

ORIGINAL ARTICLE

Chondromyxoid fibroma of the skull base: Differential diagnosis and radiotherapy: Two case reports and a review of the literature

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Abstract

Chondromyxoid fibromas are uncommon tumours mostly arising in long bones of young males. Involvement of the skull base is extremely rare. We describe two new cases of base of the skull chondromyxoid fibromas. The tumours were incompletely excised and irradiated with protons because of the high risk of complications of another surgical procedure. The rationale for proton therapy was based on the intimate relations between the tumour and the organs at risk. Skull base chondromyxoid fibroma is a very rare, slowly growing benign tumour that can cause severe disabilities due to tumour compression of critical structures. Only surgical resection has been shown to be relatively effective. We report two cases of incompletely excised lesions treated by postoperative high-dose radiation including proton therapy with no active disease and complication. Our review of the literature allows us to conclude that histological diagnosis of lesions in this site is a trap for pathologists and that radiotherapy is not contraindicated.

Chondromyxoid fibroma is uncommon and is estimated to represent less than 1% of all primary bone neoplasms [1].

It most frequently occurs in young adults during the second or third decades of life and usually arises from the metaphyses of major long bones of the lower extremities [2], although the tumour has been reported in numerous anatomic sites [3]. However, head and neck involvement remains a rare site. Chondromyxoid fibroma of the skull are thought to mainly arise from the synostosis at the base of the skull or from sutures. The tumour may also arise from embryonic cartilage residue [4].

The tumour is slow growing, and local pain is a common presenting symptom in extra-cranial tumours. Neurological deficits are unusual in chondromyxoid fibroma of the skull, but may appear as the tumour expands to involve adjacent structures, such as cranial nerves [4].

This tumour was originally distinguished from other aggressive cartilaginous tumours by Jaffe and Lichtenstein in 1948 [5]. The World Health Organization defined it as “a benign tumour characterized by lobules of spindle-shaped or stellate cells

with abundant myxoid or chondroid intercellular material separated by zones of more cellular tissue rich in spindle-shaped or round cells with a varying number of multinucleated giant cells of different sizes” [6]. The histological diagnosis of chondromyxoid fibroma is difficult because of its similarities with chondrosarcoma. To decrease the risk of diagnostic error, the pathological diagnosis must be established on the basis of careful correlation of clinical, radiographic and immunohistochemical findings. The distinction between these two tumours is important due to their different management.

Chondromyxoid fibroma is treated surgically by “en bloc” radical excision or curettage. Baujat et al. emphasized that complete surgical excision, rather than curettage, is required for long-term control because of a high recurrence rate after curettage [7]. The recurrence rate of appendicular skeletal chondromyxoid fibroma ranges between 13% and 22% after curettage [8]. In the skull base, the local failure rate reflects the difficulty of achieving complete resection by surgery alone [8]. Postoperative irradiation may therefore be indicated to reduce the risk of recurrence.

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To our knowledge, only 44 cases involving the head and neck have been reported (Table I). This article describes two additional cases involving the base of the skull treated by surgery and radiotherapy. Diagnosis and management, particularly by radiotherapy, are also discussed.

Case Reports

Case No. 1

This 19-year-old man with no relevant medical history, presented with a two-year history of horizontal diplopia. MRI with contrast enhancement demonstrated a well circumscribed $2.9 \times 3 \times 2.6$ cm calcified process, located in the left cavernous sinus with a low T1 and high heterogeneous T2 signals (Figure 1). Gross subtotal resection was performed in July 2002. The tumour impinged on the left cavernous sinus and abutted the optic chiasm superiorly and the brain stem posteriorly. The patient recovered with transient diplopia and paresthesias. The pathology report was consistent with chondromyxoid fibroma. Spindle cells and stellate cells were arranged in a lobular pattern in a chondroid and myxoid matrix. Immunohistochemical staining was positive for epithelial membrane antigen, vimentin, and S-100 protein. In September 2003, the patient experienced another episode of paresthesias and MRI demonstrated local recurrence. The patient was referred to the proton therapy center for consideration of high precision radiotherapy because of the high risk of complications of another surgical procedure. A total dose of 59 CGE was administrated combining photons and protons. Photon irradiation was delivered once a day, 5 days per week to a dose of 45 Gy with 1.8 Gy per fraction. The proton part was delivered once a day, 5 days per week to a dose of 14 CGE with 2 CGE. The gross tumor volume was viewed and delineated on a fused CT and MRI. The clinical target volume was created with an expansion of 6 mm from the gross tumor volume taking in account the natural and anatomical barriers. The planning target volume was defined as CTV plus 3 mm margin. The target volumes were identical for photon and proton treatments.

With follow-up of one year, paresthesias have resolved and MRI remains stable.

