the tumour is of plasma-cell nature; exclusion of the possibility that the lesion is the first evidence of generalized myelomatosis; there must be radiological proof that no skeletal lesions are present, both at the time of examination and at subsequent examinations at repeated intervals; and Bence Jones proteosuria shall be absent on repeated examinations.

The validity of this last criterion is questioned by Lumb (1948), who found Bence Jones proteose in the urine of a case proved at necropsy to be one of solitary plasmocytoma of the sacrum. He concludes that the proteosuria is consequent on actual tumour volume—namely, the amount of bone-marrow involvement.

Plasmocytomas of soft tissue are much less often encountered. Hellwig (1943) found 127 published cases in the literature reviewed between 1905 and 1942, to which he added a case of his own. The lesions in most cases are situated in the upper air passages, especially the nasopharynx, maxillary antrum, and oral cavity. Cases have

also occurred in the conjunctivae, while odd sites recorded include the testis and uterus (Andersen, 1949) and pancreas (Hefferman, 1947).

The occurrence of extramedullary plasmocytoma in cervical lymph nodes unassociated with other lesions is referred to by Hellwig (1943) and by Andersen (1949). Andersen quotes a personal case, occurring in a submaxillary lymph node. Hellwig was able to find four cases, of which three subsequently developed lesions elsewhere. McNamara and Rogers (1943) recorded a case of extramedullary plasma-cell tumour of a tonsil with metastasis in a cervical lymph node, the interval between the removal of the primary lesion and the appearance of the metastasis being six years. In our case the lesion appears to be localized to a group of glands. A gland had previously been removed for biopsy elsewhere, and at the more recent biopsy a further complete gland was removed.

The possibility of a metastasis from a primary growth in the nasopharynx, antra, tonsils, etc., was considered. Radiological examination of the antra was negative, as was a complete clinical examination by an oto-laryngologist.

The late development of multiple myeloma in some cases of solitary plasmocytoma has led to certain conjectures regarding the pathogenesis of the two conditions. Some thought that the multiple lesions were due to a form of metastasis (Cutler *et al.*, 1936). Geschickter and Copeland (1928) found myeloma cells in marrow blood vessels, interpreting this finding as evidence of that possibility. Other authors, however, consider that the disease is multifocal in origin. The various forms of the disease, they say, should not be regarded as separate entities but as different manifestations of the same process (Lumb and Prosser, 1948; Lumb, 1948; Snapper, 1949). If this theory be accepted a solitary plasmocytoma must be regarded as a single focus of disease, which more usually presents in a multifocal form (Lumb, 1948). It is suggested by Willis, however, that as a plasmocytoma of the bone may remain solitary for years, and that, as a generalization, when it occurs it usually does so early, it is more probable that there are two separate types of the disease. He is of the opinion that "if thorough radiographic examination one year from the date of tentative diagnosis is unequivocally negative and proteosuria has been regularly absent, it is improbable that signs of generalized myelomatosis will appear later, and the tumour may be diagnosed with reasonable certainty as a solitary one."

Many cases of extra osseous deposits occurring in multiple myeloma have been recorded (Churg and Gordon, 1950; Hayes *et al.*, 1952). Any organ may be so implicated, but most commonly those of the extraosseous haemopoietic system—namely, spleen, lymph nodes, and liver. Churg and Gordon state that in their experience the more lymph nodes taken for section the more commonly is myelomatous infiltration found. The retroperitoneal nodes are involved most commonly, the hilar glands less frequently, superficial adenopathy being rare. In our case multiple myeloma was regarded as probably eliminated in view of the negative radiological findings and the absence of Bence Jones proteose. The marrow pictures were equivocal.

The history of attacks of high pyrexia was difficult to associate with a diagnosis of solitary or multiple myeloma. No abnormal pyrexia was noted during the patient's stay in hospital. Bailey and Haines (1951) found fever significant in only 1 to 3% of cases of multiple myeloma, and seldom was the temperature in excess of 100° F. (37.2° C.). Unfortunately, it was not possible to obtain the sections of the lymph-node biopsy reported on as Hodgkin's disease in April, 1952. The histological picture of Hodgkin's disease may be simulated by various kinds of chronic lymphadenitis, notably brucellosis, glandular fever, and torulosis. In view of the febrile history, it is possible that this biopsy may have shown a picture different from the latter one. Agglutination tests for brucellosis were negative.

