MYELOMA OF THE SPINE

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In a recent article, Geschicter and Copeland [1] review all the literature and summarize the available data on all cases of multiple myeloma which have been reported since 1848. These authors give a fairly comprehensive review of our present knowledge of history, etiology, clinical characteristics, and treatment of the condition. In this paper I wish to report in detail another case of multiple myeloma, with particular reference to the diagnosis of the disease as it attacks the spine. The above authors do not emphasize this feature. Osgood and others have pointed out the difficulties in the antemortem diagnosis of myeloma of the spine, but none of them has given a very clear conception of the criteria upon which the diagnosis may be based.

From time to time during the study of the case here reported, various diagnoses were suggested by the symptoms and signs present. The patient gave a history suggesting a degenerative disease covering a six months' period prior to coming under observation. His history also suggested tuberculosis, and upon several occasions the chest findings tended to bear out this diagnosis. There was a peculiar blood picture which could not be explained upon the basis of any condition of which we were aware. Interesting alteration in the blood chemistry was also noted. There were never any symptoms referred to the long bones, pelvis or skull, and yet at autopsy these structures were found to be widely invaded by tumor. Because of the unusual and apparently misleading symptoms, the physical, röntgenological and pathological findings, it will be of interest and value to present the detailed history and laboratory data.

Case Report.—A Roumanian laborer, age thirty-one, came with the complaint of weakness dating from an acute illness six months previously. This attack had been characterized by cough and pain in the right side of the chest. These symptoms persisted for six weeks. The patient never regained strength and was unable to return to work. He had lost about seventeen pounds weight. There were no symptoms referable to any other organs than the lungs, except for a recurring eruption on the arms and face. The rest of the past history and family history offered no clues as to the cause of the complaint.

Physical examination revealed evidence of recent weight loss. There was an extensive follicular eruption over the upper extremities and face. The percussion note over the right lower chest was markedly impaired and the breath sounds were diminished. A few dry wheezing rales were heard throughout the chest, and rather numerous fine subcrepitant rales over both bases. There was slight tenderness in the right flank on deep palpation but none over the lower ribs on the right. The spine revealed normal clinical findings. The temperature was normal but the leucocyte count was 16,000, with a differential count of 57 per cent. polymorphonuclears, 1 per cent. eosinophiles, 33 per cent. small mononuclears, and 9 per cent. large mononuclears. Urinalysis revealed a

few hyaline casts, red blood cells and a trace of albumin. The blood Wassermann was negative.

Because of the suspicious deep tenderness in the right flank, and the urinary findings, a kidney lesion was suspected. Routine röntgenograms were found negative. That portion of the ribs, spine and pelvis seen in these films appeared normal. A cys-