Case No. 2

This 28-year-old woman with an unremarkable medical history was referred to the proton therapy center for consideration of proton therapy in May 1999. Following a seven-year history of intermittent diplopia (first noted during pregnancy), her cranial

neurological status deteriorated with additional right hearing loss and sixth nerve palsy. MRI demonstrated a well circumscribed lobulated tumour measuring $4.5 \times 2.4 \times 6.1$ cm, which invaded the sphenoid body (Figure 2). The patient was operated twice in October 1998 and February 1999 via temporal and posterior incisions. Both resections were deemed incomplete macroscopically. The pathology report was initially consistent with grade 1 chondrosarcoma and then with chondromyxoid fibroma. Fractionated radiation therapy delivered a total dose of 59 CGE with a combination of photons and protons. Photon irradiation was delivered once a day, 5 days per week to a dose of 45 Gy with 1.8 Gy per fraction. The proton part was delivered once a day, 5 days per week to a dose of 14 CGE with 2 CGE. The clinical target volume included a 6 mm safety margin around the gross tumor volume; the planning target volume, a 6 mm margin around the clinical target volume. The rationale for proton therapy was based on the intimate relations between the tumour, the optic chiasm and the right temporal lobe superiorly and the brainstem posteriorly. At four-year follow up, the patient was alive with no active disease and no complications. MRI showed minimal radiological abnormalities.

Discussion

Chondromyxoid fibroma of the skull base represents a diagnostic and therapeutic challenge.

Clinical features

According to Rahimi et al., 28% of chondromyxoid fibroma are located in the upper part of the tibial shaft [1]. In a large series of 365 cases, chondromyxoid fibroma was diagnosed in the third decade in 75% of patients [9]. However, ages ranging from 20 days to 79 years have been reported [10,11]. According to Unni, there is a slight male predominance for chondromyxoid fibroma in the second and third decades [12]. Patients with skull base chondromyxoid fibroma appear to be older [8].

According to Zillmer et al., the bone sites of chondromyxoid fibroma vary according to age [3]. All chondromyxoid fibromas in patients between the ages of 1 and 10 years are located in long bones. In the second decade of life, chondromyxoid fibroma lesions are predominantly observed in long bones. In the third decade, chondromyxoid fibromas are almost all diagnosed in the small bones of the hands and feet. In the fourth decade, equal numbers of tumours are seen in long bones, flat bones, and ribs [3].

Table I. Summary of published cases of skull chondromyxoid fibromas.

Cases	Authors	Site	Age/ Gender	Treatment	RT yes/no	Follow-up-Outcome	Details
1	Everke et al. 1966 [26]	Petrosphenoidal junction	26y/M	Excision	no	NA	
2	Rahimi et al. 1972 [1]	Occipital bone	NA	NA	NA	NA	
3	Okubo et al. 1973 [27]	Petrous pyramidal	NA	NA	NA	NA	
4	Chalapati et al. 1976 [28]	Right frontal bone	30y/F	NA	NA	NA	
5	Inoue et al. 1978 [20]	Intrasellar tumor	30y/ F	Subtotal excision	no	Recurrence 6 years and 7 years after first surgery (removed each time). NED 9 years after first treatment.	
6	Szmeja et al. 1981 [29]	Ethmoid labyrinth	NA	NA	NA	NA	
7	Miyamoto et al. 1981 [30]	Frontal bone	15y/F	Excision with a rim	no	NED 10 months	
8	Frank et al. 1987 [31]	Petrous-sphenoid junction	26/M	Gross tumour resection	no	NA	Extension into the posterior clinoid process, sella, cavernous sinus
9	Viswanathan et al. 1987 [32]	Parasellar tumour	33y/M	Intracapsular removal	no	NA	Ipsilateral total internal carotid artery occlusion
10	Morikawa et al. 1987 [33]	Skull base extending from middle fossa to posterior fossa	57y/F	Excision	no	NA	Stenosis of cavernous portion of internal carotid artery.
11	Kitamura et al. 1989 [34]	Mastoid bone	48y/M	Excision	no	Recurrence 1 year and re-excision. NED 1 year after last surgery	Tumour extending into the occipital bone, invading the foramen magnum and jugular foramen
12	Morimura et al. 1992 [35]	Frontal bone	41y/M	Excision	no	NA	
13	Dumas et al. 1994 [36]	Occipital bone	43y/F	Surgery	no	NA	Extension into the petrous ridge of the temporal bone, the jugular foramen, the carotid canal. Thrombosis of the sigmoid sinus and the internal jugular vein
14	Maruyama et al. 1994 [37]	Petrous temporal bone	67y/M	NA	NA	NA	Extension into the jugular foramen Intracranial chondromyxoid fibroma in an elderly person is rare
15	Koay et al. 1995 [18]	Nasal bone	57y/F	Excision	no	NED 6 months	Extension into the frontal and ethmoidal sinuses.
16	Nazeer et al. 1996 [11]	Sphenoid sinus	66y/F	Curettage	no	Recurrence 1 year and re-curettage. NED 6 months	Extension into the nasopharynx
17		Left ethmoid sinus	20day/ M	Excision	no	NED 1 year	Congenital chondromyxoid fibroma
18	Keel et al. 1997 [8]	Clivus	34y/F	Curettage + 68 Gy	yes	NED 11 months	
19		Clivus	65y/ F	Excision	no	NED 26 months	
20		Sphenoid sinus	66y/ F	Excision	no	Recurrence 6 months: excision, 61 Gy. NED 20 months	Extended into ethmoid sinus, cavum
21		Clivus	42y/M	NA	NA	NA	
22		Sphenoid, ethmoid sinus	51y/F	NA	NA	NA	
23	Wolf et al. 1997 [4]	Left inferolateral frontal bone	35y/F	Gross total remove	no	NA	
24	LeMay et al. 1997 [4]	Left temporal bone	22y/M	Excision	no		Tumour arising from the superior and medial portion of the left mastoid

