Spinal chordomas

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A series of 54 patients with spinal chordomas were treated at Memorial Sloan-Kettering Cancer Center between 1949 and 1976. Thirty-six lesions were located in the sacrococcygeal region and 18 involved the vertebral column at a higher level. The male to female ratio was 35:19. Vertebral chordomas generally occurred in a younger age group. Our radiological findings suggest that there is marked soft-tissue extension anterior to the vertebral column at the time of initial diagnosis. Eleven of 18 vertebral chordomas and 10 of 36 sacral chordomas were found to have disseminated metastases during their course. Analysis of the various modes of therapy reveals that the median survival for both groups is approximately 6 years. However, the 5-year survival for the sacrococcygeal group was 66% as opposed to 50% for the vertebral group. Radiation therapy produced significant palliation but objective evidence of tumor regression was difficult to assess. Chemotherapy in a small number of patients did not have any effect on the tumor. With the advent of computerized tomography scanning, further studies should be done to document the response of this tumor to radiation therapy.

KEY WORDS □ chordoma □ sacrococcygeal and vertebral lesions □ surgical treatment □ radiation therapy □ chemotherapy □ spinal tumor

Chordomas are generally regarded as slowly growing, localized neoplasms arising from rests of the notochord. The notochord, associated with the development of the axial skeleton, appears in the fourth week of embryonic life and regresses by the seventh week. The cephalic end of this structure closely approaches the inner surface of the future sphenoid bone in the region of the dorsum sellae and extends caudally in the midline on the pharyngeal surface of the developing occipital bone. The spinal column is derived from condensation of mesoderm around the notochord. Although the centrum of the nucleus pulposus is believed to be the only derivative of this structure, remnants of chordal tissue can persist in the adult from the clivus to the coccyx.

The supposition that chordomas arise from notochordal rests is based primarily on the fact that these neoplasms occur almost exclusively in the axial skeleton and histologically resemble embryonic notochord by both light and electron microscopy. Furthermore, Ribbert and subsequently, Congdon demonstrated experimentally in rabbits that proliferating tissue following puncture of the intervertebral disc resembles chordoma. However, there are reports of chordoma arising in the maxilla, sinuses, and larynx, but no convincing evidence for origin from the one structure traditionally associated with notochord, the intervertebral disc.

Whatever their true origin, chordomas are relatively uncommon; about 600 have been reported in the literature. Approximately 50% originate in the sacrum, 35% in the clivus, and 15% in the true vertebrae. In spite of their slow growth, cure by surgery is rare, perhaps because they are seldom diagnosed at a stage that would permit total excision. Radiation therapy has been advocated for the treatment of chordomas in conjunction with surgery or as the sole treatment. As is the case with other slowly growing neoplasms, evaluation of the efficacy of various modes of therapy is difficult because of the length of follow-up period necessary and because accurate assessment of small changes in tumor size is usually not possible. For these reasons the natural history of patients with chordomas is poorly understood.

In an attempt to define the course of patients who have undergone various treatments for this neoplasm, a retrospective survey of spinal chordomas treated at...
Memorial Sloan-Kettering Cancer Center over a 27-year period was carried out. Clival lesions were too few in number to be included in the survey.

Summary of Cases

Clinical Material

A total of 54 patients with histologically verified spinal chordomas was treated between 1949 through 1976. Of these, 34 have been included in a previous report from this Center, and six from this group have been the subject of case reports. Thus, 20 new patients are included in this series. The male to female ratio is 35:19, or approximately 2:1 as reported in most series. Thirty-six lesions were located in the sacrococcygeal region and 18 involved the vertebral column at a higher level (Fig. 1). The youngest patient in our series was 2½ years old, and the oldest was 74 years old. The age distribution is given in Table 1. The mean age of the sacrococcygeal group was 56.1 years, while tumors originating in the true vertebrae (vertebral chordomas) generally occurred in a younger age group in whom the mean age was 46.6 years.

