Intracranial chondrosarcoma: review of the literature and report of 15 cases

Arthur G G C Korten, Hans J W ter Berg, Geert H Spincemaille, Ronald T van der Laan, Antoinet M Van de Vel

Abstract
The available data in the literature (177 cases), two current clinical patients, and cases which occurred in The Netherlands (13) were reviewed concerning the clinical presentation, pathological features, radiological data, and treatment options of chondrosarcoma of the cranial base. The mean age of patients was 37 years, the male/female ratio 1:1.1. The most frequent complaints were diplopia with ocular motor disorders (51%), headache (31%), and decreased hearing, dizziness, and tinnitus with statoacoustic dysfunction (21%). The mean duration of symptoms before diagnosis was 27 months.

The chondrosarcomas were located in the petrosal bone in 37% (47 cases), in the occipital bone and clivus in 23% (30 cases), in the sphenoid bone in 20% (25 cases) and to a lesser extent in frontal, ethmoidal, and parietal bones (14%). In 6% (eight cases) the primary location was in dural tissue. Radiological examinations showed bone destruction and variable calcification (CT), involvement of neuronal and vascular structures (MRI), and mostly hypovascularity on angiography. On histological examination 51% of tumours were classified as grade I, 11% grade II, 30% mesenchymal, and 8% myxoid. The mesenchymal type was the most malignant as illustrated by a strong tendency to intradural and cerebral growth and possibly occurrence in younger age groups. The treatment of choice until recently was surgery because of the critical location and local aggressive nature. Regrowth of tumour after surgery occurred in 53% of the patients (average after 32 months). Charged particle irradiation gave a five year survival of 83–94% and a local control rate of 78%–91%. Both in surgery and radiotherapy there is treatment related morbidity and mortality that should be considered when offering these therapies.

Recent promising results imply that charged particle radiotherapy, in combination with surgery, may be the therapeutic choice of the future.

Keywords: chondrosarcoma; cranial base neoplasm

Tumours originating from bone at the base of skull are rare. One such tumour, the chondrosarcoma, the most malignant cartilage tumour, represents 0.15% of all cranial space occupying lesions and 6% of all skull base tumours. It is assumed that chondrosarcomas originate from remnants of embryonal cartilage or from metaplasia of meningeal fibroblasts.

To the best of our knowledge, the last detailed review of the literature disclosed only 50 cases until 1985. This led us to review the available literature since 1985 in detail. This report also concerns two of our own clinical patients and 13 other patients treated in different hospitals throughout The Netherlands. The clinical history, pathological features, radiological findings, and treatment options are discussed. From these data we give an overview of the current diagnostic procedures and therapeutic options of intracranial chondrosarcoma.

Methods
In addition to the study by Hassounah et al, analysis of the literature from 1985 disclosed 127 cases.4–37 Our own two clinical patients and 13 other cases retrieved from the files of the Dutch Committee on Bone Tumours, University Hospital Leiden, and the reported cases since 1985 along with the 50 cases from the review of Hassounah et al4 were analysed. Table 1 shows summarised data of the 15 Dutch patients.

Patients with chondrosarcoma from the nasopharynx or the paranasal sinus and extending into the skull base and chondrosarcoma as part of the syndromal diseases Maffucci or Ollier were excluded. The 27 patients of the series of Castro et al were also excluded because of paucity of detailed information.

Results
The sex ratio was 1:1.1. In 16 cases, the sex of the patient was not reported. The average age was 37 years (range 3 months–76 years). Age was not reported in 67 cases.

Signs and symptoms at initial presentation were described in 67 patients (table 2). The median time period between initial symptoms and moment of diagnosis was 15 months (ranging from 1 month to 144 months). This information was available in only 36 cases.