Table I. (Continued)

Cases	Authors	Site	Age/ Gender	Treatment	RT yes/no	Follow-up-Outcome	Details
25	Mendoza et al. 1998 [38]	Ethmoid	NA	NA	NA		Congenital chondromyxoid fibroma
26	Hashimoto et al. 1998 [39]	Ethmoid sinus	32y/M	Excision	no	NED 2 years	
27	Patino-Cordoba et al. 1998 [40]	Clivus	41y/F	Biopsy	yes	Recurrence 6 years after first surgery: excision	
28	Wu et al. 1998 [2]	Mastoid bone	20y/M	Excision	no	NA	
29		Frontal Bone	NA	Excision or curettage	no	NA	
30		Frontal Bone	NA	Excision or curettage	no	NA	
31		Frontal Bone	NA	Excision or curettage	no	NA	
32		Sphenoid bone	NA	Excision or curettage	no	NA	
33		Sphenoid bone	NA	Excision or curettage	no	NA	
34		Sphenoid bone	NA	Excision or curettage	no	NA	
35		Occipital bone	NA	Excision or curettage	no	NA	
36		Occipital bone	NA	Excision or curettage	no	NA	
37		Ethmoid	NA	Excision or curettage	no	NA	
38	Suzuki et al. 1999[41]	Left temporal bone	49y/M	Excision	no	NA	The recurrence involved the sphenoid body, superior nasal cavity and posterior ethmoid sinuses.
39	Skek et al. 1999 [17]	Nasal cavities	6y/F	Excision	no	Recurrence 4 years after first surgery (debulking tumor). Last surgery, 10 years after first surgery. Irradiation 50 Gy after the third surgery.	
40	Tarhan et al. 2000 [42]	Left temporal bone (tympanic portion)	44y/F	Total excision	no	NA	
41	Wang et al. 2000 [43]	Nasal septum	60y/F	Total excision	no	NED 6 months	
42	Baujat et al. 2001 [7]	Nasal bone with extension into the frontal and ethmoidal sinuses	50y/F	Macroscopic completely resection	no	NED 18 months	
43	Azorin et al. 2003 [44]	Right frontal sinus	46y/M	En bloc resection	no	NED 22 months	
44	Bloom et al. 2004 [45]	Clivus and right occipital condyle	NA	Resection	no	NA	
45	Our study	Right sphenoid bone	28y/F	Partial resection + 59CGE	yes	Recurrence: 11 months: 61 Gy NED 48 months after radiotherapy	
46	Our study	Left cavernous sinus	19y/M	Biopsy + 59 CGE	yes	NED 1 year	

RT: radiotherapy; NED: No evidence of disease; NA: Not available; Gy: Gray; CGE: Cobalt Gray Equivalent.