Clinical Symptoms and Signs

Symptoms of spinal chordomas obviously varied with the location and extent of the tumor. In general, symptoms associated with sacrococcygeal tumors (Table 2) were present for more than a year before diagnosis. The most frequent symptom was pain, either in the low back or localized to the sacrum or coccyx. Occasionally, the patients complained of pain in the buttocks or perineum. There were no characteristic features of the pain, which was described variously as dull, sharp, continuous, or intermittent. Since the onset of pain was insidious and nonspecific, this early symptom was often ignored by the patient or his physician. Fifteen percent of the patients related the pain to a prior history of trauma to the low back. Rectal dysfunction (change in bowel habits, tenesmus, or bleeding per rectum) was noted as an initial symptom in 42%. Occasionally, the patient reported urinary incontinence. In six cases, the patient noted a mass over the coccyx and on two occasions this mass was excised under the assumption that it was a pilonidal cyst. Radicular pain in the sciatic distribution associated with sensory loss was noted by only four patients as an initial symptom. Many patients were treated for degenerative arthritis, disc disease, coc-
cydinia, or hemorrhoids for several months before the true nature of the disease was recognized. In every instance, when examined at this institution there was a palpable presacral mass that did not involve the rectal mucosa.

The symptoms in the majority of patients with vertebral chordomas had been present for less than 1 year before diagnosis. While pain in the involved region of the spine, often with a radicular component, was noted by most patients, two patients with cervical chordomas complained of dysphagia, which was caused by a retropharyngeal mass, and another presented with a paracervical mass. In patients with lumbar tumors, the diagnosis was sometimes delayed because patients complained of pain referred to the corresponding dermatome rather than pain over the involved spine. Thus, patients with L1–2 lesions complained of pain in the hip, knee, groin, or in the sacroiliac region. Two of the lumbar chordomas presented as intra-abdominal masses for which exploratory laparotomies were performed without the spinal origin of the tumor being found. Paraparesis was the presenting symptom in the two cases of thoracic chordomas and thus led to an early diagnosis.
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Radiological Features

The most consistent radiological finding in sacral chordomas was destruction of several segments associated with a soft-tissue mass anterior to the sacrum (Fig. 2). Calcification in the tumor was noted in 15% of these cases. Chordomas occurring in vertebrae above the sacrum appeared to originate in a single vertebral body, initially producing lytic changes (Fig. 3 left) and ultimately leading to vertebral collapse (Fig. 3 right). The adjacent intervertebral disc spaces were usually spared. In four patients, contiguous vertebrae were involved with radiological sparing of the discs. In addition to lytic changes, noted to be the main radiological feature in other series, secondary sclerotic changes were present in more than one-half of our cases. Tomography and/or computerized tomography (CT) scanning is imperative if the extent of bone involvement is to be determined. Myelography was carried out routinely in the cases with tumors above the sacrum and in several patients with sacral lesions. Epidural extension of tumor was evident in all these patients. For this reason, myelography should be routinely employed even in the absence of neurological signs or symptoms.

Extension of these lesions into the surrounding soft tissues has not been adequately studied. During the past few years, we have used intravenous pyelography, ultrasound, arteriography (Fig. 4), venography, and, more recently, CT scanning (Fig. 5) in a number of cases in an attempt to define extravertebral extension. These studies have led us to the conclusion that the main bulk of the tumor is usually anterior to the vertebral column. Depending on the site of the tumor, anterior extension can be demonstrated by displacement of the ureters and major vessels. In addition, although chordomas are relatively avascular lesions, a tumor stain could often be identified by angiography with subtraction techniques. Computerized tomography scanning has proved to be the most useful single test for demonstration of the full extent of these tumors (Fig. 6).