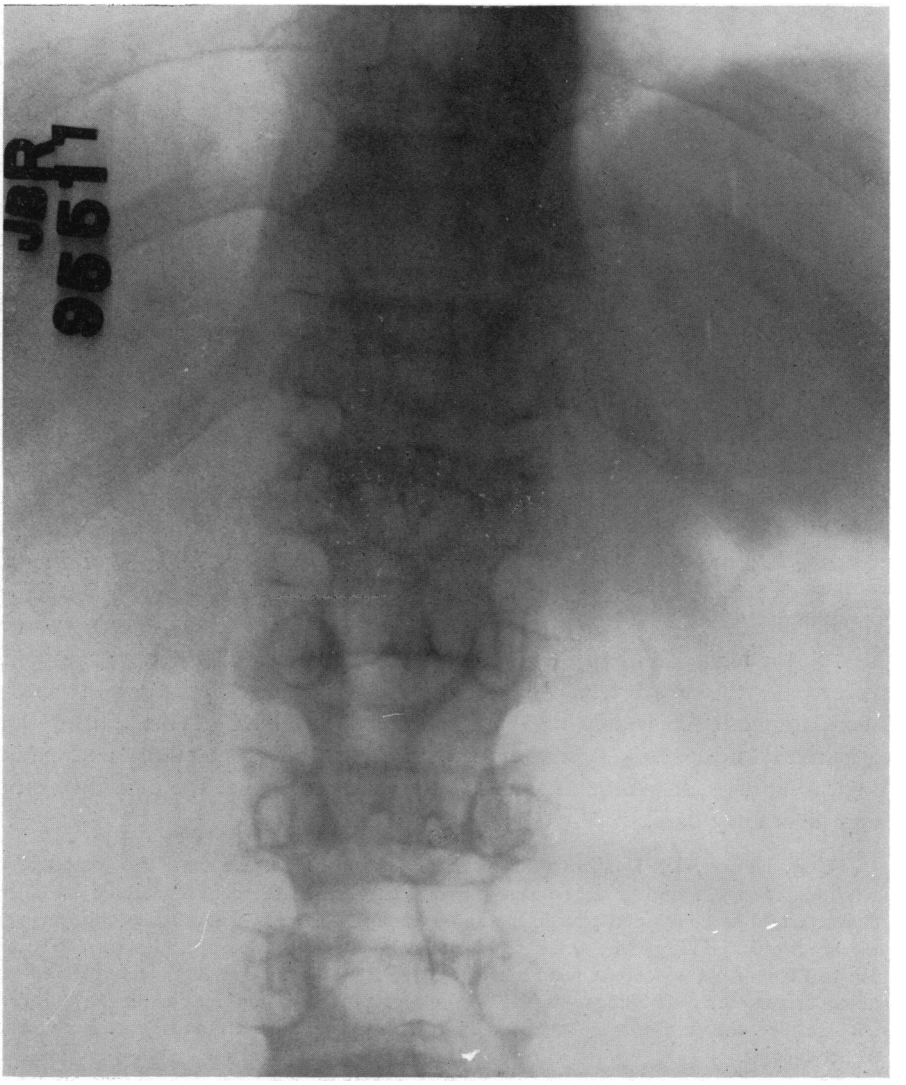

FIG. 1.—Showing marked osteoporsis of all vertebræ and definite narrowing of the twelfth dorsal and first, second and third lumbar.

toscopic examination was done and small calibre strictures of both ureters demonstrated. The urologists were uncertain as to the relation between these findings and the patient's symptoms.

Stereoscopic films of the chest gave evidence of a slight amount of fluid in the right costophrenic angle and of a tuberculous process in the left upper lobe. The ribs appeared normal.

As the patient continued under observation the findings remained about the same. Both ureters were dilated. Urine from the kidneys did not contain pus and was negative to culture on ordinary media. At each visit the leucocytosis in the neighborhood of 17,000 persisted in spite of clearing of the skin infection and apparent resolution of the chest pathology.

About eight weeks after the original examination the patient was sent into the hospital on the medical service with a recurrence of chest pain and eruption on the face and arms, and with the additional new symptoms of nausea and vomiting. The admission temperature was normal but there was again a leucocytosis of 18,000 with a high polymorphonuclear count. The patient received symptomatic treatment and gradually improved. About a month later he developed pain in the back so severe at times that he would fall to the floor. It was then that he first came under my observation. I believe the physical findings at that time were characteristic of myeloma of the spine, but I did not recognize them. The patient stood in a slightly stooped position, the weight of the body carried forward on the balls of the feet, and the feet wide apart. The spine was practically straight, the normal anteroposterior curves being decidedly decreased. All motions were executed with extreme caution and were considerably limited and very painful. There was tenderness along the lower dorsal and lumbar spine, both over the articular facets and directly over the spinous processes.

