

## Case Report

# Intracranial Extraskelatal Myxoid Chondrosarcoma: Case Report and Review of the Literature

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## Summary

**Background.** We describe a patient with an intracranial extra skeletal myxoid chondrosarcoma (EMC), an unusual neoplasm of the deep soft tissues of the extremities. Very rarely are they localised as an intracranial lesion, and we believe it is very important to accurately distinguish EMC from other intracranial tumours such as classical or “skeletal” chondrosarcomas, mesenchymal chondrosarcoma, enchondroma, and myxoid tumours (chordoma, and chondromyxoid fibroma) in order to determine their prognostic implications. Furthermore, this case presents with the second local recurrence, higher-grade cellular areas, such an event has never been reported in intracranial cases.

**Method.** A 17 year-old female presented with tonic and clonic seizures, episodic left hemiplegia and intense right-sided headaches. Computed tomography and magnetic resonance of the skull showed a right fronto-parietal cortical lesion. Complete surgical excision of the lesion through a right parieto-temporal craniotomy was performed. The tumoral lesion recurred locally twice (16 and 19 months after the initial surgery respectively).

**Findings.** First and second surgical specimens were diagnosed as extra skeletal myxoid chondrosarcoma. Microscopically, the third specimen (second local recurrence) showed abrupt transition from areas of conventional myxoid chondrosarcoma to high-grade cellular areas with fusiform features.

**Interpretation.** Extra skeletal myxoid chondrosarcoma is very rarely described as an intracranial lesion. Reference on this topic is very confusing as there is no clear-cut distinction between skeletal chondrosarcomas with prominent myxoid matrix and extra skeletal myxoid chondrosarcoma which is a definite entity first defined by Enzinger and Shiraki in 1972 in deep soft tissues of the extremities. We review the cases reported in the literature with the diagnosis of myxoid chondrosarcoma either of extra skeletal origin or with skeletal attachment, and analyse their clinic and pathological features.

**Keywords:** Brain neoplasm; extra skeletal myxoid chondrosarcoma; intracranial tumour; myxoid neoplasm.

## Introduction

Cartilaginous tumours constitute 0.16% of all cranial/intracranial lesions [4, 16]. They include chondromas and chondrosarcomas.

The largest and most recent survey of cranial/intracranial chondrosarcoma in the literature included 192 cases which represented 0.15% of all intracranial space occupying lesions, and 6% of those at the base of the skull where they are most frequently located; only rare cases arose from the dura [12]. Cranial/intracranial chondrosarcomas are usually solitary lesions except in the context of Maffucci's syndrome in which they are associated with extracranial tumours such as multiple enchondromas, peripheral chondrosarcomas, ovarian thecomas, paragangliomas, etc. [2, 6].

There are three types of cranial/intracranial chondrosarcoma: *classic or “skeletal” chondrosarcoma*, subdivided into three histological grades of increasing malignancy (I, II, and III) depending on cellular density, nuclear size, mitotic rate, and multiple nuclei in each lacuna [7]; histologically they are neoplastic proliferations with evident chondroblastic differentiation always with areas of hyaline cartilage matrix; *mesenchymal chondrosarcoma*, the most frequent and aggressive variant at this location, histologically resembles primitive cartilaginous mesenchyma with a biphasic pattern of primitive small undifferentiated