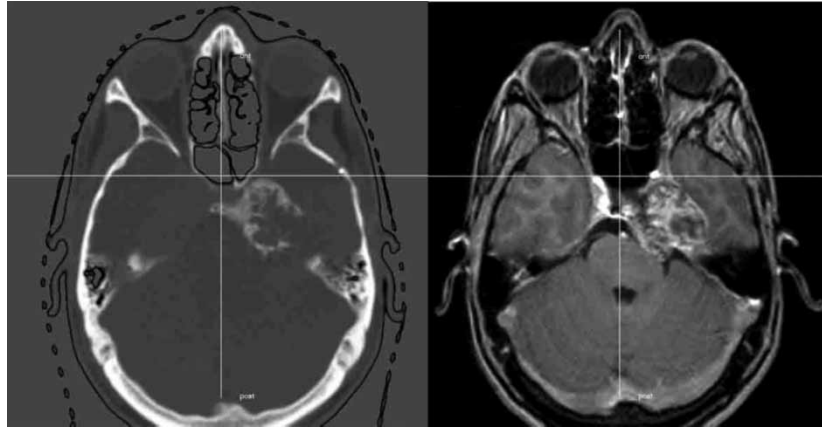


Figure 1. Case 1- Axial CT of the head in bone window showed calcified matrix and a thin peripheral calcified rim in petro-sphenoidal junction. Gadolinium-enhanced MRI, T1-weighted image shows mixed signal intensity in the tumour at the diagnosis.

The duration of symptoms prior to diagnosis is difficult to determine from the available information, but appears to range from ten days to 20 years [3].

Radiographically, most chondromyxoid fibroma of the skull base are well-defined tumours, but locally invading vital structures such as cranial nerves, carotid arteries, and the cavernous sinus. Calcification within the lesion, as observed in our cases, has been rarely described [8]. Wilson et al. reported that the difficulties of the radiological diagnosis of chondromyxoid fibroma resulted more from the diversity of sites of involvement and from the relative rarity of the tumour than from its radiographic features [9]. MRI with its superior soft tissue details allows more detailed characterization of chondromyxoid fibroma. Hypointensity on T1-weighted images and hyperintensity on T2-weighted images indicate that the tumour has a significant water content [13]. Classically, the tumour is intensely enhanced by gadolinium.

Differential diagnosis

More than 55 years after Jaffe and Lichtenstein described the difficulty of differentiating chondromyxoid fibroma from chondrosarcoma, the diagnosis still remains a challenge [5]. Our two cases emphasize the need to consider this tumour in the differential diagnosis of an intracranial chondroid tumour. The eight cases described by Jaffe and Lichtenstein were originally classified as chondrosarcoma [5], as in the second case reported here. The histological differential diagnosis of chondromyxoid fibroma of the skull base mainly includes chordoma and chondrosarcoma. It is important to distinguish chondromyxoid fibroma from chondrosarcoma and chordoma, as they present a different natural history and prognosis. Chordoma can be distinguished easily from chondromyxoid fibroma by immunohistochemistry, as it usually expresses epithelial antigens such as keratin and epithelial membrane antigen, whereas chondromyxoid

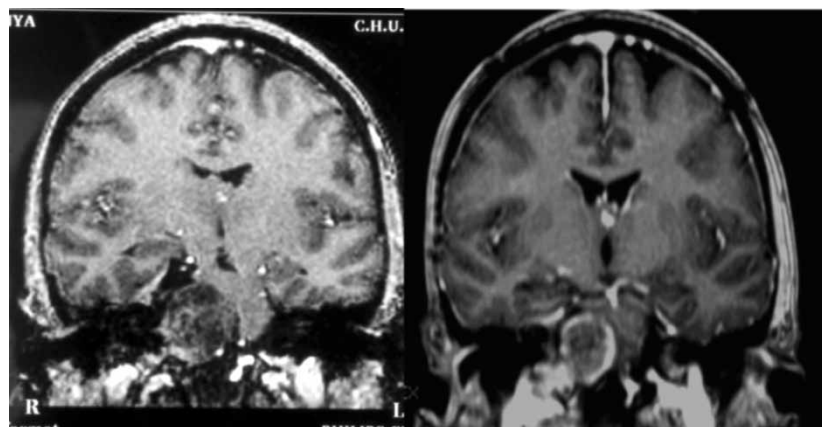


Figure 2. Case 2- MRI, coronal T1-weighted images of chondromyxoid fibroma in right sphenoid bone before radiotherapy (left) and 4 years later (right).

fibroma does not stain with antibodies against these proteins. Chondrosarcoma has a lobular growth pattern similar to that of chondromyxoid fibroma and also frequently contains myxoid areas, hence the difficulty of distinguishing chondrosarcoma from chondromyxoid fibroma on light microscopy. Immunohistochemistry is not helpful to distinguish chondrosarcoma from chondromyxoid fibroma because both tumours are known to express vimentin and S-100 protein. Recent studies suggest that possible aberrations at chromosome 6q are non-random and recurrent in chondromyxoid fibroma [14,15]. These results indicate the probable value of cytogenetic analysis, which should be performed in all cases with unusual or clinicopathologically borderline features.

