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 pathological entity—surgical seeding of tumor cells.

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 at the cervical spine. There were two male (33%) and four female patients (67%) whose mean age was 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 (mean 12 months) after surgery. 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 confirmed histologically.

Conclusions. Seeding of chordomas occurs along the operative route and at distant locations where tissue is harvested. Early diagnosis and aggressive surgery are recommended. Based on the results of this study, the authors suggest that surgical techniques, postoperative radiotherapy, 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. Their propensity for local recurrence, direct extension from the primary site, and systemic and cerebrospinal fluid metastasis are well known. Distal metastasis most often occurs in young patients, those with sacrococcygeal or vertebral tumors, and those with atypical chordoma histological features. Predictably, a poor prognosis is demonstrated in patients with metastasis.[1–12,15–20,22–50] Radical resection followed by high-dose radiotherapy "sterilizes" the field and controls the tumor locally. The surgical route, however, is outside the region of the primary tumor and outside the irradiated area and is therefore vulnerable to tumor seeding by surgical implantation.

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

Abbreviation used in this paper: MR = magnetic resonance.

Clinical Material and Methods

We retrospectively analyzed a series of patients with chordoma in whom surgery or evaluation was performed by the senior author (O.A.M.) over a period of 10 years (9/1990–10/2000) at 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).

In the series of 82 patients with chordomas, 62 underwent surgery and 20 underwent evaluation. There were 35 male (43%) and 47 female patients (57%) 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, in six (7.3%) there was documented evidence of surgical seeding of the tumor. Data from each patient's medical chart, follow-up examinations, neuroradiological studies, and histological reports were reviewed. In cases in which patients could not be followed on a regular basis, we obtained medical, operative, radiological, and pathological reports or contacted the patients directly through phone interviews or questionnaires.

Results

In all six patients the classic histological picture of chordoma was demonstrated. In five patients (83%), the site of the primary tumor was the clivus; in one patient (17%), it

TABLE 1

Characteristics and outcome in six patients with surgical seeding of chordomas

Case No.	Age (yrs), Sex	Primary Tumor Site	Seeding Op Approach	Type of Radiation	Diagnosis of Seeding (mos)*	Seeding Site/Tissue	Outcome
1	29, F	clivus	transmaxillary	proton beam	15	maxillary sinus/bone mucosa	died 8 mos postop
2	51, F	bilat petroclivus, pterygoid plates	transnasal	proton beam	12	inferior nasal cavity, nasal septum palate, upper & lower lips, tongue/bone, cartilage, mucosa	alive
3	52, M	clivus, dorsum sellae	transnasal	conventional	15	anterior nasal septum, hard palate, maxilla/bone, cartilage, mucosa	died 2 mos postop
4	44, F	C3–6	anterolat to cervical spine	conventional	5	anterolat neck/muscle & subcutaneous tissue	alive
5	15, F	clivus	transoral	proton beam	10	abdominal wound/subcutaneous tissue, fat	died 8 mos postop
6	14, M	clivus	petrosal	none	13	posterior petrous, retroauricular area/dura, tentorium, subcutaneous tissue	alive

* Time between operation and diagnosis of surgical seeding.

was the cervical spine. Four patients were female (67%) and two were male (33%), and they ranged in age from 14 to 52 years (mean 34 years). After the initial surgery five patients underwent radiotherapy (three with proton-beam and two with conventional radiation). All patients underwent multiple surgeries for the treatment of either their primary tumor, recurrence, or seeding; the number of surgeries ranged from two to eight (mean four surgeries/patient). 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). In five patients there was a single site of seeding, which occurred in the following various tissues: mucosa (nasal, sinus, oral, or labial), facial bones (vomer, hard palate, or maxilla), the petrous bone, the tentorium, the petrous dura, muscle, and subcutaneous tissues (abdomen or neck). In one patient 17 different seeding sites present in the mucosa of the nose, lips, and tongue, were treated surgically as they appeared and were diagnosed (Table 1, Figs. 1–3).