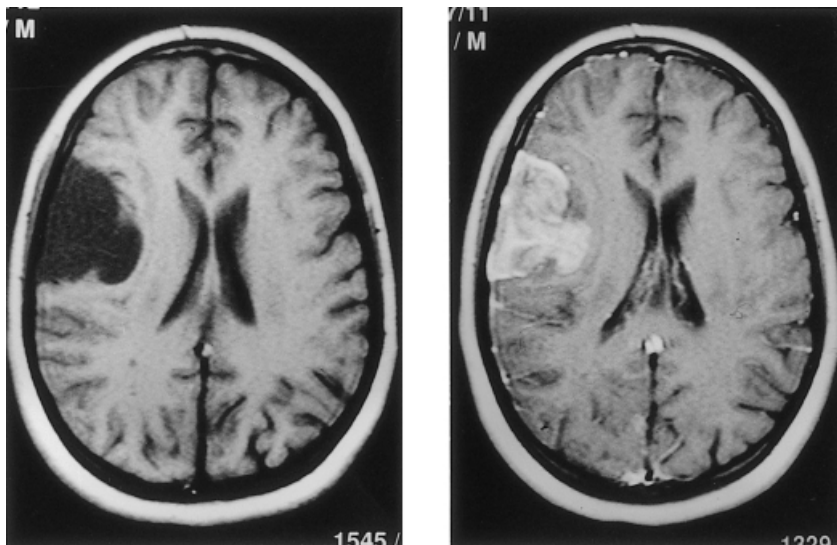


Fig. 1. T1-weighted MR imaging with (right) and without (left) contrast-enhancement of the well delimited primary tumour in fronto-temporal cortical location. Note the geographic contours of the neoplasm and the heterogeneous contrast-enhancement

mesenchymal cells, and other areas of well differentiated cartilage [11]; and *myxoid chondrosarcoma*, the rarest variant which lacks hyaline cartilage areas and has a prominent myxoid matrix between small round or stellate cells arranged in cords. This variant is reviewed in this paper.

We report an exceptional case of fronto-temporal location with dural attachment and two local recurrences, the last of which suffered dedifferentiation. We review the clinic and pathological features of the previously reported cases.

### Case Report and Methods

The patient was a 17 year-old female with partial idiopathic epilepsy in her childhood. In the last three years she had had five episodic and transient left hemiplegias and intense right-sided headaches lasting a maximum of 24 hours. During the last episode, she had associated status epilepticus and needed intensive care support; there she received anti-epileptic therapy (phenitoin, barbiturates, clonazepam).

Computed tomography (CT) and magnetic resonance (MR) of the skull showed a well-defined cortical lesion in the fronto-parietal area of the right hemisphere. The lesion showed heterogeneous signal intensity with contrast-enhanced techniques (Fig. 1).

### Results

Complete surgical excision of the lesion through a right parieto-temporal craniotomy revealed a yellowish nodular mass strongly attached to the dura covering the cortex.

The tumour recurred locally 16 months later when the patient suffered left-sided tonic and clonic seizures.

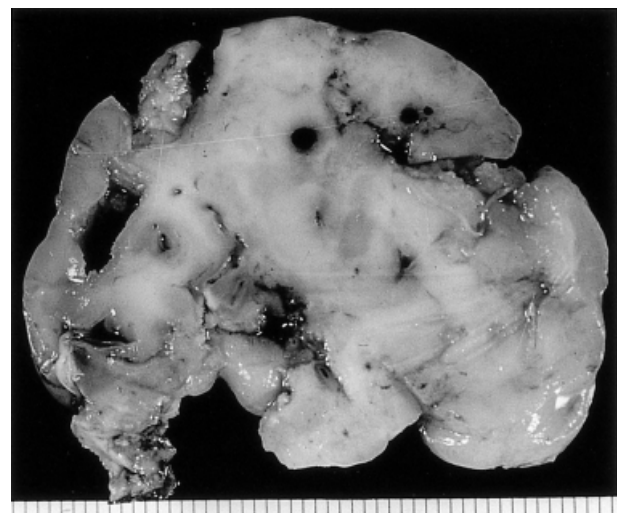


Fig. 2. Macroscopic appearance of the primary tumour. Note the lobulated, jelly-like appearance

The tumour was completely re-excised and the patient was treated with 6000 Gy local radiotherapy.

Both surgical specimens showed identical features. Macroscopically they were well defined, white and elastic nodules measuring less than 3 cms. (2.3 × 2 cms. The second one) (Fig. 2).