Pathology

Grossly, the lesions presented as a lobulated gray, partially translucent, cystic or solid mass resembling a cartilage tumor or occasionally a mucin-producing adenocarcinoma. The consistency varied from firm and focally ossified or calcified, to soft, myxoid,

**Fic. 5. Computerized tomography scanning.** Left: Extensive destruction and calcification are seen in a sacral chordoma (dotted line). Right: Massive lateral extension into the retroperitoneal space by a lumbar chordoma (dotted line) is visualized.

gelatinous, or even semi-fluid. They appeared to be well circumscribed with pseudocapsule formation, that is, compression of the adjacent tissue mimicking a true capsule. This apparent encapsulation was usually evident only in the soft tissues but was completely lacking in the region of the bone extension by tumor. Intact but elevated periosteum covered sacral tumors.

Microscopically, the lesions were characterized by a distinctly lobular architecture formed by the "physaliphorous" (dewdrop-like) cells with ample vacuolated cytoplasms, and "signet-ring" type of cells. A thick layer of peripheral fibrous investment could occasionally be seen which appeared to be focally incomplete and was often invaded by infiltrating tumor cells. This incomplete encapsulation and microscopic involvement by strands of chordoma cells at some distance from the major tumor mass may explain the high local recurrence rates of this neoplasm. The intracytoplasmic mucus droplets varied greatly in size and showed a positive staining reaction for both glycogen and mucin. The smaller, better preserved, tumor nodules demonstrated oval or polygonal cells in close proximity to each other with a distinct resemblance to carcinoma cells with mucin production. The larger tumor lobules showed ample extracellular mucin production with only a few cells scattered about, especially in the peripheral areas. Marked variation in nuclear size and chromatin was seen. Binucleate forms and multinucleated giant cells were also featured. Mitotic figures were rarely discerned. Cellular anaplasia and increased mitotic rate did not seem to presage a more virulent clinical course. The infiltrating capacity was well documented by the frequent finding of clusters or columns of chordoma cells invading between muscle planes and along nerve trunks. On occasion, the histological distinction between chondrosarcoma and chordoma, especially in the sphenoid-occipital region may present considerable difficulties. The tendency for both intra- or extracellular mucin production and the complete lack of calcification of chordomas help to distinguish them from cartilaginous tumors. According to Crawford,11 chondromas show a positive staining reaction with phosphotungstic acid hematoxylin (PTAH), and are readily impregnated by silver reticulin. These reactions leave chordomas largely unaffected.

Ultrastructural studies emphasize two distinct types of tumor cells with transitions between them.6,16,26,28 These cells are either large and appear to be epithelial in character, or elongated and spindly. Recurrent lesions or those that were treated by radiation therapy showed a prominent component of a spindle-cell sarcoma, thereby obscuring the true identity of the lesion.3 This feature was seen in three patients in our series.

**Metastases**

The tendency of chordomas to recur locally is well known, but the propensity of these tumors to metastasize may not be.7,9 In our current series, 11 of 18 vertebral chordomas and 10 of 36 sacral chordomas were found to have disseminated metastases. The difference between the two groups was statistically significant (chi-square = 3.96, p < 0.05). Metastases appeared uniformly throughout the course of therapy. They were discovered as early as 1 year and as late as 10 years after tissue diagnosis and, therefore, did not appear to be merely a reflection of a long follow-up period. There also did not appear to be any obvious correlation between the incidence of
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metastases and the mode of treatment of the primary tumor. The sites of metastases included soft tissues, lymph nodes, lung, bone, liver, and other intra-abdominal viscera. Occasionally, widely disseminated metastases including the heart, pleura, and brain were found (Table 3).

Treatment

Of the 18 patients with vertebral chordomas, initial treatment in 14 consisted of decompressive laminectomy with removal of varying amounts of tumor in the extradural space and involved bone. In the remaining four patients, the diagnosis of chordoma was not entertained before surgery: two patients underwent laparotomy for an intra-abdominal mass and two had biopsy of a retropharyngeal tumor. Multiple operations (laminectomy and/or fusions) were performed in 14 patients within 2 years of initial surgery for recurrent symptoms. There were no operative deaths. Seventeen patients received postoperative radiation therapy.