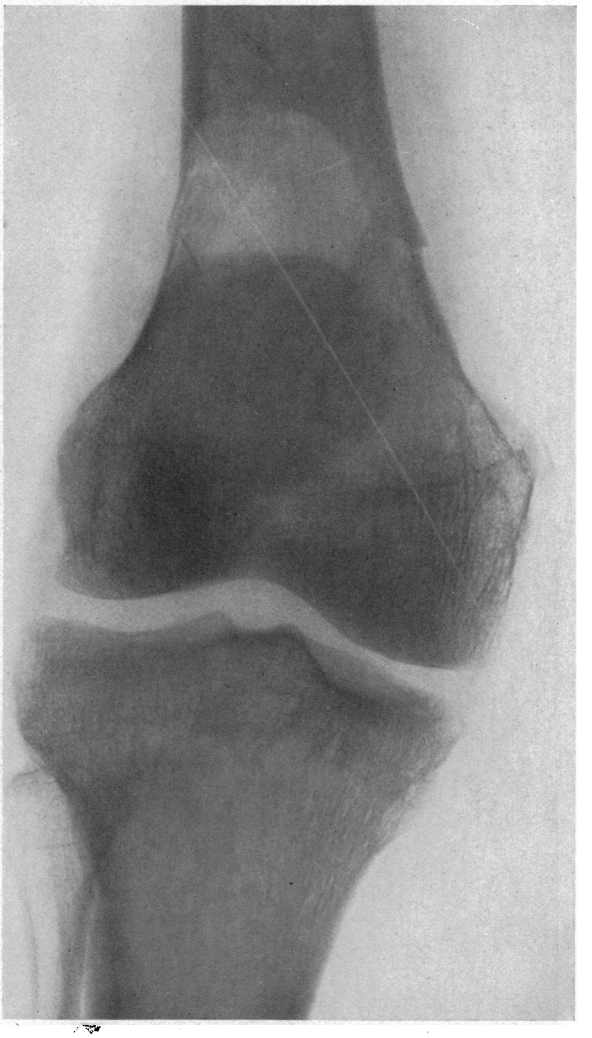

FIG. 2.—Showing circumscribed tumor in right femur. Fracture was produced with some force post-mortem.

Röntgenograms of the spine showed a fusiform shadow about the level of the eleventh dorsal vertebræ suggesting the possibility of a peri-vertebral abscess. The vertebræ and ribs appeared normal. I felt at this time that the symptoms and physical findings warranted a diagnosis of acute spinal arthritis, but that early Pott's disease, not demonstrable by X-ray, might be strongly suspected. Accordingly immobilization of the spine in plaster was advised and accepted by the patient.

Subsequent to the application of the plaster jacket the patient was very comfortable. A fortnight later the pain recurred with as much severity as before. The cast was

removed and the patient placed on a Bradford frame. The following day he developed severe nausea, vomiting, distention and inability to pass flatus. Peculiarly, the temperature was normal but the leucocytes numbered 26,000, with 74 per cent. polymorphonuclears. The following day the leucocytes had risen to 39,000, and physical signs of an acute lobar pneumonia and symptoms suggesting an early meningitis had developed. The