Surgery, recurrence and spontaneous malignant transformation

Surgery remains the cornerstone of therapy. Many investigators have advocated that surgery should be performed according to an "en bloc" procedure, but this approach is associated with considerably increased morbidity [1,10,12,16,17]. Curettage alone is not recommended because of the probability of leaving small tumour lobules in the spongiosa in the vicinity of the tumour mass that would contribute to recurrence [16]. Zillmer et al. reported a higher local recurrence rate (22%) after this type of procedure in young children [3]. Another argument against partial surgery for skull base chondromyxoid fibroma is the higher risk of a cerebrospinal fluid leak and post-operative meningitis after curettage [7]. Another reason to attempt surgery as complete as possible is the possibility of spontaneous malignant transformation, although this risk remains extremely low [7]. However, several cases of spontaneous malignant transformation have been reported in the international literature, but Unni considered that malignant change in chondromyxoid fibromas has been rarely convincingly documented [12]. For such cases, doubts remain about the accuracy of the initial diagnoses, and whether these lesions really correspond to myxoid chondrosarcomas misdiagnosed as chondromyxoid fibromas. Wu et al. described the case of a 45-year old man with a high-grade malignant fibrous histiocytoma diagnosed 5 months after chondromyxoid fibroma of the pubis. The patient died with metastases and autopsy revealed both chondromyxoid and malignant fibrous histiocytoma in the pubic bone. Although this case is probably one of the rare well-documented examples in the literature, it seems impossible to distinguish between a random association of chondromyxoid fibroma and malignant fibrous histiocytoma or a

spontaneous malignant transformation of chondromyxoid fibroma [2].

Contrasting with radical resection of long bone chondromyxoid fibroma, wide excision of tumour involving the craniofacial skeleton is difficult and may result in severe functional and cosmetic morbidity [18]. The surgical approach in skull base lesions is often limited to drilling the tumour in order to remove as much tumor as can be safely resected without causing further neurological deficit. The local failure rate reflects the difficulty of achieving complete resection in this anatomical site, which becomes surgically more inaccessible and less curable with successive relapses [8].

In the case of craniofacial chondromyxoid fibroma excision, some authors recommend very long-term careful periodic surveillance especially after curettage [18]. Shek et al. described an uncommon case of skull base chondromyxoid fibroma in a teenage girl with multiple recurrences over a 10-year period after the initial operation [17]. In another study, a thoracic spine chondromyxoid fibroma recurrence was described 30 years after initial curettage [19].

Skek et al., who consider repeat resection to be the treatment of choice for resectable recurrent tumour, raised the question "what is the possible role of adjunctive therapies after surgery?" [17,19].

Radiotherapy

Given that it is often impossible to completely remove tumours situated in the skull base, several authors have argued that postoperative irradiation may be indicated to reduce the risk of tumor recurrence [8,12]. A similar interdisciplinary concept of cranial base surgery and postoperative radiation therapy has been advocated in the management of chordomas and chondrosarcomas of the skull base. In contrast, for other authors, radiotherapy is contraindicated in the treatment of chondromyxoid fibroma due to a suspected irradiation-related risk of malignant transformation [1,3,4].

In fact, the role of radiotherapy is uncertain. English language publications are rare, and are limited in terms of the number of cases and follow-up. Among 44 cases of skull chondromyxoid fibroma (Table I), Inoue and Shek reported only two cases, one of which was irradiated, followed for 10 years [17,20].

Limited data are available concerning the post-irradiation prognosis of skull chondromyxoid fibromas, but we believe that radiotherapy is now part of standard treatment for chondromyxoid fibroma. We propose a flow diagram (Figure 3) for treatment, although each case must be discussed in a multidisciplinary meeting. Our proposal is based on

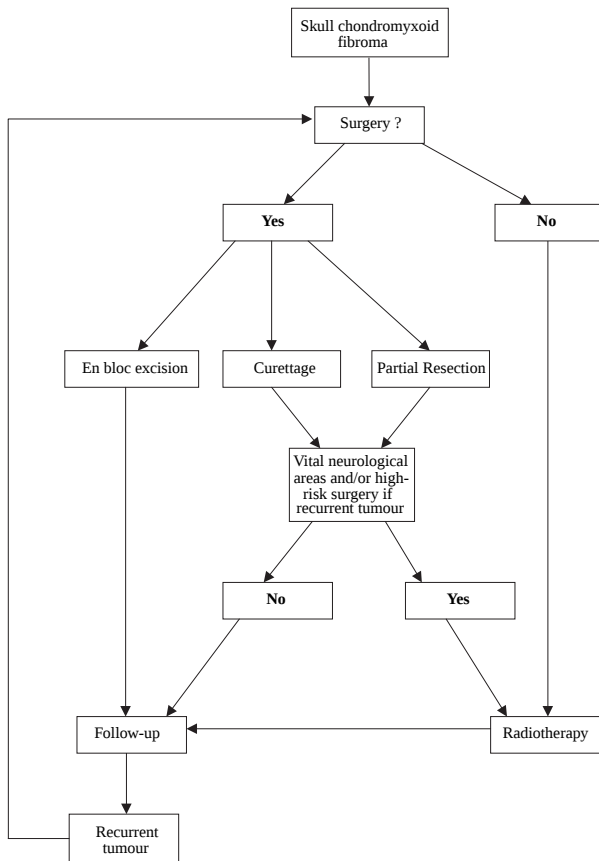


Figure 3. Flow diagram- role of radiotherapy for skull chondromyxoid fibromas.

different parameters, which are discussed according to the possibility of surgery: site of the tumour (neurological functional areas), operative risks, patient preference and possibility of close follow-up.