Over the years, different radiological evaluation methods have been used. Plain skull radiography, CT, MRI, and angiography were the most often used diagnostic tools. On T1 weighted MRI, chondrosarcomas had a low to intermediate signal intensity and were isointense or hypointense to grey matter. On proton density and T2 weighted images, they had high signal intensity and were hyperintense to grey matter.
Table 1 Characteristics of 15 Dutch patients

<table>
<thead>
<tr>
<th>No</th>
<th>Age/sex</th>
<th>Location</th>
<th>Pathology</th>
<th>Size</th>
<th>Symptoms/signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>31/M</td>
<td>PS; extension in pons and in Scav; destruction of Sph</td>
<td>Grade I</td>
<td>2½×3 cm</td>
<td>Headache 2 y; 1 y diplopia; sensory disturbance OD. Posis / VI dysfunction OD; cornea reflex R=L; sensory disturbance V branch 1 and 2 R Pain face 1 y; paraesthesias. V dysfunction L; possibly VII dysfunction L</td>
</tr>
<tr>
<td>2</td>
<td>26/F</td>
<td>FM; SS</td>
<td>Grade I</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>18/F</td>
<td>PS; extension in clivus and SCav; petroclival junction</td>
<td>Grade II</td>
<td>1×2 cm</td>
<td>Several months diplopia on looking L; headache. VI dysfunction L</td>
</tr>
<tr>
<td>4</td>
<td>15/F</td>
<td>PS; extension in SPh</td>
<td>Grade I</td>
<td>3×2×2 cm</td>
<td>1 y Diplopia; headache. Dysfunction III L</td>
</tr>
<tr>
<td>5</td>
<td>23/M</td>
<td>PS; Clivus; SCav</td>
<td>Grade I</td>
<td></td>
<td>1 y Intermittent frontoparietal headache; diplopia horizontally. VI dysfunction R</td>
</tr>
<tr>
<td>6</td>
<td>72/M</td>
<td></td>
<td>Grade II</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>38/M</td>
<td>Pontomedullary angle</td>
<td>Grade I</td>
<td></td>
<td>Dysfunction VII - XII R</td>
</tr>
<tr>
<td>8</td>
<td>33/M</td>
<td>Os petrosum</td>
<td>Grade II</td>
<td>3×2×2 cm</td>
<td>12 y Strabism; later unsteady gait and decreased hearing AD. Sensory disturbance V branch 2 R; paresis in trapezius and sternocleidom. R; tongue deviating to R; dyssodiaochokinesis and ataxia R</td>
</tr>
<tr>
<td>9</td>
<td>47/F</td>
<td>Behind os petrosum; extension to PS</td>
<td>Grade I</td>
<td>4×4×4 cm</td>
<td>Hemiparesis R; disorder of speech; memory disturbance</td>
</tr>
<tr>
<td>10</td>
<td>64/F</td>
<td>Cranial clivus; SS up to Monro</td>
<td>Grade I</td>
<td>4×4×6 cm</td>
<td>3½ y Decreased visual acuity OD; 3 months amaurosis OD and decreased visual acuity OS. Quadrant-anopsia and L VI dysfunction</td>
</tr>
<tr>
<td>11</td>
<td>72/F</td>
<td>Clivus; PS; Sphenoïd and SCav</td>
<td>Grade I</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>45/M</td>
<td>FM and FP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>60/M</td>
<td>Petroclival</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>44/M</td>
<td>Foramen jugulare and in tympanic cavity; Clivus and SCav</td>
<td>Grade II</td>
<td></td>
<td>2 Months pain R neck/ear; diziness; nausea; decreased hearing and tinnitus AD; diplopia. Sensory disturbance R mouth, VII dysfunction R and hearing AD&lt;AS</td>
</tr>
<tr>
<td>15</td>
<td>16/M</td>
<td>FM; Petrosal bone</td>
<td>Grade II</td>
<td></td>
<td>2 y Diplopia when looking R; paraesthesias maxillar and mandibular R, diplopia. No cornea reflex R; hypaesthesia V branch 1-2-3 R</td>
</tr>
</tbody>
</table>

Table 2 Clinical presentation, tumour location, and pathological subtypes of chondrosarcoma of the cranial base