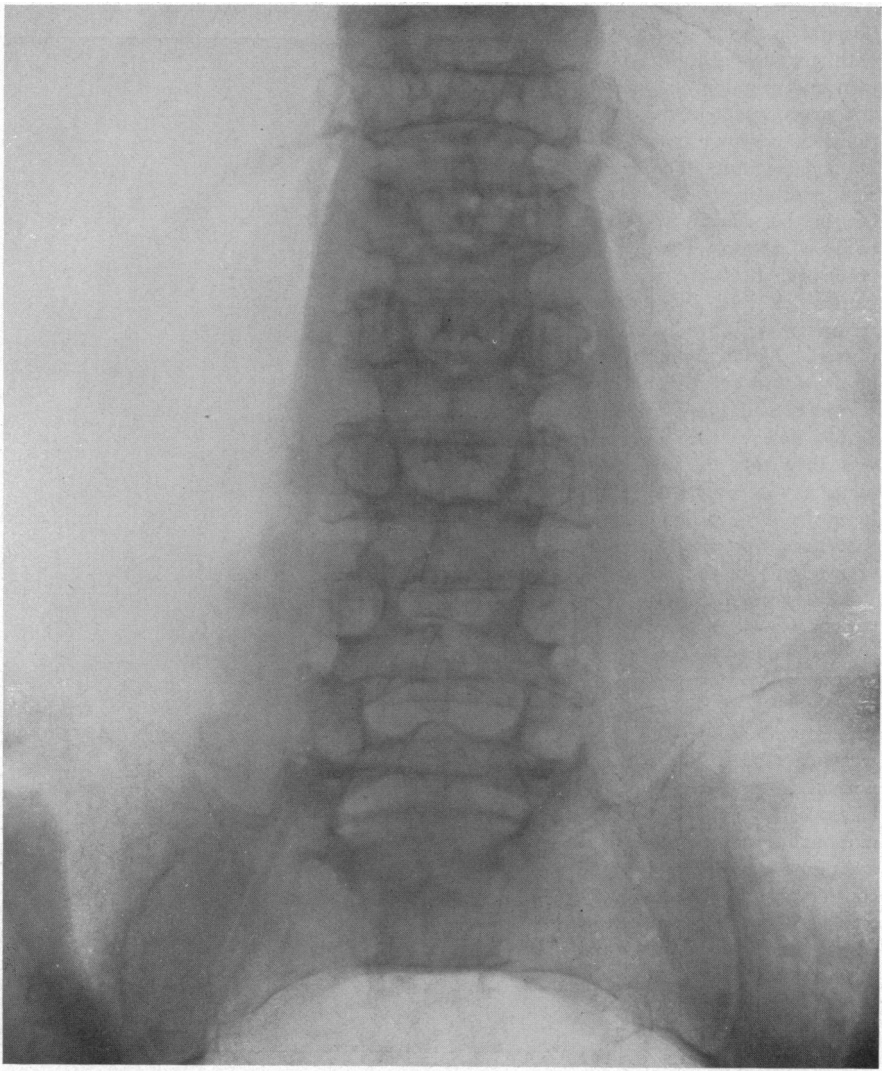

FIG. 3.—Taken post-mortem. Showing widespread involvement of all bones. Appearance of spine is typical. Compare lateral view (Fig. 5).

temperature rose to 103, the pulse was rapid and weak, but the respirations were normal in rate. Within four days the temperature had returned to normal, the above symptoms had all disappeared, but the leucocytes remained elevated. Repeated studies of blood smears showed slight change in size, shape and staining qualities of the red cells, occasional stippling of the red cells, but never any abnormal white cells. The color index was below 1.

A spinal puncture done because of the suspicious cerebral symptoms, revealed a

typical paretic gold curve and a positive Pandy. It will be recalled that there was no history or clinical evidence of syphilis and that the blood Wassermann was negative.

Blood chemistry studies showed a non-protein nitrogen of 26, urea nitrogen 14.9, creatinine 1.5, sugar 91, phosphorus 3.36–4.08 and calcium 16.1. Unfortunately the importance of the abnormal calcium and its possible relationship to the disease were overlooked and only the single determination made.

From this time on, the patient's course was apparently one of gradual improvement with periods of relapse in which he was very ill. Röntgenograms of the spine (Fig. 1)