According to Rahimi et al., eleven of the total of 14 recurrences occurred within 2 years, two after 3 years, and one after 6 years. Eleven of the 14 recurrences developed in patients less than 15 years old. Tumours with the largest myxoid components and the largest nuclei were more frequently observed in younger patients, who were most likely to develop recurrence after curettage [1]. Age and histological subtype should be taken into account in the indications for adjuvant radiotherapy.

The therapeutic efficacy of radiotherapy must be weighed up against therapy-induced damage to normal tissue. This becomes very important in the treatment of benign tumours in young patients, as benign tumours are associated with long life expectancy and the probability of late side effects increases with time. Untoward side effects such as impairment of intellectual functioning and development of secondary tumours can be observed after moderate- to high-dose radiation therapy [21]. Charged particles provide the advantage of a high physical selectivity

and reduced integral dose to surrounding tissues compared with alternative 3D conformal techniques with photons. This advantage with proton therapy is secondary to the Bragg peak deposition of dose leading to a higher dose delivered to the target volume with enhanced sparing of the surrounding normal tissue. For these reasons and to minimize acute and late side effects, we combined proton beam to treat patients with tumours situated close to structures at risk [22].

In various series, the doses delivered to the tumour range from 50 to 60 Gy (Table I). In fact, no recommendations are available for chondromyxoid fibroma irradiation techniques. We propose a total dose of 55 – 60 Gy for the treatment of some benign tumors [23].

Malignant transformation after irradiation

Two cases of malignant transformation after irradiation have been reported. Wu et al. reported a 58-year-old woman who developed a grade 3 fibrosarcoma in the proximal tibia 6 years after treatment for a chondromyxoid fibroma including radiation with a dose of 50 Gy [2]. In 1989, Zillmer et al. reported the case of a 20-year-old woman with a chondromyxoid fibroma involving the seventh cervical vertebra treated by intralesional excision and radiation [3]. Radiation therapy was delivered on the basis of an erroneous initial diagnosis of giant cell tumour. Seven years later, this patient presented with acute spinal cord compression caused by tumour combining recurrent chondromyxoid fibroma and malignant fibrous histiocytoma [3]. The authors consequently concluded that radiation therapy is not indicated except for very rare surgically inaccessible lesions [1,2,12]. However, some authors have used radiotherapy for local relapses following surgical excision or for unresectable tumour without malignant transformation with follow-ups ranging from 11 months to 10 years [1,8,17]. The definition for so-called radiation-induced tumours as proposed by Cahan et al. includes the following criteria: it arises in the zone of irradiation, at least 5 years after irradiation, with a different histological type from that of the initial tumour [24,25]. The two cases reported by Wu et al. and Zillmer et al. present all of these criteria. The possible role of radiotherapy in malignant transformation needs to be further investigated and clarified.

In conclusion, only two well-documented cases of post-radiation transformation have been described, contrasting with the large number of patients with chondromyxoid fibromas treated by irradiation who did not develop any complications during follow-up. In addition, only one well-documented spontaneous

malignant transformation has been described in a patient treated without irradiation [2]. Another case of spontaneous transformation is not convincing [3]. Moreover, an initial incorrect diagnosis cannot be excluded, leading to an erroneous conclusion of malignant transformation when the initial tumour was already malignant. Radiotherapy therefore cannot be excluded from the management of skull base chondromyxoid fibroma on the basis of such limited data.

Conclusion

Skull base chondromyxoid fibroma is a very rare, slowly growing benign tumour that can cause severe disabilities due to tumour compression of critical structures. Only surgical resection has been shown to be relatively effective. We report two cases of incompletely excised lesions treated by postoperative high-dose radiation including proton therapy, increasing the total number of cases reported in the international literature to 46 cases. A good knowledge of this entity should avoid incorrect diagnosis. Although surgery is the cornerstone of treatment, radiotherapy should also be discussed. Proton therapy appears to be a useful irradiation modality to minimize late effects of radiation.

