

# Intracerebral metaplastic meningioma with prominent ossification and extensive calcification

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## Abstract

We present a patient (male 26 years) with a short history of recurrent seizures induced by a largely intracerebrally located frontal lobe meningioma. The tumor displayed a heretofore unpublished combination of extensive metaplastic bone formation and prominent non-psammomatous calcifications with focal chicken-wire pattern.

## Introduction

Meningiomas are relatively common tumors derived from arachnoidal cells and most frequently occur in association with intra-cranial meninges. They make up about 30 per cent of primary brain and central nervous system tumors.<sup>1</sup> Whilst psammomatous meningiomas may be associated with metaplastic bone formation, metaplastic meningiomas with significant ossification are distinctly uncommon. In this study, we present a metaplastic meningioma which in addition to widespread ossification also exhibited extensive calcifications which focally displayed a distinctive pattern of non-psammomatous (*chicken-wire*) calcification. This combination of histological features has, to the best of our knowledge, not been reported previously.

## Case Report

The patient is a previously healthy 26-year-old man who developed recurrent generalized tonic-clonic seizures over a period of 3 months. A magnetic resonance imaging (MRI) of the brain showed a 4 cm large, rounded, heavily calcified tumor predominantly located in the brain parenchyma (right frontal region), causing underlying edema and left sided midline shift.

The tumor was attached to the dura by a very thin tail (Figure 1). The tumor was excised.

## Materials and Methods

The tissue was fixed in formalin and embedded in paraffin. Four-micron thick sections were cut and stained with Hematoxylin and Eosin (H&E). An immunohistochemical study was performed with progesterone receptor antibody (Ventana) and the following primary antibodies from DAKO: epithelial membrane antigen (EMA [1:200]), CD34 (1:200) and S-100 protein (1:2000).

## Results

The excision specimen revealed firm tissue with white, gritty and granular cut surface.

Routine histological examination disclosed a heterogeneous tumor composed of large areas of mature osseous tissue, conspicuous calcified nodules of varying sizes and intervening more cellular areas (Figure 2A).

The cellular areas of the tumor were composed of plump to spindly elongated cells forming a fascicular pattern in some areas, and syncytial sheets and whorls in others. The cells had indistinct cell borders and oval nuclei containing delicate chromatin and small nucleoli (Figure 2B). In the non-mineralized areas, a significant lymphoplasmacytic infiltrate was present (Figure 2C). The tumor was highly vascularized. In addition to numerous small caliber vessels, scattered large blood vessels with a dysplastic appearance, including walls showing very irregular thickness and focally myxoid features (Figure 2D).

A striking feature of the neoplasm was prominent calcified nodules of varying sizes that were seen throughout the tumor. The calcifications formed crystalline deposits with no (psammomatous) concentrically laminated rings, and merged with spicules of woven bone which displayed no definite osteoblastic rimming (Figures 2E and 3). In several calcified areas, wire-like streaks of calcification could be seen surrounding ghost cell outlines, forming patterns reminiscent of chicken wires (Figure 2F). Focally, the osseous islands showed myxoid-edematous degenerative changes. In the immunohistochemical study, the cells uniformly showed cytoplasmic expression of EMA and some of the cells displayed nuclear expression of progesterone receptor (Figure 4A and B). Only scattered cells expressed S-100. No expression of CD34 was detected.

## Discussion

Whilst all meningiomas show characteristic ultrastructural features of well-formed desmo-

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somes and interdigitating processes on electron microscopy, there is a great diversity in morphological presentation on a light microscopical level. Metaplastic meningioma (MM) constitute an uncommon subset of low grade meningiomas that contain a significant component of fat, bone, cartilage or myxoid tissue. Reportedly, the most commonly encountered mesenchymal tissue component in metaplastic meningioma is mature adipose tissue.<sup>2</sup> Extensive ossification in MM is distinctly uncommon. To date, it is not known how these metaplastic changes occur. Bone morphogenetic protein-2 (BMP2), a cytokine involved in osteogenesis, was found to be expressed in a case of ossified en plaque psammomatous meningioma of the thoracic spine.<sup>3</sup> However, it has not been shown if BMP2 plays a direct role in the ossification process or if it is also