The initial treatment of the 36 patients with sacrococcygeal lesions can be divided into three major categories: seven underwent biopsy and radiation therapy; nine underwent major surgical resection only; and 20 underwent surgery and radiation therapy. Of the entire group, 17 patients underwent further surgery for recurrent tumor. While the rationale for choosing a particular mode of therapy was not always clear, it could be generally inferred that postoperative radiation was omitted if the surgeon believed that tumor resection was complete. Those patients judged too ill to undergo a major operation and those in whom the extent of tumor made total resection unlikely underwent biopsy only. There were two immediate postoperative deaths in the surgical group. Five patients underwent cordotomy for treatment of intractable pain several years after the initial surgery.

Since this study covers a period from 1949 to 1976, radiotherapy techniques varied considerably. During the earlier period 250 kV x-rays were used, particularly for palliative treatment. However, most patients in this series received supervoltage radiation including 1 MeV, 2 MeV, and 6 MeV x-rays, telecobalt, and high-energy electron beam therapy. Two patients received interstitial implantation of radioactive isotopes. Some of the techniques used have been described in an earlier paper.18 Radiation dosages depended on the aim of treatment as well as whether or not the patient had had prior radiotherapy. In general, doses of 6000 to 7000 rads in 6 to 10 weeks were given for radical treatment and 4000 to 5000 rads in 4 to 6 weeks were given for palliation. The dose given for recurrent cases depended on previous radiation therapy factors and the condition of the normal tissues.

In recent years, newer and improved techniques have been developed that are capable of providing more accurate and precise treatment to the tumor mass, with sparing of surrounding normal tissues. These include the use of wedge filter techniques to shape the beam, and rotation therapy using gravity-oriented blocks to protect vital structures such as the spinal cord. The latter technique has been described in detail elsewhere.22

Chemotherapy was used to treat either recurrent or disseminated disease in a small number of patients. Eight patients (six with vertebral and two with sacral chordomas) had a number of chemotherapeutic agents singly or in combination, including epoxy-piperazine, vinblastine, cyclophosphamide, methotrexate, 5-fluorouracil, actinomycin D, and chlorambucil. An additional seven patients were given multiple doses of radioactive sulfur-35.

Results of Treatment

Forty-one of the 54 patients have been followed up to death, and 10 patients were alive at the time of the study. Three patients were lost to follow-up review. In the sacral group, 25 patients survived 5 years or

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<td>lung</td>
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FIG. 6. Computerized tomography scan showing extension into the soft tissue (dotted line), bone, and spinal column (arrow).

TABLE 3

Metastases in spinal chordomas

(21 of 54 cases)
longer, as did eight of the vertebral group. Using the Kaplan-Meier product-limit method, we computed the probability of survival for patients with sacrococcygeal and vertebral lesions. The median survival for both groups was approximately 6 years. The 5-year survival for the sacrococcygeal group was 66%, as opposed to 50% for the vertebral group. Approximately 40% of patients with sacral chordomas lived 10 years. The number of patients with vertebral tumor followed to 10 years was too small to permit analysis. Statistical analysis revealed no correlation between survival and age or sex of the patients. With few exceptions, the presence or absence of metastases also did not affect survival. Although the survival period for patients with sacral chordomas appeared somewhat better than for those with vertebral chordomas, the difference was not significant. Only four patients in the entire series were free of disease at 5 or more years. Of these four patients, two died 17 and 20 years, respectively, after surgery alone, and were shown to have no residual disease at autopsy. A third patient, also treated by surgery only, was lost to follow-up review after being free of disease for 14 years. The fourth patient is still alive 8 years after biopsy and radiation therapy. A comparison of different modalities of treatment used in the sacrococcygeal group shows no significant difference in survival between those who underwent surgery plus radiation therapy versus those treated by radical surgery alone. Response to chemotherapy was poor. Two patients reported varying degrees of pain relief, but no patient had evidence of tumor regression. Sulfur-35 caused the regression of tumor mass in one patient.