The fact that albuminuria was present but Bence Jones proteose absent calls for cautious comment. Magnus-Levy (1932) (quoted by Bailey and Haines, 1951) thought that

where these findings occurred the albuminuria was largely due to the Bence Jones fraction and that negative reports of its absence were erroneous. In Bailey and Haines's series of cases, 29 out of 32 patients suffering from multiple myeloma had albuminuria. This was equal to 90% of their cases, and was the most frequently observed positive laboratory investigation in their series.

More than a year has elapsed since the first biopsy was made in our case, and in view of the normal findings on recent radiological examination it is most likely that the lesion was a primary extramedullary plasmocytoma. Diffuse plasma-cell myelomatosis with little or no radiographic evidence of bone lesions does occur, and this is still a possibility in view of the equivocality of the marrow picture. The continued absence of Bence Jones proteosuria is, however, a strong point in favour of the former diagnosis.

Summary

A case of extramedullary plasmocytoma is reported. The differential diagnosis, the interrelationship of the three main types of plasma-cell tumours, and the significance of the main findings are discussed.

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REFERENCES

- Andersen, P. E. (1949). *Acta radiol. scand.*, **32**, 365.
 Bailey, H. A., and Haines, R. D. (1951). *Sth. med. J.*, **44**, 62.
 Chesterman, J. T. (1936). *Brit. J. Surg.*, **23**, 727.
 — (1948). *Ibid.*, **35**, 440.
 Churg, J., and Gordon, A. J. (1950). *Amer. J. clin. Path.*, **20**, 934.
 Cutler, M., Buschke, F., and Cantril, S. T. (1936). *Surg. Gynec. Obstet.*, **62**, 918.
 Geschickter, C. F., and Copeland, M. M. (1928). *Arch. Surg., Chicago*, **16**, 807.
 Hayes, D. W., Bennett, W. A., and Heck, F. J. (1952). *Arch. Path., Chicago*, **53**, 262.
 Hefferman, A. (1947). *Lancet*, **1**, 910.
 Hellwig, C. A. (1943). *Arch. Path., Chicago*, **36**, 95.
 Leedham-Green, J. C., *et al.* (1938). *Brit. J. Surg.*, **26**, 90.
 Magnus-Levy, A. (1932). *Z. klin. Med.*, **119**, 307.
 Lumb, G. (1948). *Brit. J. Surg.*, **36**, 16.
 — and Prosser, T. M. (1948). *J. Bone Jt Surg.*, **30B**, 124.
 McNamara, W. L., and Rogers, R. J. (1943). *Arch. Path., Chicago*, **36**, 89.
 Rogers, H. (1930). *Brit. J. Surg.*, **17**, 518.
 Snapper, I. (1949). *Medical Clinics on Bone Diseases*, 2nd ed., p. 261. Inter Science Publishers, New York.
 Willis, R. A. (1941). *J. Path. Bact.*, **53**, 77.

The Tobacco Industry Research Committee in the U.S.A. has invited university, hospital, and other medical research organizations to submit proposals for specific cancer research projects for consideration by the committee's scientific advisory board. The board is said to be now reviewing 60 applications and inquiries already received. An initial fund of \$500,000 has been appropriated for research. The Tobacco Industry Research Committee is composed of the large cigarette-manufacturers, tobacco-growers, and warehousemen. The scientific advisory board is guiding the development of long-term research to be conducted in institutions outside the tobacco industry. The industry will not set up any research facilities. No industry funds will be given to tobacco company laboratories. All projects will be in addition to research carried on by companies. The members of the advisory board are: Dr. CLARENCE C. LITTLE, director of the Roscoe B. Jackson Laboratory; Professor MCKEEN CATTELL, head of the department of pharmacology at Cornell University Medical College; Dr. LEON JACOBSON, professor of medicine at the University of Chicago; Dr. PAUL KOTIN, assistant professor of pathology at the University of Southern California Medical School; Dr. KENNETH LYNCH, professor of pathology at the Medical College of South Carolina; Dr. STANLEY P. REIMANN, scientific director of the Institute for Cancer Research, Philadelphia; and Dr. WILLIAM F. RIENHOFF, Jr., associate professor of surgery at the Johns Hopkins School of Medicine, Baltimore.