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

Discussion

Surgical Seeding of Chordoma

Although a few cases of "surgical pathway tumor recurrence" have been reported in other series,[4,13,14,21] the seeding of chordomas as a surgery-induced complication is underrecognized. In the series reported by Austin, et al.,[4] recurrence was demonstrated in two patients along the surgical pathway that was not part of the target volume. Later, reporting from the same institution, Fagundes, et al.,[13] noted that, of 204 patients with skull base and cervical chordomas in whom proton-beam radiotherapy was performed, treatment failure occurred in 63 (31%). Of these 63 patients, recurrence was demonstrated in three along the surgical pathways (neck, palate, and nasal cavity, respectively). Hug, et al.,[21] have reported that, of 58 patients in whom chordomas and chondrosarcomas were treated with proton irradiation, a failure of treatment occurred in 10 (17%); in one of these, recurrence was observed in the nasal cavity along the surgical pathway, which was outside the radiation field. Recently, Fischbein, et al.,[14] have described three cases of clival chordoma recurrence demonstrated along the surgical pathway that occurred 4, 2, and 2 years postoperatively, respectively, all in the sinonasal cavity. The approaches used in these patients were the transsphenoethmoidal, the sublabial transsphenoidal, and the transoral, respectively. The first two patients underwent subsequent 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 indicate, surgical seeding of chordomas is a consequence of the implantation of tumor cells along the surgical route or where fat is harvested. The rate of chordoma seeding in our 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 interval 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 produce symptoms.

As data from this and other series[4,13,14,21] indicate, radiotherapy, regardless of whether proton-beam or conventional radiation is used, does not routinely include the surgical route. One may speculate that this plan of treatment facilitates tumor growth. Undoubtedly, we should reevaluate the planning and methods used in the radiotherapeutic intervention in patients with chordomas.

Despite the fact that the classic histological forms of chordoma without atypical features were present in all six patients, the chordoma cells were selective for neither the new host tissue nor 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.

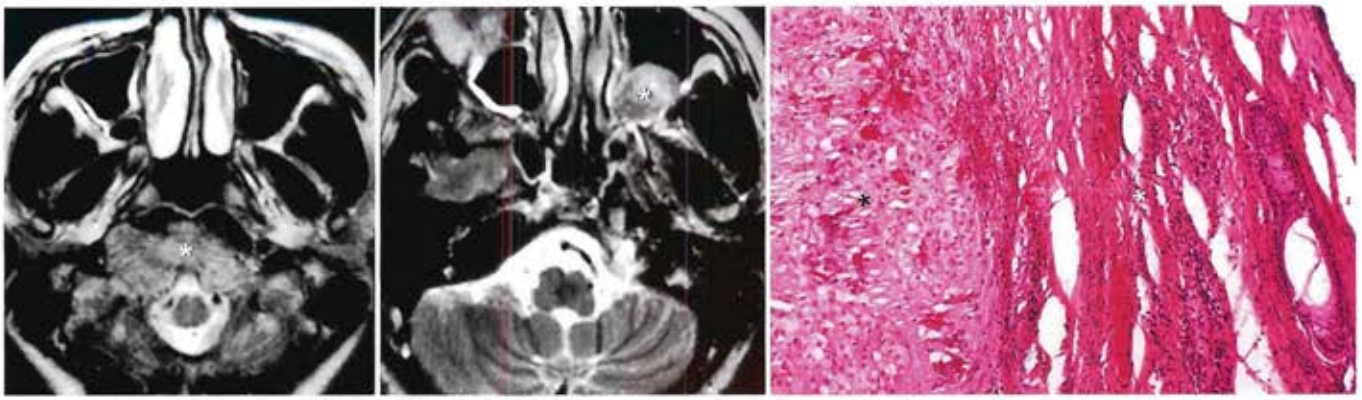

FIG. 1. Case 1. *Left:* Axial T_2-weighted MR image obtained at initial presentation, revealing the hyperintense tumor *(asterisk)*, which was resected in two stages (via transcondylar and the transmaxillary approaches). *Center:* Follow-up T_2-weighted MR image obtained 15 months later demonstrating chordoma seeding in the left maxillary sinus *(asterisk)*; the mass was removed surgically. *Right:* Photomicrograph of the surgical specimen showing the tumor *(black asterisk)* and the mucosa of the maxillary sinus *(white asterisk)*. H & E, original magnification × 33.