References

- [1] Rahimi A, Beabout JW, Ivins JC, Dahlin DC. Chondromyxoid fibroma: a clinicopathologic study of 76 cases. *Cancer* 1972;30:726–36.
- [2] Wu CT, Inwards CY, O’Laughlin S, Rock MG, Beabout JW, Unni KK. Chondromyxoid fibroma of bone: a clinicopathologic review of 278 cases. *Hum Pathol* 1998;29:438–46.
- [3] Zillmer DA, Dorfman HD. Chondromyxoid fibroma of bone: thirty-six cases with clinicopathologic correlation. *Hum Pathol* 1989;20:952–64.
- [4] LeMay DR, Sun JK, Mendel E, Hinton DR, Giannotta SL. Chondromyxoid fibroma of the temporal bone. *Surg Neurol* 1997;48:148–52.
- [5] Jaffe HL, Lichtenstein L. Chondromyxoid fibroma of bone: a distinctive benign tumor likely to be mistaken especially for chondrosarcoma. *Arch Pathol Lab Med* 1948;45:541–51.
- [6] Fletcher CD, Unni KK, Mertens F. World Health Organization classification of tumors. Pathology and genetics of tumors of soft tissue and bone. LYON: IARC press; 2002.
- [7] Baujat B, Attal P, Racy E, Quillard J, Parker F, Evannou A, et al. Chondromyxoid fibroma of the nasal bone with extension into the frontal and ethmoidal sinuses: report of one case and a review of the literature. *Am J Otolaryngol* 2001;22:150–3.
- [8] Keel SB, Bhan AK, Liebsch NJ, Rosenberg AE. Chondromyxoid fibroma of the skull base: a tumor which may be confused with chordoma and chondrosarcoma. A report of three cases and review of the literature. *Am J Surg Pathol* 1997;21:577–82.
- [9] Wilson AJ, Kyriakos M, Ackerman LV. Chondromyxoid fibroma: radiographic appearance in 38 cases and in a review of the literature. *Radiology* 1991;179:513–8.
- [10] Feldman F, Hecht HL, Johnston AD. Chondromyxoid fibroma of bone. *Radiology* 1970;94:249–60.
- [11] Nazeer T, Ro JY, Varma DG, de IH, Jr, Ayala AG. Chondromyxoid fibroma of paranasal sinuses: report of two cases presenting with nasal obstruction. *Skeletal Radiol* 1996;25:779–82.
- [12] Unni KK. Chondromyxoid Fibroma. Dahlin’s Bone Tumors General Aspects and Data on 11,087 cases. Lippincott-Raven, Philadelphia US, 1996;2:59–69.
- [13] Mitchell M, Sartoris DJ, Resnick D. Magnetic resonance imaging of chondromyxoid fibroma of the third metatarsal. *J Foot Surg* 1990;29:613–7.
- [14] Safar A, Nelson M, Neff JR, Maale GE, Bayani J, Squire J, et al. Recurrent anomalies of 6q25 in chondromyxoid fibroma. *Hum Pathol* 2000;31:306–11.
- [15] Tallini G, Dorfman H, Brys P, Dal Cin P, De WI, Fletcher CD, et al. Correlation between clinicopathological features and karyotype in 100 cartilaginous and chordoid tumours. A report from the Chromosomes and Morphology (CHAMP) Collaborative Study Group. *J Pathol* 2002;196:194–203.
- [16] Schajowicz F. Tumor and Tumorlike Lesions of Bone and Joints. Berlin Heidelberg New York: Springer; 1981. p. 148–60.
- [17] Shek TW, Peh WC, Leung G. Chondromyxoid fibroma of skull base: a tumour prone to local recurrence. *J Laryngol Otol* 1999;113:380–5.
- [18] Koay CB, Freeland AP, Athanasou NA. Chondromyxoid fibroma of the nasal bone with extension into the frontal and ethmoidal sinuses. *J Laryngol Otol* 1995;109:258–61.
- [19] Kikuchi F, Dorfman HD, Kane PB. Recurrent chondromyxoid fibroma of the thoracic spine 30 years after primary excision: case report and review of the literature. *Int J Surg Pathol* 2001;9:323–9.
- [20] Inoue K, Sugiyama Y, Ishii R. Intracellar fibromyxochondroma. *Surg Neurol* 1978;10:167–70.
- [21] Silber JH, Radcliffe J, Peckham V, Perilongo G, Kishnani P, Fridman M, et al. Whole-brain irradiation and decline in intelligence: the influence of dose and age on IQ score. *J Clin Oncol* 1992;10:1390–6.
- [22] Goitein M, Lomax AJ, Pedroni ES. Treating Cancer With Protons. *Physics Today* 2002;September:45–50.
- [23] Noel G, Renard A, Valery C, Mokhtari K, Mazon JJ. Role of radiotherapy in the treatment of cerebral meningiomas. *Cancer Radiother* 2001;5:217–36.
- [24] Cahan WG, Woodard HQ, Higinbotham NL, Stewart FW, Coley BL. Sarcoma arising in irradiated bone: report of eleven cases. 1948. *Cancer* 1998;82:8–34.
- [25] Cahan WG. Radiation-induced sarcoma—50 years later. *Cancer* 1998;82:6–7.
- [26] Everke H. A myxochondroma—chondromyxoid fibroma—of the base of the skull with expansion in the spinal canal. *Acta Neurochir (Wien)* 1966;15:150–8.
- [27] Okubo T, Ryunchan K, Takaku A. A successfully operated case of chondromyxoid fibroma originated from the petrous pyramidal. *No To Shinkei* 1973;25:355–9.
- [28] Chalapati RKV, Subba RB, Reddy CRRM. Chondromyxoid fibroma of the frontal bone: a report on a case. *Indian J Orthop* 1976;10:137–9.
- [29] Szmaja Z, Obrebski A, Strzyzowski M, Lukaszewski B. Chondromyxofibroma ossificans of the ethmoidal labyrinth in a child. *Int J Pediatr Otorhinolaryngol* 1981;3:151–6.
- [30] Miyamoto E, Kuriyama T, Iwamoto M, Tsuji N, Shizuki H. Cranial chondromyxoid fibroma. Case report. *J Neurosurg* 1981;55:1001–3.
- [31] Frank E, Deruaz JP, de Tribolet N. Chondromyxoid fibroma of the petrous-sphenoid junction. *Surg Neurol* 1987;27:182–6.

