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# Original research article

# Tumour seeding in the surgical pathway after resection of skull base chordoma



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#### ABSTRACT

Aim: The aim of this study is to review the clinical series in which tumour seeding was reported after skull base surgery for chordomas.

*Background*: The occurrence of implantation of cancer cells during surgical procedures for the removal of chordoma is a rare event described by a number of authors in a few patient series and case reports.

Materials and methods: Literature search was performed by PubMed and Scopus by using the words "surgical tumour seeding, tumour implantation, surgical pathway recurrence, skull base chordoma, and clivus chordoma".

Results: Six retrospective series and 7 case reports were included in the analysis. In total, 34 patients are described with pathway recurrence, 30 at a single site and 4 at multiple sites.

In the 5 largest chordoma series, the rate of occurrence of surgical seeding ranged from 1.3% to 7.3% (3.9%). In the 34 patients diagnosed with tumour seeding, the most frequent surgical approach was trans-nasal/trans-sphenoidal, that was used in 12 cases. The median time from primary treatment to surgical pathway tumour seeding ranged from 7 to 78 months. Data of the treatment of seeding are available in 26/34 patients. All of them underwent a new surgery, 6 received additional external beam radiotherapy, and 2 intraoperative radiotherapy.

Conclusions: The risk of surgical seeding should be taken into consideration when deciding on the surgical approach and the planning treatment volume for postoperative radiation therapy. The surgical pathway should be included in follow-up studies to diagnose this peculiar type of treatment failure possibly at an early phase.

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### 1. Background

Chordoma is a rare cancer arising from notochord remnants. Its incidence is 0.08 per 100,000 with predominance of male and a peak between 50 and 60 years. Chordoma occurs at skull base in 30-40% of cases.<sup>1,2</sup> Although it is usually a slow growing cancer and looks relatively benign histologically, it is locally aggressive and frequently recurs following treatment. Normally, surgical resection is the first line treatment. The "en bloc" resection aims at local control but is usually difficult to achieve, due to the close proximity of this tumour to critical structures such as brainstem, cranial nerves, and major intracranial vessels. Radiation therapy is used to sterilize surgical field and treat residual, recurrent or unresectable disease. Local recurrence is the most common form of treatment failure, local recurrence free survival at 5 years being in the range of 17-33% in historical series treated by conventional radiotherapy and 50% in more recent series treated by stereotactic radiotherapy. 3-5 Particle therapy, mainly by protons, has substantially improved local control and long term outcome. 3,6,7 Chordoma has also the potential to metastasize to regional lymph nodes, distant sites and cerebrospinal fluid. 1,2,7,8 A rare and peculiar pattern of failure is tumour seeding along the surgical access pathway that is reported in less than 5% of cases.8 These sites, such as the nasal cavity and surrounding soft tissue, are often outside the treatment field of radiation and can be subject to iatrogenic tumour implantation.

#### 2. Aim

The aim of this study is to perform a review the literature about the occurrence and the natural history of tumour seeding after a surgical approach for skull base chordoma.

#### 3. Material and methods

Literature search was performed by PubMed and Scopus by using the following words: surgical tumour seeding, tumour implantation, surgical pathway recurrence, skull base chordoma, and clival chordoma. No limits of time period were used. Only English-language studies were included. Only studies with tumour seeding related to surgical procedures for skull base chordoma were included. No selection basing on type of studies was adopted. Abstracts from scientific meetings were considered when relevant, i.e. including large series of skull base chordoma. Case reports were considered as well.

#### 4. Results

From literature search, we found 6 retrospective series and 7 case reports of patients who experienced surgical pathway recurrence after excision of skull base chordomas<sup>9–21</sup> (Table 1). No prospective trials were found. Five out of 13 series included not only skull base but also cervical spine tumours. An abstract was also considered since it specifically updated the results on skull base chordoma of one of the largest series about skull base and cervical chordoma.<sup>20</sup>

In total, 34 patients were described with pathway recurrence, 30 at a single site and 4 at multiple sites: one patient with 4 sites, another patient with 3 sites and two patients with 2 sites.

Postoperative radiotherapy was mainly delivered by protons or protons/photons.

In the 5 largest chordoma series coming from 4 different institutions, the rate of occurrence of surgical seeding ranged from 1.3% to 7.3% (median 3.9%). Considering the total number of patients affected by skull base chordoma from these 5 series, the mean incidence of surgical seeding was 2.7% (25/930). In the 34 cases with 39 sites of surgical seeding, the surgical approaches were as follows: trans-nasal/trans-sphenoidal in 12 cases, cervical skin and soft tissues in 5 cases, trans-maxillary in 2 cases, trans-oral in 6 cases, trans-petrosal in 1 case (3 sites), infra-temporal or trans-condylar in 2 cases, rhinoseptal in 2 cases, trans-latero nasal and temporozygomatic in 1 case, at the level of craniotomies in 4 cases and in the abdominal wound after a procedure for tissue graft in one case

The median time from primary treatment to surgical pathway tumour seeding reported in the 3 large series ranged from 12.5 to 78 months and the same time in the 7 case reports ranged from 7 to 72 months.

Data concerning treatment of seeding were available in 26 out of 34 patients. All of them underwent a new surgery, 6 received external beam radiotherapy, and 2 intraoperative radiotherapy.

Three articles described the series from MGH.<sup>9,10,20</sup> The most recent one<sup>20</sup> includes 8 patients with 11 sites of surgical seeding observed in a series of 203 cases of clivus chordoma (3.9%) who underwent 302 surgical procedures: 7 after 187 trans-facial approaches (3.7%), 2 after 101 craniotomies (2.0%), and 2 after 14 infratemporal approaches (14.3%). The authors reported 5 and 10 years overall survivals rates worse for the 8 cases with surgical seeding compared to the other 195 patients. Of the 8 cases with surgical seeding, 3 (37.5%) developed systemic metastases, compared to 5/195 (2.6%) cases without surgical seeding.

Fischbein et al.<sup>11</sup> reported on 3 patients out of 70 (4.3%) operated for skull base chordoma at the University of California, San Francisco, who recurred along the surgical pathway. All the three patients, aged 33–47, were operated by trans-sphenoidal approach in two cases and by transoral approach followed by external spheno-ethmoidectomy for recurrence in one case. All three patients were treated postoperatively by proton beam radiation therapy. Tumour seeding occurred in the nasal cavity in the first two cases and in the ethmoid region in the third case. All the three patients required further surgery associated with radiation in 2/3. They remained without tumour progression after 2–4 years after the treatment for tumour seeding.

Arnautovic et al.<sup>12</sup> reported surgical seeding in 6 out of 82 patients (7.3%) operated for chordoma of the skull base and cervical spine at the University of Arkansas. The 6 patients were aged from 14 to 52 years and 5 of them had undergone postoperative radiotherapy with protons in 3 cases and photons in 2. All the 6 patients had received 2–8 surgical procedures for their primaries and recurrences. Five developed a single site of seeding, including the site of abdominal wound

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