Histologically they were neoplastic proliferations of moderate cellular density, constituted by interconnected ribbons and cords of round cells in an abundant myxoid stroma, which contained neutral and acid mucopolysaccharides. Cytoplasm were very scanty and sometimes with a stellate shape. Nuclei were small and with low pleomorphism. Mitotic rate was low. There

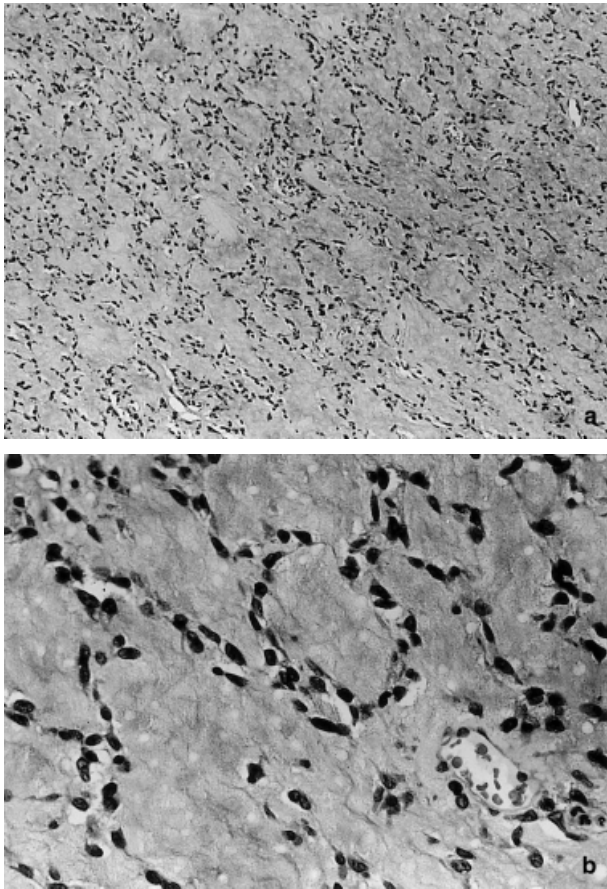


Fig. 3. (a) (HE  $\times 100$ ) Microscopic appearance of the tumour, Note the interconnected ribbons of small, oval neoplastic cells in an abundant myxoid matrix. (b) (HE  $\times 200$ ) Cellular detail of the neoplasm. Note the absence of atypia or pleomorphism

were many small vessels and occasionally larger ones with hyalinized walls. The tumours had a lobulated pattern with increasing cellularity at the periphery of the lobules. There was no hyaline cartilage nor osteoid formation (Fig. 3). Neoplastic cells were positively stained with vimentin (V9, DAKO, 1:1000), and focally with S-100 protein (rabbit S-100, DAKO, 1:2000). They were negative with EMA (E29, DAKO, 1:1000)  $\alpha$ -smooth muscle actin (1A4, DAKO, 1:50) and neuronal specific enolase (BB/NC/VI-H14, DAKO, 1:1000) Ultra structure showed a neoplastic proliferation with low cellular density and abundant nonspecific extra cellular matrix. The neoplasm was constituted by polygonal cells with oval nuclei and cytoplasmic rough endoplasmic reticulum cisterna without any other signs of differentiation compatible with the diagnosis of myxoid chondrosarcoma.