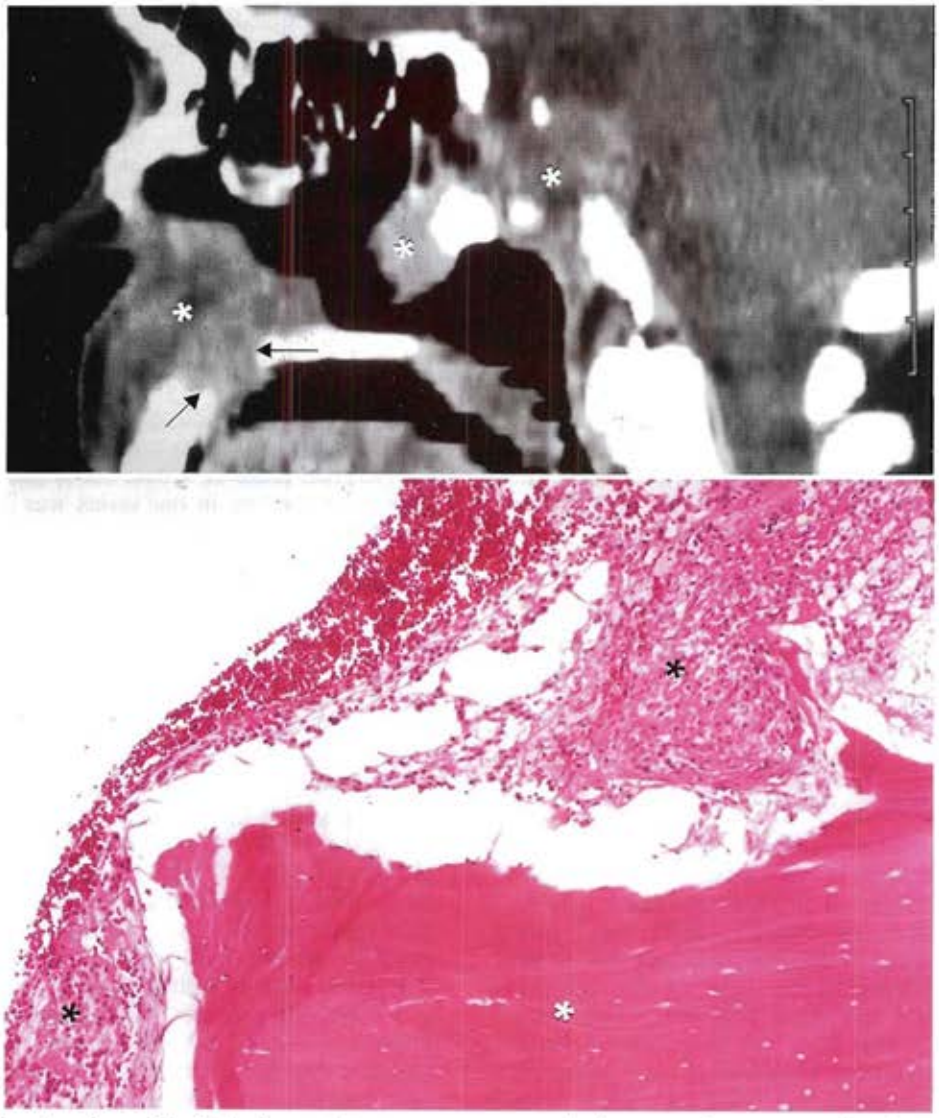

FIG. 2. Case 3. *Upper:* Sagittal reformatted postcontrast computerized tomography scan revealing the tumor recurrence at the clivus area *(asterisk)* and chordoma seeding *(asterisk)* penetrating the hard palate *(arrows)*. *Lower:* Photomicrograph showing the bone of the hard palate *(white asterisk)* and the tumor *(black asterisk)*. H & E, original magnification × 33.