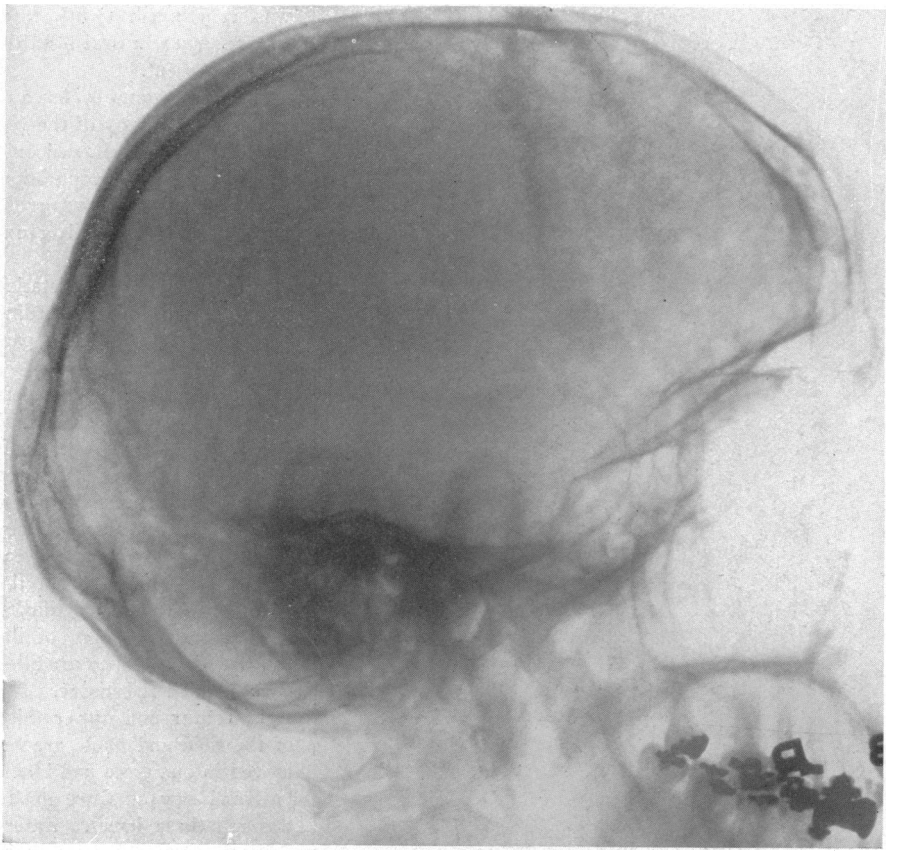

FIG. 4.—Showing typical "worm eaten wood" appearance of myeloma in skull.

taken about six weeks after the original ones, showed marked narrowing of the upper three lumbar vertebræ and of the last dorsal but no narrowing of the joint spaces. The lower ribs were normal. After a careful study of these films a diagnosis of myeloma was made on the basis of them. Because of the expense the patient would not permit X-ray studies of the entire skeleton. Bence Jones bodies were then demonstrated in two urine specimens after examining every specimen voided over a ten-day period.

The patient was then given deep X-ray therapy to the spine. Improvement was really remarkable. After two exposures he experienced complete relief of pain and was able to leave the hospital two weeks later. He was equipped with a spinal brace.

Of the subsequent history nothing is known. The patient died two months later at the county infirmary. The terminal symptoms were evidently pulmonary, as the

cause of death was given as tuberculosis. Fortunately I was able to have the body returned for an autopsy. This was performed by Dr. C. Z. Garber. A résume of the important findings having a bearing on the subject of this paper follow.

Pathological Report.—It is worthy to note that the lungs showed no evidence of tuberculosis, either old or recent. Both pleural cavities were nearly completely obliterated by dense fibrous adhesions and the visceral pleura was very much thickened. There was considerable œdema present.

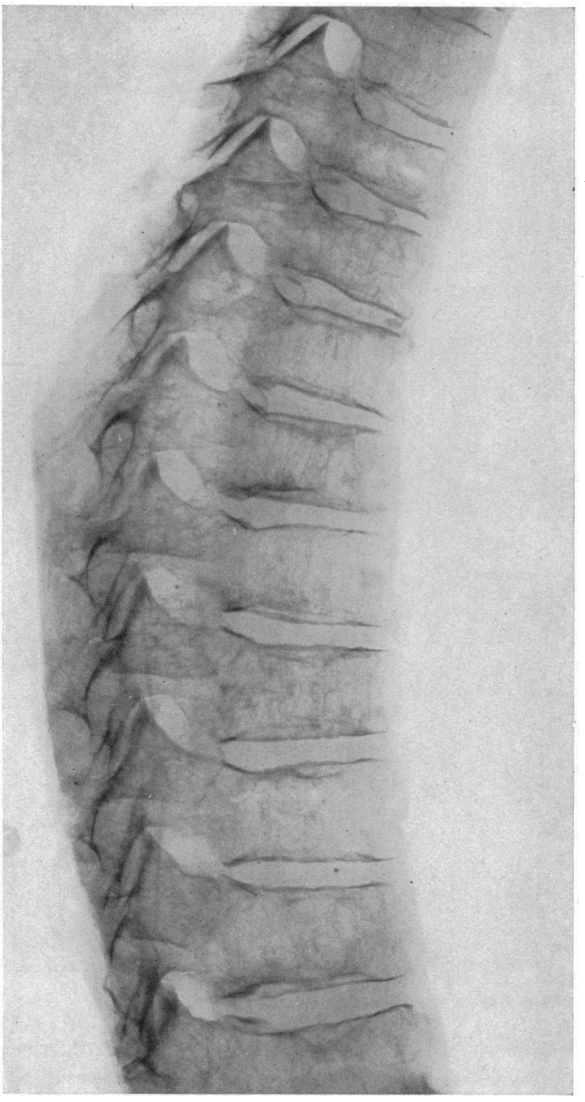

FIG. 5.—Showing typical X-ray appearance of myeloma of the spine. Taken post-mortem with the spine dissected free and hemisected.