<table>
<thead>
<tr>
<th>Symptoms/signs</th>
<th>Cases</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysfunction of eye movement</td>
<td>37</td>
<td>51</td>
</tr>
<tr>
<td>Headache</td>
<td>22</td>
<td>31</td>
</tr>
<tr>
<td>Hearing loss, diziness, and tinnitus</td>
<td>15</td>
<td>21</td>
</tr>
<tr>
<td>Sensory disturbances of the face</td>
<td>15</td>
<td>21</td>
</tr>
<tr>
<td>Decreased visual acuity</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td>Dysfonia</td>
<td>9</td>
<td>13</td>
</tr>
<tr>
<td>Ataxia</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>(Hemiparesis</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>Dysthria/dysphagia</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Tongue paresis</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Facial palsy</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Nasal obstruction</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Decreased memory</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Palatal mass</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

Bone parts

| Os frontale | 2 |
| Os ethmoidale | 3 |
| Os sphenoidale | 25 |
| Os petrosum | 47 |
| Os parietale | 13 |
| Os occipitale or clivus | 30 |
| Origin in dura | 8 |

Subtypes

| Grade I | 54 | 51 |
| Grade II | 12 | 11 |
| Grade III | 12 | 11 |
| Mesenchymal | 30 | |
| Myxoid | 8 | 8 |

Intracranial tumour growth can be present. The origin has been reported to be in different bone parts (table 2). In eight cases an origin in the dura was described. A pathological diagnosis was reported in 106 cases (table 2). Four subtypes of skull base chondrosarcomas were described in the literature: grade I, II, mesenchymal, and myxoid type. No further pathological grading was given for mesenchymal and myxoid subtypes. The figure lists the pathological subtypes and their age of occurrence. The extension in dural tissue of the chondrosarcoma, confirmed through postmortem data (10 cases) or radiological imaging only, was explicitly mentioned in 30 cases. Of these, 10 were diagnosed as chondrosarcoma grade I, three were diagnosed as grade II, 16 were diagnosed as mesenchymal type, and one as myxoid.

The usual methods of treatment were neurosurgery and conventional or proton radiotherapy. Stereotactic radiosurgery has been reported in only two cases. Adjuvant chemotherapy was scarcely mentioned. A local recurrence rate of 53% after neurosurgical treatment (34 out of 64 cases) has been reported with clinical and radiological signs of regrowth after a mean interval of 32 months. In 40 cases information on the extent of the operation was reported: in 80% of the operation was reported: in 80% (32 cases) resection was subtotal and in 20% (eight cases) total.

Thirteen of the 15 Dutch patients were operated on. Two received proton radiotherapy and one conventional radiotherapy postoperatively. Recurrence occurred in 54% (seven cases). The mean time to recurrence was three years. Recurrence free survival rates at 2, 3, and 5 years were calculated at respectively 67%, 56%, and 43%.

Discussion

This review of the literature and of our own cases (in total 192) illustrates the very low frequency of occurrence of intracranial chondrosarcoma. The incompleteness of data in the case reports is of such an extent that the clinical picture had to be made using a substantially smaller part of the published cases.

For patient characteristics, no sex dominance existed. The mean age was 37 years (our own series 43 years). Chondrosarcoma occurred in both very young and old age groups, from 3 months to 76 years of age. The mesenchymal subtype showed a tendency to occur at a younger age (figure).

The signs and symptoms at the first manifestation of the tumour were mainly caused by oculomotor dysfunction, related to
the preferable location of chondrosarcoma in
the petrosal part of the skull base. A more lat-
eral localisation explains initial VIIIth nerve
dysfunction. Cerebral lesions caused by intra-
dural and intracerebral expansion were re-
ported in 30 cases. Most cases were described
as originating from the skull base (table 2), pos-
sibly from remnants of embryonal cartilage.
However, a few were reported to originate from
dural tissue, suggestive of metaplasia of menin-
geal fibroblasts.12

On radiological examination, plain skull
radiography showed only bone destruction and
calcifications. Before 1980, angiography was
used to evaluate the intracranial extension. Skull CT with intravenous contrast also
disclosed bone destruction and calcification
with more detailed demarcation of the tumour
extension.

