Surgical seeding of chordomas

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Object. Chordomas have a high propensity for local recurrence and progression, as well as for systemic and cerebrospinal fluid metastasis. The authors identified and analyzed a series of patients with chordomas, focusing on an underrecognized entity—surgical seeding.

Methods. In a retrospective analysis of 82 patients with chordomas treated over a 10-year period (1990–2000) the authors found six patients (7.3%) in whom surgical seeding had occurred. In five (83%) of these patients the primary tumor was located at the clivus. In one (17%) the tumor was present in the cervical region. There were two male (33%) and four female patients (67%) with a mean age of 34 years. The seeding sites, which were separate from the primary tumor, were located along the operative route or in the abdomen where fat was removed. The seeding was diagnosed 5 to 15 months after surgery (mean 12 months). One seeding site was present in five patients and 17 seeding sites were present in one patient. The involved tissues included mucosa, bone, dura, muscle, and fat. After resection, all seedings were documented histologically.

Conclusions. Seeding of chordomas occurs along the operative route and at distant locations where fat is harvested. Early diagnosis and aggressive surgical treatment are recommended. Based on the results of this study, it is suggested that surgical techniques, postoperative irradiation, the neuroradiological follow-up protocol, and even research on chordomas should be reevaluated.

KEY WORDS • chordoma • skull base • surgical seeding • tumor • cervical spine • clivus

Chordomas are rare, aggressive, slow-growing, invasive, and locally destructive tumors that arise from the notochordal remnants along the cerebrospinal axis. In half of the patients with chordomas, they occur in the sacrococcygeal region. Other sites are the sphenoooccipital area (35%) and the upper cervical spine (15%). Males are affected more frequently than females, and radical resection and postoperative radiotherapy are well established as the treatment modalities. This tumor’s propensity for local recurrence, direct extension from the primary site, and systemic and cerebrospinal fluid metastasis are well known. Metastasis most often occurs in young patients, those with sacrococcygeal or vertebral tumors, and those with atypical chordoma histological features. Predictably, patients with metastasis have a poor prognosis.

Surgical seeding of tumor cells along the operative route or at distant locations where fat is harvested is an underrecognized surgery-related complication in the treatment of chordomas. We found six patients in whom seeding of the tumor into tissues occurred separate from the primary tumor. In this article we focus on this underrecognized entity. We discuss the impact this phenomenon may have on future surgical and radiation treatments as well as pathology research. We also describe modifications of surgical technique that can prevent or at least minimize this problem.

CLINICAL MATERIAL AND METHODS

We retrospectively analyzed a series of patients with chordoma surgically treated or evaluated by the senior author (O.A.M.) over a 10-year period (September 1990–October 2000) in three institutions: the University of Mississippi Medical Center (1990), Loyola University Medical Center (1991–1993), and the University of Arkansas for Medical Sciences (1993–2000).

Of 82 patients with chordomas, 62 underwent surgery and 20 underwent only evaluation. The series was composed of 35 male (43%) and 47 female (57%) patients, ranging in age from 5 to 87 years (mean 40 years). The early part of this series has been described previously.1,6

Of the 82 patients, surgical seeding of the tumor was documented in six (7.3%). We reviewed data obtained from each patient’s medical chart, follow-up examinations, neuroradiological review, and histological analysis. For patients who could not be followed on a regular basis, we obtained medical, operative, imaging, and pathology reports, or we contacted the patients directly through phone interviews or questionnaires. Four of these patients...
were female (67%) and two were male (33%) and they ranged in age from 14 to 52 years (mean 34 years) (Table 1, Figs. 1–4).

RESULTS

In all six patients there was a classic histological picture of chordoma. In five patients (83%) the site of the primary tumor was the clivus. In the remaining patient (17%) it was the cervical spine. Five patients underwent radiotherapy (three proton beam and two conventional) after the initial surgery. All patients underwent multiple surgeries for the treatment of the primary tumor, recurrence, or seeding; the number of surgeries ranged from two to eight, with a mean of four. In each patient, seeding of the tumor occurred during the first surgery. In two patients, a chordoma was not considered in the differential diagnosis before the first surgery. The time between the primary surgery and the diagnosis of chordoma seeding ranged from 5 to 15 months (mean 12 months). Five patients had only one site of seeding, which occurred in various tissues: mucosa (nasal, sinuses, oral, and labial), facial bones (vomer, hard palate, and maxilla), the cartilage, the petrous bone, the tentorium, the petrous dura, muscle, and subcutaneous tissues (abdomen and neck). One patient had 17 different seeding sites in the mucosa of the nose, lips, and tongue that were treated surgically as they appeared and were diagnosed.