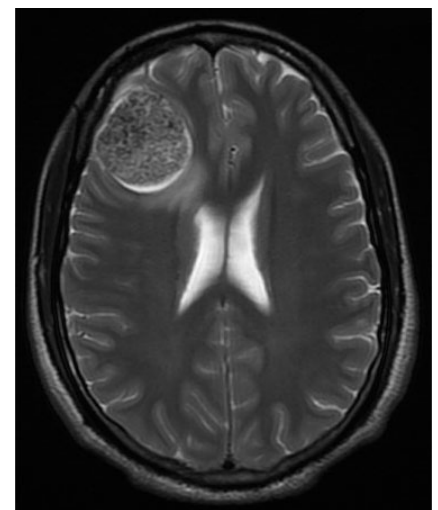
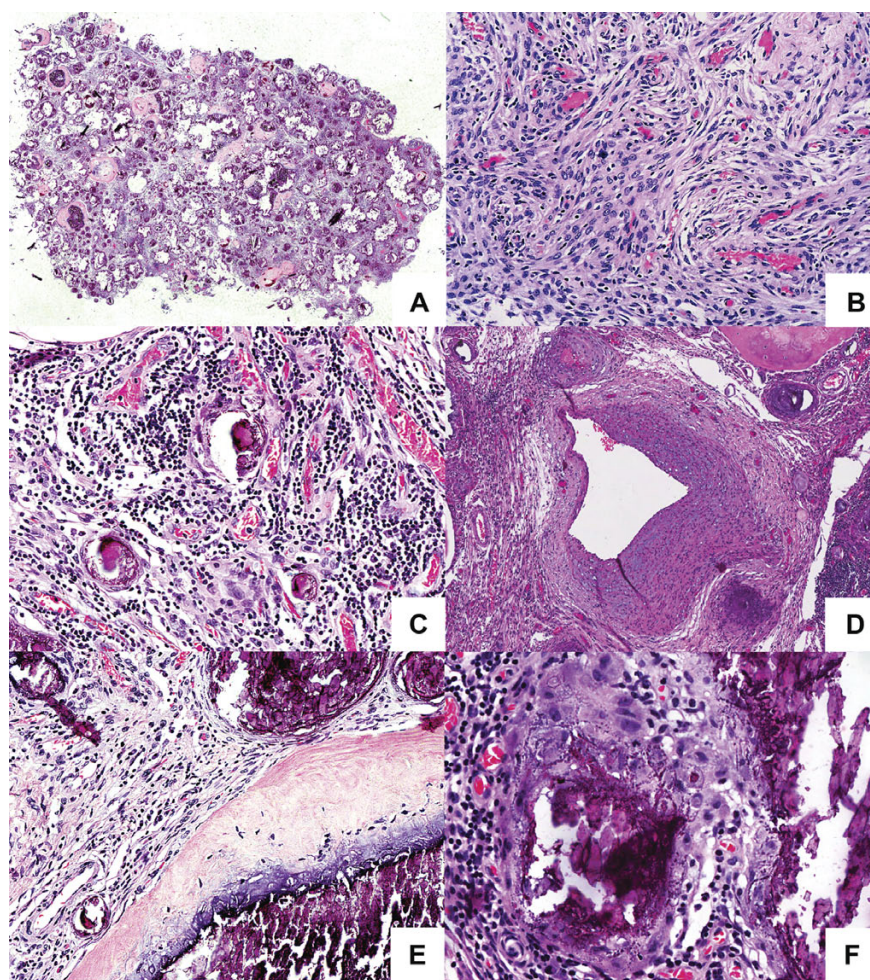


Figure 1. A right frontal lobe tumor. Magnetic resonance imaging scan of the brain was performed and revealed a 4.0- cm calcified tumor associated with edema of the adjacent brain parenchyma.

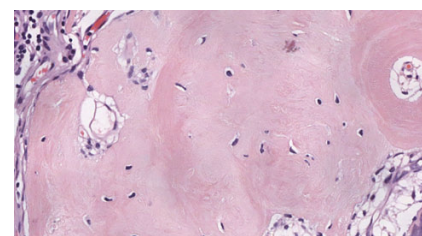
expressed in the more common meningothe-  
lial meningiomas. It is also not clear if the  
ossification process in psammomatous menin-  
giomas and metaplastic meningiomas are sig-  
nificantly different, although they are classi-  
fied as distinct histologic subtypes. To the best  
of our knowledge, the vast majority of reported  
cases of extensively ossified meningiomas  
have contained psammoma bodies.<sup>3-6</sup> However,  
one case of a meningioma (in the lacrimal  
fossa) which showed osseous metaplasia with-  
out significant non-osseous calcifications is  
on record.<sup>7</sup> In our case, the extensive calcium  
deposits formed crystalline structures rather  
than the characteristic concentric laminations  
of psammoma bodies and the basophilic calci-  
fications transitioned seamlessly into woven  
bone in many areas. An interesting finding in  
the tumor presented herein was the *chicken-*

*wire*-type calcifications. This pattern of calci-  
fication is very similar to what is commonly  
encountered in chondroblastomas (CB) and  
has not previously been reported in a meta-  
plastic meningioma. Chondroblastomas are  
rare primary bone tumors (1% of all primary  
bone neoplasms) which most commonly occur  
in the epiphysis of long bones with only 1%  
seen in the skull (Kobayashi Y 2001).  
Especially on small biopsy specimens with a  
paucity of lesional cells, the rare examples of  
the latter category may pose differential diag-  
nostic difficulties to a MM where this type of  
calcification pattern is encountered. However,  
paying close attention to the morphological  
features of CB should help to resolve this. CB  
has a characteristic matrix (*pink cartilage*)  
and the lesional cells are rounded-epithelioid  
with round to ovoid grooved nuclei and the