There was no evidence of new growth in any of the viscera. The liver showed only chronic passive congestion. The spleen showed no gross evidence of pathological change.

The following dictation by the pathologist regarding the skeletal tissues is of particular interest.

"Section through the sternum shows a large central cavity filled with very soft coarsely granular, pinkish-red tissue. The ribs look to be smaller than normal. They are broken and cut with great ease. It is easier to cut the ribs than the costal cartilages. The central cavities of the ribs are small. They are filled with pinkish-red tissue. The right femur and upper third of the tibia and fibula are removed in one piece and longitudinal saw cuts are made through these bones. Externally they are not remarkable except for the fracture at the lower end of the femur, which was made while handling the body. The marrow cavity of the femur is seen to contain a very abundant amount of pinkish-red, coarsely granular, soft tissue. The cortex appears to be of normal thickness except at the ends of the bones, where it is thinned out to a mere shell. This is most marked in the lower end of the femur in the region of the fracture. There is no new bone formation. The area at the lower end of the femur shows the marrow cavity enlarged and occupied by a soft, mottled, pinkish-gray and brownish-gray tumor mass. Section of the tibia shows the marrow cavity rather large and containing yellow adipose tissue and showing some mottling of pink.

Section of the fibula shows a small marrow cavity which is yellowish-pink in color. Except for the upper cervical region the vertebral column is removed intact, the ribs being cut easily by means of an ordinary knife. The vertebral column is sawed in two and the bodies of the vertebræ are seen to be pinkish-red in color. The bony trabeculæ have largely been destroyed, and many of the vertebral bodies are filled with soft, coarsely granular, pinkish-red tissue which is not much different from hyperplastic bone marrow in appearance. The process of sawing through the vertebral column is done very easily, showing the great loss of bone. The intervertebral cartilages are intact.

"The skull is easily sawed through. The calvarium measures 5 to 6 mm. in thickness. There is a larger amount of pinkish-red, marrow-like tissue than is usually found. There are no large definite areas of tumor. Dura is not remarkable. Numerous sections of the brain show no abnormalities. The posterior clinoid processes of the sphenoid are much more easily broken than is usually the case."

At this point it is well to emphasize the fact that even though those parts of the femur, tibia and fibula which were removed from the body showed gross evidence of rather diffuse tumor involvement, only the ends of those bones revealed very definite X-ray evidence of the disease. Röntgenograms taken post-mortem of all the long bones showed rather circumscribed areas of rarefaction near the epiphyses.

Microscopic Notes.—Sections through the large mass of tumor at the lower end of the right femur show it to be composed of a network of rather small, definitely outlined, irregularly shaped cells with rather scanty bluish-pink staining cytoplasm often extending in the form of delicate processes and fairly large round oval nuclei which stain dark bluish-black or show chromatin in more open, coarsely granular form. A few mitotic figures are found. There is a lace-like, delicate, fibrous, connective tissue stroma and the tumor cells appear to grow out from it so that there is a suggestion of an alveolar arrangement. Capillaries containing red blood cells are occasionally visible in the stroma. There is a little variation in the size of the tumor cells and some have two nuclei. A few red blood cells are noted scattered among the tumor cells of certain areas but no normoblasts are identified. Several narrow bone trabeculæ are seen with a good deal of rather loosely woven connective tissue round about.

A section taken through the marrow at the upper end of the right femur shows some evidence of normal bone marrow structure in that there are hollow spaces which are judged to have formerly contained fat. There is a delicate fibrous connective tissue stroma which is more diffuse and shows no suggestion of alveolar arrangement. There are some normoblasts and irregularly-shaped cells similar to those described above except that they contain numerous small pink or bluish-pink staining granules. Many cells show lobulated nuclei.