Three patients died during the follow-up period. One died of a stroke 2 months after his last surgery. The other two patients died of local recurrence of the tumor at the primary site 8 months after their last surgery.

DISCUSSION

Local Tumor Recurrence and Progression

Both the use and combination of modern skull base surgical techniques have significantly improved the outcome of patients with skull base chordomas, clearly extending the boundaries of their treatment. At the same time, the use these techniques has brought about certain contemporary developments and complications previously unknown. These techniques have allowed a radical tumor resection rate of approximately 50%, a mortality rate of approximately 5%, and a major complication rate of approximately 10%. The 5-year recurrence-free interval in patients with a chordoma is approximately 76%. To achieve radical resection, multiple skull base approaches

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**TABLE 1**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Primary Tumor Site</th>
<th>Seeding Op Approach</th>
<th>Type of Radiation</th>
<th>Time Between Op &amp; Diagnosis of Seeding (mos)</th>
<th>Seeding Site/Tissue</th>
<th>Mos Until Death After Last Op</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>29, F</td>
<td>clivus, transmaxillar</td>
<td>proton beam</td>
<td>15</td>
<td>maxillary sinus/bone, mucosa</td>
<td>8</td>
<td>alive</td>
</tr>
<tr>
<td>2</td>
<td>51, F</td>
<td>bilat petroclivus, petrogyoid plates, transnasal</td>
<td>proton beam</td>
<td>12</td>
<td>inferior nasal cavity, nasal septum, hard palate, upper &amp; lower lips, tongue/bone, cartilage, mucosa</td>
<td>2</td>
<td>alive</td>
</tr>
<tr>
<td>3</td>
<td>52, M</td>
<td>clivus, transnasal</td>
<td>conventional</td>
<td>15</td>
<td>anterior nasal septum, hard palate, maxilla/ bone, cartilage, mucosa</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>44, F</td>
<td>C3–6, anterolateral to cervical spine</td>
<td>conventional</td>
<td>5</td>
<td>anterolateral neck/muscle &amp; subcutaneous tissue</td>
<td>alive</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>15, F</td>
<td>clivus, transoral</td>
<td>proton beam</td>
<td>10</td>
<td>posterior wound/subcutaneous tissue, fat</td>
<td>8</td>
<td>alive</td>
</tr>
<tr>
<td>6</td>
<td>14, F</td>
<td>clivus, petrosal</td>
<td>none</td>
<td>13</td>
<td>posterior petrous, retroauricular area/dura, tentorium, subcutaneous tissue</td>
<td></td>
<td></td>
</tr>
</tbody>
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**Fig. 1.** Case 1. *Upper Left:* Axial T2-weighted magnetic resonance image obtained at initial presentation, demonstrating the hypointense tumor (asterisk), which was resected in two stages (the transcondylar and the transmaxillary approach). *Upper Right:* Follow-up T2-weighted magnetic resonance image obtained 15 months later, revealing the chordoma seeding in the left maxillary sinus, which was removed surgically. *Lower:* Photomicrograph showing the tumor (black asterisk) and the mucosa of the maxillary sinus (white asterisk). H & E, original magnification × 33.
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Fig. 2. Case 2. Magnetic resonance images. Upper: Coronal T$_1$-weighted postcontrast image with fat suppression, demonstrating one of the patient’s 17 chordoma seedings that occurred after initial surgery via the transnasal approach conducted at another institution. This seeding was located in the right inferior nasal cavum (asterisk). Lower: Axial T$_2$-weighted image revealing the hyperintense tumor (asterisk).