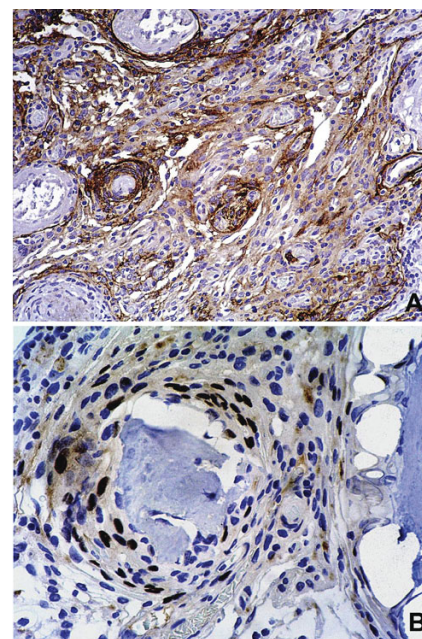
presence of multinucleated giant cells in CB  
are in contrast to the whorls and spindly mor-  
phology of most meningothe-  
lial cells which also frequently display nuclear  
inclusions. Of note is that immunohistochemi-  
cally, in addition to expressing S-100 protein,  
chondroblastomas have been shown to express  
EMA.<sup>8</sup> Osteoblastomas may arise both in the peri-  
osteum of the calvarium (calvarial periosteal  
osteoblastomas<sup>9,10</sup> and in an extra-osseous and  
intracranial locations with similar radiologic  
features as a meningioma.<sup>11</sup> This is especially  
important since in one case located in the cal-  
varium, EMA expression was detected.<sup>9</sup> Another  
differential diagnosis that should be  
contemplated is the calcifying pseudotumor of  
the neural axis. This rare lesion presents as a  
granular mass located in the meninges and is  
characterized by amorphous calcifying materi-



**Figure 2.** A heterogeneous tumor with areas of calcification and bone formation. (A) Tumor seen at low power showing cellular areas with areas of calcification and ossification. (B) The cellular areas are composed of plump, elongated cells with meningothe-  
lial features. (C) Prominent lymphoplasmacytic infiltrate is present within the cellular areas. (D) The highly vascularized tumour also contain dysplastic blood vessels. (E) The areas of calcification show crystalline deposits of calcium merge seamlessly with woven bone. No osteoblastic rimming is seen. (F) An interlacing *chicken-wire*-like calcification is seen in several areas.



**Figure 3.** Bone formation within the tumour. Bony trabeculae with no osteoblastic rimming is seen within the tumour.



**Figure 4.** The tumor expresses epithelial membrane antigen and progesterone receptor. Sections of the tumor were stained with anti-EMA and anti-progesterone receptor primary antibodies and counterstained with hematoxylin. (A) Diffuse expression of cytoplasmic EMA is seen. (B) Scattered cells show nuclear expression of progesterone receptor.

al surrounded by palisading epithelioid cells. Importantly, published histological features of the calcifying pseudotumor of the neural axis that overlap with those seen in our case are: an interlacing linear pattern of calcification, occasional ossification and EMA expression of the epithelioid cells.<sup>12,13</sup> Ossifying fibroma (OF), especially the juvenile psammomatoid (JPOF) variant<sup>14</sup> of the skull is also a differential diagnostic possibility. OF is composed of a fibroblastic stroma admixed with woven and lamellar bone and basophilic cementum-like material. The proportions of the various components may vary significantly. Furthermore (which adds to the potential differential diagnostic difficulties), JPOF may contain thread-like calcifications in hyaline deposits of collagenous tissue. However, the osseous tissue in all variants of OF characteristically shows osteoblastic rimming that was conspicuously absent in our case. In addition, bone-invading meningioma could mimic a metaplastic meningioma especially in small biopsies and close correlation with biopsy site will be necessary.

The prominent lymphoplasmacytic infiltration present in our case gave a vague association to the recently described IgG4-related sclerosing pachymeningitis.<sup>15</sup> In our case, the absence of areas of sclerosis and obstructive phlebitis and the observation that the majority of the cells were lymphocytes (although with focally significant numbers of plasma cells), the predominantly intracerebral location and the results of the immunohistochemical study, strongly militate against this diagnostic possibility. In addition, the patient did not show any clinical features to suggest the possibility of IgG4-related sclerotic disease elsewhere.

In summary, we present a case of a metaplastic meningioma with widespread ossifica-

tion and extensive non-psammomatous calcification with focal areas forming linear *chicken-wire* patterns. The unique pattern of calcification and bone formation has, to the best of our knowledge, not been reported previously and may give rise to a number of interesting, some of which probably just as rarely occurring, differential diagnostic possibilities.

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