Discussion

There have been only a few large series of chordomas reported in the English literature. In none of these, has the follow-up period been long enough to define the life history of patients with this neoplasm. While there have been several small series in which a high proportion of patients have survived for long periods, analysis of the present series demonstrates that survival varied considerably (from 1 to 12 years), and that the risk of death remained relatively constant throughout this period. For these reasons, and the fact that there was no apparent correlation of survival with age, sex, type of treatment, or site, we infer that chordomas exhibit a wide spectrum of biological behavior. Clinically, this diverse behavior was shown by obvious indolent growth of the tumors in some patients as contrasted to rapid and massive recurrence with disseminated metastases in others.

There are conflicting reports in the literature regarding the incidence of metastases from a low of 5% to a high of 43%. While some of the discrepancy may be explained by the fact that there is a high incidence of metastases in necropsied cases, we cannot explain the striking difference in the incidence of metastases between our series and that reported from the Mayo Clinic. Dahlin and MacCarty stated that radical surgical excision is the treatment of choice for sacrococcygeal lesions if the second sacral segment is intact. In our own series, three of our long-term survivors were those who had small lesions involving the coccyx and lower sacral segments and who underwent complete surgical excision. However, the number of patients who would be amenable to total surgical excision is extremely small, since most patients come to the attention of the surgeon with involvement of the second sacral segment at the initial diagnosis. Hemimorporectomy has been suggested for an occasional patient with lesions below the second lumbar segment; however, the indication for this operation seems very limited, even excepting psychological considerations, in view of our radiological findings that suggest large paravertebral soft-tissue extension before the diagnosis is made.

The number of vertebral chordomas potentially amenable to cure by radical excision is undoubtedly even smaller than for those occurring in the sacrococcygeal area. However, in selected cases in which the location and extent of the tumor appears to lend itself to total removal, we feel such an attempt is justifiable in view of the unpredictable nature of these neoplasms and the fact that, in our experience, patients undergoing limited resection have all manifested recurrence within 2 years. Before deciding on radical excision, however, it is imperative to determine the full extent to which the spine and surrounding structures are involved with tumor so that the proper surgical approach (anterior, posterior, or combined) can be planned, and provisions made for stabilization of the spine. In those patients in whom total surgical excision is not feasible, decompressive laminectomy combined with removal of all gross tumor from the spinal canal can provide worthwhile short-term benefits that may be extended by repeated operations. In this regard, we have been impressed with the value of posterior intertransverse fusion at initial operation as a means of prevention of vertebral body collapse and its consequence of cord compression and pain.

In spite of the tumor's known radio-resistance, the value of radiation therapy has been stressed in several series. Although radiation therapy produced significant subjective relief of pain in a number of patients in our series, objective evidence of tumor regression was difficult to evaluate in the vast majority. We could not show a significantly prolonged survival in those patients with sacrococcygeal lesions treated with postoperative radiotherapy; however, the
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two treatment groups are not strictly comparable. Patients with smaller lesions underwent surgical excision alone, while patients with obviously unresectable lesions received radiation therapy in addition to surgery. With the advent of CT scanning, which permits accurate assessment of tumor extent and volume, it should now be possible to deliver relatively large dosages of radiation to the neoplasm while sparing uninvolved tissue, and to evaluate the efficacy of such treatment.

Conclusions
1. Chordomas exhibit a wide spectrum of biological behavior, with a significant number (39%) manifesting distant metastasis during their clinical course.
2. At the present time, complete surgical resection is possible in only a small number of cases because of widespread extension into soft tissue and bone at the time of primary diagnosis.
3. Radiation therapy probably affords palliation in the majority of cases, but further studies are needed to document by CT scanning the tumor’s radio-response.

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References

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