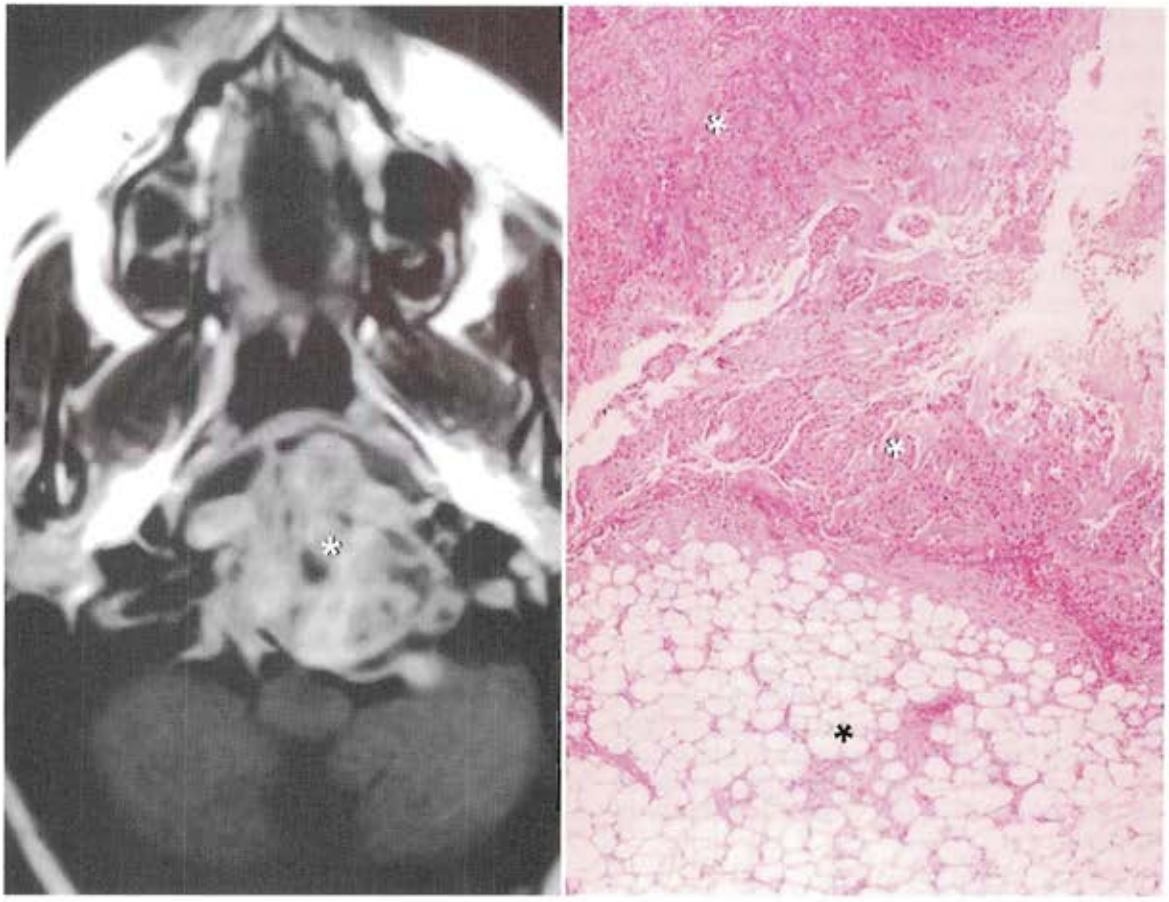

FIG. 3. Case 6. *Left:* Axial postcontrast T_1-weighted MR image demonstrating the contrast-enhanced clivus tumor *(asterisk)*, which was subsequently resected at an outside institution via a two-stage procedure (the transoral and the transcondylar approaches). At that time, fat was harvested from the abdomen to serve as a graft. The patient presented to us with local tumor recurrence but also pain and swelling at the site at which the fat was harvested. We resected the clival tumor recurrence and also explored the abdominal harvest site. To our surprise, a chordoma seeding was found. *Right:* Photomicrograph of a specimen obtained after exploration of earlier fat harvest site and removal of the tumor. Note the abdominal fat *(black asterisk)* and the chordoma *(white asterisks)*. H & E, original magnification × 33.

Similarly, chordomas metastasize nonselectively to almost any organ or tissue. This combination of chordoma metastasis and seeding should inspire new pathological studies in which investigators focus on the cultivation of chordoma cells and the development of new culture lines. Such studies could shed light on the molecular, biochemical, cellular, and tissue levels that pertain to the invasive nature of chordomas. Further 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 the skull base approaches to chordomas including fat, muscle, or bone.

Prognostic, Diagnostic, and Surgery-Related Implications

With regard to prognosis, the results from this and other series[4,13,14,21] paradoxically indicate that the surgical seeding of chordoma per se does not contribute to the final outcome of most of the patients. Rather, these findings were better indicators of the aggressive behavior of the tumor in every patient and a harbinger of repeated 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 resection of all tumors in this series may have kept seeding from becoming a more unfavorable prognostic factor.

On follow-up neuroimaging, the surgical route should be routinely scrutinized for a recurrent tumor. The use of T_2-weighted MR images are particularly useful for this purpose. Until proven otherwise, a hyperintense lesion demonstrated along the surgical route on the T_2-weighted MR image should be considered tumor seeding rather than a benign postoperative change, a nasal cyst, or a polyp.

Finally, but most importantly, the surgical techniques and approaches used to remove chordomas should be tailored to meet new circumstances. During preoperative planning, the surgeon should consider that a clival tumor may in fact be a chordoma. In fact, in two patients in this series, chordoma was not suspected preoperatively. We have modified our operative techniques based on the lessons learned from this series. After the approach is completed but before we remove the tumor, we coat the walls of the operative tunnel with fibrin glue and large cotton patties; at the end of surgery, we carefully remove the cot-

ton patties along with the fibrin glue. Grafts are then introduced into the "tumor-free" area (gross totally resected tumor). Before closure, all contaminated drapes and towels are replaced, and a clean set of instruments and new gloves are used to perform closure. We also use a clean set of instruments and new gloves and drapes when harvesting fat from the abdomen. In general, all instruments that came in contact with the tumor are considered contaminated. If seeding of the chordoma is diagnosed during the follow-up period, it is treated aggressively and radically, as is any recurrence at the primary site or metastasis. As the results of this study suggest, no particular surgical approach is predisposed to the seeding of tumor cells. Rather, surgical seeding appears to be tumor implantation.

Conclusions

The seeding of a chordoma may occur along the operative route or at a distant site where tissue 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, consideration might be given to including this area in the postoperative irradiation treatment if possible. Furthermore, on follow-up MR images, 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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