- [32] Viswanathan R, Jegathraman AR, Ganapathy K, Bharati AS, Govindan R. Parasellar chondromyxofibroma with ipsilateral total internal carotid artery occlusion. *Surg Neurol* 1987;28: 141–4.
- [33] Morikawa E, Sasaki T, Basugi N, Hashimoto K, Iwata J. Chondromyxoid fibroma of the skull base extending from the middle fossa to the posterior fossa—case report]. *No Shinkei Geka* 1987;15:1233–8.
- [34] Kitamura K, Nibu K, Asai M, Shitara N, Niki T. Chondromyxoid fibroma of the mastoid invading the occipital bone. *Arch Otolaryngol Head Neck Surg* 1989;115:384–6.
- [35] Morimura T, Nakano A, Matsumoto T, Tani E. Chondromyxoid fibroma of the frontal bone. *AJNR Am J Neuroradiol* 1992;13:1261–4.
- [36] Dumas MD, Munk PL, Munoz DG, Pelz D. Chondromyxoid fibroma of the occipital bone. *Can Assoc Radiol J* 1994; 45:303–6.
- [37] Maruyama R, Nagaoka S, Todaka T, Nakahara T, Kishida K. Intracranial chondromyxoid fibroma extending into the jugular foramen. *Pathol Int* 1994;44:857–9.
- [38] Mendoza M, Gonzalez I, Aperribay M, Hermosa JR, Nogues A. Congenital chondromyxoid fibroma of the ethmoid: case report. *Pediatr Radiol* 1998;28:339–41.
- [39] Gonzalez-Lois C, Cuevas C, Abdullah O, Ricoy JR. Intracranial extraskelatal myxoid chondrosarcoma: case report and review of the literature. *Acta Neurochir (Wien)* 2002; 144:735–40.
- [40] Patino-Cordoba JJ, Turner J, McCarthy SW, Fagan P. Chondromyxoid fibroma of the skull base. *Otolaryngol Head Neck Surg* 1998;118:415–8.
- [41] Suzuki S, Oka H, Tanaka R, Kawano N, Fujii K, Dobashi Y, et al. A chondromyxoid fibroma-like tumor of the cranial convexity: immunohistochemical and ultrastructural study. *Clin Neuropathol* 1999;18:37–41.
- [42] Tarhan NC, Yologlu Z, Tutar NU, Coskun M, Agildere AM, Arikan U. Chondromyxoid fibroma of the temporal bone: CT and MRI findings. *Eur Radiol* 2000;10:1678–80.
- [43] Wang C, Morrow T, Friedman P, Lara JF. Chondromyxoid fibroma of the nasal septum: a case report emphasizing clinical correlation. *Am J Rhinol* 2000;14:45–9.
- [44] Azorin D, Gil A, Sanchez-Aniceto G, Ballestin C, Martinez-Tello FJ. Chondromyxoid fibroma of the frontal sinus. *Br J Oral Maxillofac Surg* 2003;41:418–20.
- [45] Bloom KK, Ellen J, Kaye D. Occipital neuralgia and twelfth nerve palsy from a chondromyxoid fibroma. *J Ky Med Assoc* 2004;102:255–8.