may need to be performed in as many as 50% of patients. Nonetheless, radical resection remains one of the most important prognostic factors in the treatment of chordomas in any location. The other important treatment modality and prognostic factor is postoperative radiotherapy. Proton-beam radiotherapy (or conventional radiotherapy as an alternative in patients with spinal lesions) in combination with radical surgery offers the best chance for long-term tumor control in patients with chordoma.1,2,6,15,17,26,30,50

The most common failure in the treatment of skull base (78%) and spinal chordomas is local tumor recurrence or progression.1,2,6,17,30,50 If the tumor recurs, radical surgery and radiotherapy (if the patient is eligible) may be repeated. Another failure in the treatment of these challenging tumors, which may also be an initial presentation of the disease, is local extension of the tumor from the primary site. The most common sites of tumor extension in the skull base are the nasopharynx, maxilla, and the frontal sinus.5,21,31,35,39,48

Metastasis of Chordomas

Chordomas metastasize in 3 to 48% of the patients harboring these lesions. Tumors in the sacrococcygeal and vertebral locations are more prone to metastasis and metastasis is more likely to occur in children younger than age 5 years than in older children. Atypical histological patterns are found in 86% of metastases, whereas classic and chondroid patterns are found in 7% each. Most of the patients with metastatic disease die within a mean follow-up period of 40 months. In descending order of occurrence, the organs and tissues involved by metastasis include the lungs, lymph nodes, liver, bone, skin, muscle, peritoneum, heart, pleura, retroperitoneum, spleen, dura mater, kidney, and the adrenal glands.1,3–10,13,18,22,25,27,29,30,32,33,35,36,38,39,41–50 Markwalder, et al.,29 have suggested that metastasis is more common with spinal rather than clival chordomas because most tumor cells reach the circulation by invading large veins. Chambers and Schwinn10 have suggested that irradiation may play some role in the genesis of metastasis, whereas surgery, length of survival, age, and sex do not.

Cerebrospinal fluid drop metastasis of skull base chordomas is rare, but several cases have been reported.13,25,33,40,42 Presumably, the tumor cells detach after the tumor penetrates the dura and dislodge distally along cerebrospinal fluid pathways.

Surgical Seeding of Chordoma

Although a few cases of “surgical pathway tumor recurrence” have been reported in the neuroradiological and radiotherapeutic literature,4,13,14,20 the seeding of chordomas as a surgery-related complication is an underrecognized entity. Austin, et al.,4 reported that among 141 patients with skull base and cervical chordomas treated with proton-beam irradiation, recurrent disease was demonstrated in 26. Of these 26 patients, recurrence along the surgical pathway, which was not part of the target volume, occurred in two (7.7%). Fagundes, et al.,13 noted that of 204 patients with skull base and cervical chordomas who underwent proton-beam irradiation, in 63 (31%) treatment failed. Of these 63 patients, in three the recurrence was present along the surgical pathways (neck, palate, and nasal cavity, respectively). All of these patients underwent surgical removal of these lesions, but two eventually died of local recurrence and local and distal tumor recurrence, respectively. Both of these teams published on series of patients that were collected at the same institution and thus these series may actually overlap. Hug, et al.,21 have reported that of 58 patients harboring chordomas and chondrosarcomas treated with proton beam irradiation, failure of treatment occurred in 10 (17%). In one of the 10 patients recurrence was demonstrated in the nasal cavity along the surgical pathway, which was outside the radiation field. Recently, Fischbein, et al.,14 reported three cases of clival chordoma “recurrence along the surgical pathway” occurring 4, 2, and 2 years postoperatively, respectively, all in the sinonasal cavity. The lesions in these patients were treated via the transsphenoidal, the sublabial transsphenoidal, and the transoral approach, respectively. The first two patients subsequently underwent proton-beam irradiation, which failed to include the surgical pathways in the treatment field. The authors stated that in these patients they could not distinguish between the two possible mechanisms of tumor recurrence along surgical pathways: direct surgical tumor implantation or hematogenous spread.