Skull MRI with administration of gadolin-
i um DTPA resulted in even better tumour
demarcation and visualisation of dural exten-
sion. The anatomical relations of the tumour
with main vessels such as the carotid arteries
and optic nerves are important guides for the
extension of neurosurgical extirpation.39

Bone biopsy was the main diagnostic tool.
The pathological classification of the subtypes
grade I - III is based on differences in
characteristics such as nuclear size, cellularity,
mitotic rate, and frequency of lacunae with
multiple nuclei.43 Our study of 177 patients in
the literature and 15 Dutch patients disclosed
no grade III chondrosarcoma. In the mesen-
chymal subtype, primitive spindle cells are
present.44 The myxoid type is composed of
strings of rounded cells in a more or less
myxoid matrix.45

With the help of tumour markers such as
vimentin, cytokeratin, and S100, the chondro-
sarcoma can be differentiated from chordoma.
Chordomas lack vimentin immunoreactivity
and chondrosarcomas fail to express cytokera-
tin. S-100 protein expression is present in
both.46

In the literature, mesenchymal and myxoid
subtypes are classified separately from the con-
ventional type I - III gradation. Lichtenstein
and Bernstein considered the mesenchymal
chondrosarcoma as a separate subtype.44 Evans
et al described a subgroup of grade III chond-
rosarcoma containing large areas exhibiting a
spindle cell pattern, but with a mitotic rate well
in excess of minimum criteria for grade III.45
Although not explicitly mentioned, their de-
scription fits the definition of mesenchymal
chondrosarcoma. It is our opinion that on the
basis of this finding, at least the mesenchymal
chondrosarcoma should be considered as a
separate subtype.

Mesenchymal chondrosarcomas mainly oc-
curred in the younger age group (10–30 years).
The grade I chondrosarcoma had no clear age
preference.

Very little data were available on the
presence of dural invasion in skull base chond-
rosarcoma. The more malignant mesenchymal
chondrosarcoma had a tendency towards a
malign growth pattern which is illustrated by
the relatively high frequency of extension into
dural and cerebral tissue. In our own series
(15 patients), dural invasion was present in five
cases: three of these were grade I and two grade
II chondrosarcoma.

Metastases of chondrosarcoma with a pri-
mary localisation in other parts of the body
were found in 10% of grade II and 71% of
grade III tumours.43 Metastases from the skull
base were mentioned by Hassounah et al in five

<table>
<thead>
<tr>
<th>Invasion</th>
<th>Postoperative course</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dural and cerebral</td>
<td>Epilepsy and persisting VI dysfunction R; no recurrence after 10 y</td>
</tr>
<tr>
<td></td>
<td>Pain maxillar and mandibular L, decreased hearing AS; recurrence after 2 y (operated)</td>
</tr>
<tr>
<td></td>
<td>Mild III/VI dysfunction; twice reoperated on; recurrence after 3 y: proton radiotherapy</td>
</tr>
<tr>
<td>Dural</td>
<td>Persistent III dysfunction L</td>
</tr>
<tr>
<td></td>
<td>1 y After operation proton radiotherapy; no recurrence 3 y after operation</td>
</tr>
<tr>
<td>Dural</td>
<td>Dysarthria, L hemiparesis and abscess cerebral, epilepsy; 4 months later recurrence</td>
</tr>
<tr>
<td></td>
<td>Recurrence after 8 y; recurrence after 2 y; death 19 y after diagnosis</td>
</tr>
<tr>
<td>Dural and cerebral</td>
<td>Reoperation 1 y later, death 11 y after diagnosis</td>
</tr>
<tr>
<td></td>
<td>Total hearing loss AD and VII dysfunction R; later stereotactical radiotherapy</td>
</tr>
<tr>
<td>Dural</td>
<td>Decreased visual acuity OD and hearing AD; hypaesthesia R face; no recurrence 3 y after operation</td>
</tr>
</tbody>
</table>

Age distribution for the different pathological subtypes of skull base chondrosarcomas.
of 50 patients. We were not able to find other cases with metastases.

Neurosurgery is one of the treatment options. In 53% of neurosurgically treated patients recurrence of the tumour was found (mean interval 32 months). The high recurrence rate is caused by partial resection due to the proximity of critical neuronal and vascular structures.