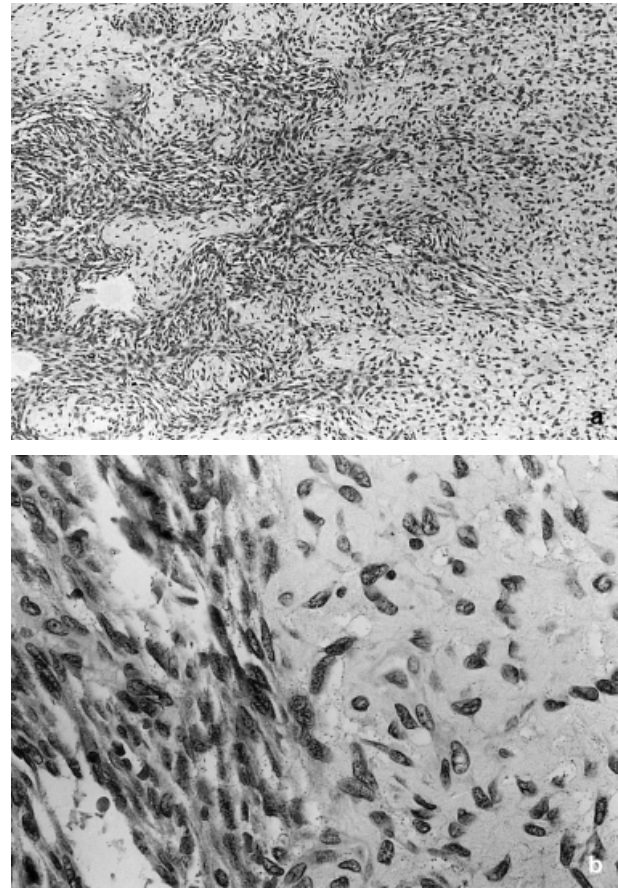


Fig. 4. (a) (HE  $\times 100$ ) Panoramic view of second recurrence of the tumour in an area of transition from areas of low cellularity (right) similar to the primary tumour to areas of high cellularity with a whorled spindle cell pattern. (b) (HE  $\times 200$ ) Note the abrupt transition from myxoid low-grade areas to high-grade fusocellular areas

4 months later the tumour recurred locally again, showing the same MR features as the primary tumour. On this occasion, microscopically examination showed extensively more cellular areas richly vascularized by medium sized curvilinear vessels with hyalinisation of their walls (Fig. 4a). Cellular density tends to be more around these vessels. There was abrupt transition from less cellular areas similar to the primary tumour (Fig. 4b). Cellular areas had less extracellular myxoid matrix than those of conventional myxoid chondrosarcoma, tending to be more fusocellular and showed more pleomorphism and numerous mitotic figures.

## Discussion

EMC is a distinct entity defined by a proliferation of small cells distributed in cords and interconnected rib-

Table 1. *Clinical Features of Myxoid Chondrosarcomas in the Literature (Modified from Hassounah et al., 1985). Ref: Reference; Postsurg. Course: Post Surgical Course*

Ref. year	Age/sex	Location/attachment	Treatment	Postsurg. course
(11), 1899	28/M	parasellar	NA	NA
(15), 1973	24/F	R petrous apex	surgery	12 days, died
(20), 1976	39/M	4th ventricle	surgery	13 days, died (ventriculitis)
(10), 1981	31/F	L petrous bone & posterior fossa	surgery & radiotherapy	8 years, alive, radiation necrosis
(21), 1981	12/M	L cerebellar hem & foramen magnum dura	surgery	13 months, alive, free of disease
(11), 1985	33/F	R posterior fossa (dura & bone)	surgery & radiotherapy	3 years, alive, free of disease
(18), 1992	28/F	L parafalcine & dura of falx	surgery & brachithery	20 months, alive, local recurrence
(5), 1992	17–46	L petrous apex,	surgery & radiotherapy	3 months–7 years alive, free of disease
	3M	R petrous apex & clivus,		
	2F	R parasellar & temporal fossa		
		R sinus cavernosus		
		Dorsum sellae (bone)		
(19), 1993	43/F	pineal gland & dura	surgery & radiotherapy & chemotherapy	3 years, dead (tumour progress)
(17), 1998	55/F	posterior fossa (dura & bone)	surgery	7 years, dead (tumour progress)
Present, 2000	17/F	fronto-temporal (dura & hemisphere)	surgery & radiotherapy	19 months, alive, local recurrence

M Male; F female; R right; L left; hem hemisphere; NA not available.

bons merged in an abundant myxoid matrix. Cells are moderately atypical. General pattern of growth is lobulated with increasing cellularity at the periphery of the lobules. This tumour characteristically lacks hyaline cartilage areas. Enzinger and Shiraki first described it in 1972 [8] as a deep soft tissue tumour of the extremities. They noticed that some of the cases had more cellular areas with higher atypia and mitotic index, which could correspond, to areas of dedifferentiation. These cases had a higher rate of recurrence. Other authors have observed this fact also in wider series [13, 14]. This feature has never been described in intracranial cases. The t(9; 22) (q22; q12) translocation seemed to be specific of extra skeletal myxoid chondrosarcoma [1]. However, some authors report a case of dedifferentiated grade IV chondrosarcoma with t(9; 22) (q34; q11–12) translocation suggesting that the different breakpoints in the t(9; 22) may reflect different histopathological subgroups of chondrosarcoma [22].