As our findings demonstrate, surgical seeding of chordoma is a consequence of the implantation of tumor along the surgical route or where fat is harvested. The rate
of chordoma seeding in this series was 7.3%. In all six patients, the seeding sites were separate from the initial tumor site, and all tumor seedings were confirmed histologically after their removal. A certain interval seems necessary between the time of surgery, when the seeding occurs, and the actual growth of a symptomatic mass. In our study, this period ranged from 5 to 15 months (mean 12 months). We hypothesize that this time is necessary for the tumor cells to adjust to a new environment, overcome the local and systemic defense mechanisms, and finally grow large enough to induce symptoms.

As analysis of data from this and other series 4,13,14,20 indicates, radiotherapy, regardless of whether proton-beam or conventional radiation is used, does not routinely target the surgical route. One may speculate that this plan of treatment facilitates tumor growth. Undoubtedly, the planning and techniques used for radiotherapy in patients with chordomas should be reevaluated.

Despite the fact that the classic histological forms of chordoma without atypical features were demonstrated in all six patients, the chordoma cells were not selective for the new host tissue or the location. “Good” tissues for tumor growth included bone (vomer, maxilla, hard palate, and petrous pyramid), the mucosa (oral, nasal, tongue, and labial), the tentorium, the petrous dura, subcutaneous fat and muscles in the neck, and subcutaneous fat in the abdomen. Chordomas metastasize nonselectively to almost any organ or tissue. This combination of metastasis and seeding should inspire new pathological studies in which investigators assess the cultivation of chordoma cells and the development of new culture lines. The results of such studies could shed light on the molecular, biochemical, cellular, and tissue levels that pertain to the invasive nature of chordomas. Additional studies could then be conducted to test the effects of different chemotherapeutic agents on this tumor. Finally, surgeons should rethink the graft techniques routinely used in skull base approaches to chordomas including fat, muscle, or bone.

With regard to prognosis, the results obtained in this and other series 4,13,14,20 paradoxically indicate that the surgical seeding of chordoma per se does not contribute to the final, dismal outcome of most patients. Instead, these findings were better indicators of the aggressive behavior of the tumor in every patient and a harbinger of recurrence and progression at the initial site. These factors ultimately caused death in almost half of the patients in this series. On the other hand, early diagnosis and radical removal of all the tumors in our patients may have prevented seeding from becoming a more unfavorable prognostic factor.

On follow-up imaging, the surgical route must be routinely scrutinized for a recurrent tumor for this purpose. Magnetic resonance T2-weighted images are particularly useful. Until proven otherwise, a hyperintense lesion demonstrated along the surgical route on a T2-weighted image should be considered tumor seeding, not a benign postoperative change, a nasal cyst, or a polyp.

Finally, but most important, the surgical techniques and approaches used to remove chordomas must be tailored to meet new findings. During preoperative planning, the surgeon should consider that a clival tumor may actually be a chordoma. In fact, in two patients in this series, the surgeons performing the initial “seeding” operations did not...
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Fig. 4. Case 6.  Left: Sagittal T1-weighted magnetic resonance image revealing the clival chordoma (asterisk) that had been resected via a two-stage procedure (via transoral and transcondylar approach) at another institution. Center: Coronal postcontrast T1-weighted magnetic resonance image demonstrating the contrast-enhancing tumor (asterisk). At that time fat had been harvested from the abdomen to serve as a graft. Right: The patient presented to us with local tumor recurrence as well as pain and swelling at the site at which fat was harvested. We resected the recurrent clival tumor and also explored the abdominal harvest site. To our surprise, a chordoma seeding was found. This photomicrograph of a specimen was obtained after exploration of earlier fat harvest site and removal of the tumor. Note the abdominal fat (black asterisk) and the chordoma (white asterisk). H & E, original magnification × 33.

CONCLUSIONS

The seeding of a chordoma may occur along the operative route or at a distant site at which fat is harvested. The surgical techniques used to remove chordomas should be modified to prevent or minimize the risk of this complication. If seeding occurs, early diagnosis and aggressive surgical treatment are recommended. Because chordoma seeding may occur in the tissues along the operative route, this area should be included in the postoperative radiation field. Furthermore, on follow-up magnetic resonance imaging the operative route should be scrutinized for possible seeding. Chordomas seem to be able to grow on any tissue, a fact of great importance in chordoma research.

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References


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