Another section from the upper end of the femur was made from a decalcified block. Some of the cortical bone remains but it is much thinner than normal. Bony trabeculæ are numerous but smaller than normal. Some normoblasts, giant cells, and neutrophilic and eosinophilic myelocytes are seen, but most of the cells are of the more embryonic type.

Sections from the vertebræ show but little fat and the marrow cells are rather close together. Myelocytes of the neutrophile and eosinophile types, and a rather small number of normoblasts, red blood cells, polymorphonuclear neutrophiles, eosinophiles and giant cells are seen, but most of the cells are of the more embryonic type, such as have been described above. They are irregular in outline and vary somewhat in size but have a moderate amount of bluish-pink staining cytoplasm and relatively large nuclei which are round or oval and have their chromatin in a granular arrangement. Bony trabeculæ are less numerous than normal and are long and very narrow. In some places they are surrounded by a zone of fibrous tissue which looks like compressed reticulum.

Another section from a decalcified block of vertebræ shows practically the same picture. The predominance of the embryonic type of cell is, however, even more marked. A few mitotic figures are seen. The cortex of the bone is largely destroyed and in

most areas the characteristic cells border directly and are sometimes seen to be invading the dense fibrous tissue of the periosteum.

Discussion.—Geschicter and Copeland emphasize the fact that the distribution of the tumors in multiple myeloma is perhaps the most outstanding diagnostic feature of the disease. These authors believe that there is multiple involvement of the ribs, sternum, or clavicles and spine in ninety per cent. of all cases, and that in rare instances the disease may involve the spine only or the ribs only. Ewing [2] states that the ribs and sternum form the usual original sites of the disease and that the skull, femur, pelvis and humerus are less often involved and in the order named. This is rather contrary to the idea conveyed by Geschicter and Copeland. In a report of thirteen cases from the Mayo Clinic, Meyerding [3] gives the impression that the spine is rather often the seat of primary involvement.

While the evidence is inconclusive, it points to the primary involvement of the spine in the case here reported. It will be recalled that at no time while under my observation did this patient complain of pain referable to any bones except the spine and ribs. The chest pain was easily explainable on the basis of lung pathology, and repeated röntgenograms of the ribs were negative for signs of neoplasm. Also in favor of the spine as the primary site of the growth was the widespread involvement of all the vertebræ in spite of protection from the effect which weight bearing and motion might have had in disseminating the growth.

The first and most outstanding symptom in all reported cases of myeloma was pain. This may be rheumatic in character and rather indefinite at first It may be referred to the corresponding nerve root areas. The pain is aggravated by movement or pressure and is subject to remissions and exacerbations. In the above patient, the initial attack of pain was brought on by cranking an automobile and was of sufficient severity to completely prostrate him. Geschicter and Copeland convey the idea in their report that in all cases of myeloma, back pain is characteristic, but they do not explain the mechanism of the pain. The cases of myeloma with spinal involvement which have been reported have had back pain as a common symptom. I believe this pain is due to erosion of the periosteum from within, by the advancing growth and to nerve root pressure accompanying the softening and collapse of the vertebræ. In the absence of definite spinal involvement back pain is difficult to explain.

The change in shape of the vertebræ mentioned above causes a progressive deformity of the spine. This is the next most characteristic clinical sign of myeloma of the spine. The stature may be actually reduced as in Paget's disease of the bone. The normal antero-posterior curves are changed as the vertebral bodies narrow. As pointed out by Geschicter and Copeland, the deformity of the trunk leads to a characteristic habitus or stance with protruding abdomen, and shoulders thrown back and the head forward, the feet well apart to give a wide base for standing.