However, primary skeletal myxoid chondrosarcoma is not well defined and is not recognised as a distinct entity. It refers to either a conventional chondrosarcoma with prominent myxoid degeneration (minimum of 95%) or a myxoid sarcoma without hyaline cartilage identical to extra skeletal myxoid chondrosarcoma but bone located [1].

Myxoid chondrosarcoma is the rarest variant of chondrosarcomas in this location.

It is worthwhile to make an accurate differential diagnosis of intracranial chondrosarcomas, as there are differences in outcome and management. Mesenchymal chondrosarcoma has the higher recurrence rate, and opposed to myxoid and “skeletal” variants, it could be treated with chemotherapy (adriamycin) and presurgical embolization being a very vascularized tumour [18]. Myxoid chondrosarcoma is described in the largest surveys as an intermediate malignant tumour [11, 12] but as they are so infrequent we cannot give a prognostic conclusions, either from skeletal or extra skeletal origin. Differential diagnosis of this entity must also include other myxoid lesions such as chordoma or chondromyxoid fibroma. Chordoma has also a lobulated pattern of growth and cord-like distribution but it shows diagnostic physaliphora cells and a distinct immunophenotype (positive with keratins and EMA). Chondromyxoid fibroma is a less cellular lesion without significant atypia and with an osteoid peripheral rim [23].

There are only 14 cases reported previously in the English literature [5, 10, 11, 15–21].

Their clinic and pathologic features are summarised in Table 1. Among them, there are low-grade chondrosarcomas of “skeletal” type but with abundant

myxoid matrix. From the cases in the literature, only 4 (including the present case reported here) fulfil the histological features of extra skeletal myxoid chondrosarcoma and an evident extra skeletal origin [18, 19, 21]. From these cases only one of them (25%) [19] died of the tumoral disease despite aggressive treatment (surgery, radiotherapy and chemotherapy) after 37 months of follow-up. Mean follow-up of the four was 22.2 months. Mean follow-up of skeletal myxoid chondrosarcomas was 75.4 months.

Comparing Bingaman's series of extra skeletal mesenchymal chondrosarcoma, and this present review of myxoid chondrosarcomas (skeletal plus extra skeletal) we conclude that myxoid chondrosarcoma is less aggressive than mesenchymal chondrosarcoma and that there are no relevant prognostic differences between extra skeletal myxoid chondrosarcoma and skeletal chondrosarcomas with prominent myxoid degeneration in the few cases reported up to now.

In most cranial/intracranial chondrosarcoma cases, it is unclear which is the exact site of attachment in order to establish the skeletal or extra skeletal nature of the tumour. At the base of the skull, they could arise from cartilaginous rests or from mesenchymal pluripotential cells of the meninges. When the tumoral mass has attachment to the falx, tentorium, or dural sinuses, the dura is thought to be the origin of the tumour [11]. There are rare tumours within the parenchyma without dural attachment, and they are thought to arise from the pia-arachnoid cells of the Virchow-Robin spaces [21]. Meningeal chondrosarcomas usually belong to mesenchymal or myxoid variants but there is also an unusual case of "skeletal" chondrosarcoma arising from dura in a child [9].

Radical surgery with complete tumoral excision is the treatment of choice, but this is often impossible due to the localisation of the tumour. Adjuvant therapies such as radiotherapy and also brachytherapy [18] improve follow-up results, although we must be aware of therapy-related morbidity and mortality [12].

## Conclusion

We present an unusual case of cellular EMC, which has been reported only 3 times previously in the literature as less cellular cases. From the few cases reported of both skeletal and extra skeletal cranial/intracranial myxoid chondrosarcoma, we conclude that there are no substantial prognostic differences between the two variants. On the other hand, extra skeletal mesen-

chymal chondrosarcoma is a much more aggressive variant of intracranial chondrosarcoma.

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