Several studies describe neurosurgical procedures and their results in treatment of intracranial chondrosarcoma. Up to nine different surgical approaches are possible, often combined or in stages. Macroscopical total resection was accomplished in 56%-67% of cases. Postoperative radiotherapy was given in 20%-44% of the patients.

Gay and Sekhar reported on 60 patients with low grade cranial base chondrosarcoma and chordoma. Fifty percent of these patients were treated previously elsewhere. All were operated on and total or near total resection was achieved in 67% of cases. Twenty per cent of the patients received radiotherapy postoperatively. They found a recurrence free survival rate at five years of 65%. The most frequent complication of the operation was leakage of CSF (30%). During follow up two patients (3%) died because of complications of radiotherapy and three (5%) because of systemic complications of surgery.

Risk of recurrence of tumour growth was found to be greater in patients who were already operated on elsewhere and in the case of only partial resection.

In general, an optimal tumour removal in one operation was advocated, because repeated surgical intervention has risks of tumour progression, development of scar tissue, and secondary spread of tumour cells.

Radiotherapy is another treatment for these tumours in the direct vicinity of essential structures. The anatomical close relation between the tumour and these critical normal structures limits the dose that can be delivered with conventional radiation treatment. Charged particle radiotherapy combined with three dimensional treatment planning results in superior dose distribution that allows delivery of high tumour dose with acceptable dose to the normal tissues.

Table 3 shows the results of the treatment of low grade chondrosarcoma of the skull base with combined proton and photon radiotherapy and with helium or neon radiotherapy. Local control rates of 78%-91% and survival rates of 83%-94%, both at five years, were achieved.

The treatment related morbidity ranged from 6% (visual complications) to 13% (auditory complications) in series of chondrosarcomas (81 cases) and chordomas (113 cases) of both the skull base and cervical spine. Castro et al reported a decline in occurrence of all radiotherapy complications from 41% in the period before 1986 to 20% after 1986, demonstrating the impact of improved imaging and treatment planning techniques. However, in the period 1977-92, five of 85 disease free patients (5%) died due to complications of therapy.

Despite the high rates of local success of charged particle radiotherapy and the fact that local recurrence always led to deterioration of the neurological condition, morbidity and mortality are considerable and should be taken into account when offering this treatment to patients.

Up to now, charged particle radiotherapy can only be carried out in highly specialised centres. It is our opinion however, that the role of radiotherapy in the treatment of skull base chondrosarcoma, possibly in combination with surgery, in the years to come will grow.

Skull base chondrosarcomas are tumours that should be considered in cases of unexplainable cranial nerve dysfunction and other associated symptoms. The reported close interval between the first symptoms and moment of diagnosis was often long. In most reports important data in defining the natural history of a chondrosarcoma were missing. Also, pathological classification should be given in more detail. In comparison with neurosurgical, mostly partial, tumour resection, charged particle radiotherapy seems to give better follow up results in terms of five year survival. Both neurosurgery and radiotherapy can cause treatment related side effects that should influence therapy choice in the individual patient.

We are indebted to the "Dutch Committee on Bone Tumours" for providing the necessary data on the patients in the Netherlands and to G Freling for his comments on pathological classification.


Table 3 Results of radiotherapy in 108 patients with low grade chondrosarcoma of the cranial base, treated with charged particles

<table>
<thead>
<tr>
<th>Reference</th>
<th>Patients</th>
<th>Follow up (months)</th>
<th>Particles</th>
<th>Dose (GyE)</th>
<th>LC-5 (%)</th>
<th>SV-5 (%)</th>
<th>Complication rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Castro et al</td>
<td>27</td>
<td>4-191 (median 51)</td>
<td>Helium, neon</td>
<td>60-80 (median 66)</td>
<td>78</td>
<td>83</td>
<td>41 (77-86)</td>
</tr>
<tr>
<td>Munzenrider et al</td>
<td>81</td>
<td>2-187 (median 37)</td>
<td>Proton</td>
<td>62.8-77.4 (median 68.5)</td>
<td>91</td>
<td>94</td>
<td>13 (auditory)</td>
</tr>
</tbody>
</table>

LC-5 = local control rate at 5 y; SV-5 = survival rate at 5 y; GyE = Gray equivalent.


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