The laboratory findings, while not particularly characteristic of myeloma of the spine, may be mentioned briefly as aids in diagnosis. In the majority of

cases there is a secondary anæmia. The white blood cell and differential counts present certain peculiarities. These are discussed in detail by Geschicter and Copeland. Suffice it to say here that a leucocytosis has been present in twenty-three per cent. of reported cases and was explained frequently by the presence of secondary infection. In others it was probably due to the disturbance in the bone marrow. The leucocytosis in our patient was certainly disproportionate to infection and fever. It seems reasonable to expect some pathological change in the histology of the white blood cells and in the count. Careful blood studies should be made in all suspected cases.

The presence of Bence Jones bodies in the urine, often looked upon as a classical sign of the disease, has been noted as early as the eleventh week and as late as the fifth year. They may be present intermittently or continuously. They sometimes appear in showers similar to the appearance of casts in certain forms of nephritis. Meyerding[4] believes these peculiar bodies to be present in the urine of eighty per cent of cases. They were found in half the cases reviewed by Ewing, but in the review of Geschicter and Copeland in sixty-five per cent. I am inclined to believe that they are present in all cases sometime during the course of the disease, but that they are difficult to find. Emerson[5] states that in those cases in which Bence Jones protein is found in the urine, it is usually present in concentrations of less than one per cent. Most patients whose urine contains Bence Jones bodies die in less than two years. One should not have to wait until these bodies are demonstrated to make the diagnosis of myeloma.

While Baetjer and Waters[6] state that myeloma is difficult if not impossible to diagnose by X-ray, Kolodny[7] and Meyerding believe that X-ray is the single most important factor in the diagnosis. The typical röntgenogram of myeloma in all bones except the vertebræ resembles worm eaten wood, with numerous areas of decreased density which vary in size and shape, most typically seen in the skull (Fig. 4).

At this point it is well to emphasize the numerous mistakes made in hospital and private practice, and freely admitted by various well-known men in the diagnosis of myeloma of the spine. While these mistakes may not have had any appreciable influence on the outcome or progress of the disease, avoiding them may obviate useless treatment and lead to an earlier and more correct prognosis. The reasons for these errors are several. First, the possibility of the disease is seldom in one's mind when examining backs in which lesions of the vertebræ are suspected. Other factors which lead to incorrect diagnoses are the rarity of the disease, the scarcity of reports in English on the subject, and the peculiar clinical course and misleading physical findings. Last, and most important, are the rather confused ideas regarding the X-ray findings.

Turner[8] states that the röntgenograms of his cases were inconclusive for spinal pathology. Osgood[9] makes the same statement in a report of three cases observed by him. Gaube[10] reports a case in which it was impossible to establish a correct diagnosis because the röntgen examination failed to reveal the true condition. Reviewing the photographic copies of röntgeno-

grams accompanying the last three mentioned reports, and comparing them with those shown by Meyerding and Kolodny, and with those of this report, one finds them practically identical. It seems that the typical X-ray picture of myeloma of the spine, that which has often been regarded as confusing and indefinite, is one of extensive rarefaction (Fig. 3 and Fig. 5) of the bone with flattening of the bodies of the vertebræ but not much narrowing of the intervertebral cartilages. The only other conditions which might present the same picture are the rapidly growing sarcomata arising from bone marrow. However, these conditions would have other distinguishing features. There should be no mistaking the diagnosis of myeloma of the spine in röntgenograms such as presented here, and especially when combined with a peculiar history similar to the one given in this paper, and with the clinical characteristics enumerated above.

The reason for the peculiar appearance of röntgenograms of myeloma of the spine as different from other bones is possibly explained by the structure of the vertebral bodies, where the total amount of compact bone is less than in other parts of the skeleton. Consequently the tumor is more rapidly destructive and infiltrating and finally replaces all the normal bone, leaving a very thin cortex.

SUMMARY AND CONCLUSIONS

1. Myeloma of the spine is a rare disease, but one which should be kept in mind when examining for spinal pathology.

2. The clinical course and findings are rather definite. The apparent indefiniteness of the clinical signs is itself typical.

3. The absence of Bence Jones bodies from the urine does not preclude the possibility of the disease. The presence of these bodies should serve as confirmatory rather than indicative evidence.

4. There is often a disturbance in the blood picture. The blood should be carefully studied in all suspected cases.

5. The röntgenological findings are diagnostic.

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