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Incidental gangliocytoma in a middle-age adult: a case report

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Objective and Importance: We present an extremely rare case of a middle age man with an asymptomatic central gangliocytoma with calcification that had been found incidentally on his plain skull X-ray. The plain skull X-ray had been performed to investigate an unrelated subcutaneous lesion in his scalp.
Clinical Presentation: A fifty-two year old man had presented complaining of a lump on his left occipital area. On plain skull X-ray he was incidentally found to have a right frontal intracranial calcified mass. The patient was further investigated with computed tomography (CT) scan and magnetic resonance imaging (MRI) of his head. He subsequently underwent a right frontal craniotomy and total resection of the mass. The resected lesion was diagnosed as a gangliocytoma based on its histopathological features.
Discussion: Asymptomatic gangliocytoma in middle age patients is very rare. Central gangliocytoma is an uncommon tumour. Most gangliocytomas occur in children or adults under the age of 30 years. Most common presentation of gangliocytoma is seizures.
Conclusion: Gangliocytoma is a very rare cause of intracranial calcification in middle-age patients. Plain X-ray study of skull can occasionally yield troubling incidental findings.

Key words: gangliocytoma • adult • middle-age • calcified tumour • skull X-ray • central

Objective and importance

We present an extremely rare case of a middle age man with an asymptomatic central gangliocytoma with calcification that had been found incidentally on his plain skull X-ray.

Clinical presentation

A fifty-two year old gentleman was referred by his physician to us with a small left occipital subcutaneous mass. The physician had ordered a skull X-ray (figure 1) for the patient, which had revealed a right frontal intracranial calcification unrelated to the presenting complaint. The patient had no significant past medical history. He had been a smoker for the past 30 years.

On general examination no abnormality was found except for a left occipital subcutaneous lesion. Neurological examination was normal.

We obtained a CT scan of his head (figure 2), which confirmed the findings of the plain skull X-ray, showing a calcified lesion in the right frontal lobe. A MRI scan of the head of the patient showed a 4x5x5 cm right frontal lesion with a cystic component and calcification(figures 2-4).

We performed a right frontal craniotomy and total resection of the right frontal lesion. The peri- and post-operative courses were uncomplicated. The patient made an excellent recovery. The patient was discharged on prophylactic anti-epileptic medication (carbamazepine 1200mg/day).

Pathology from the resection was consistent with central gangliocytoma. On light microscopy there was mature neuronal cell bodies with minor atypical features on a neurofibrillary background. The lack of a glial component

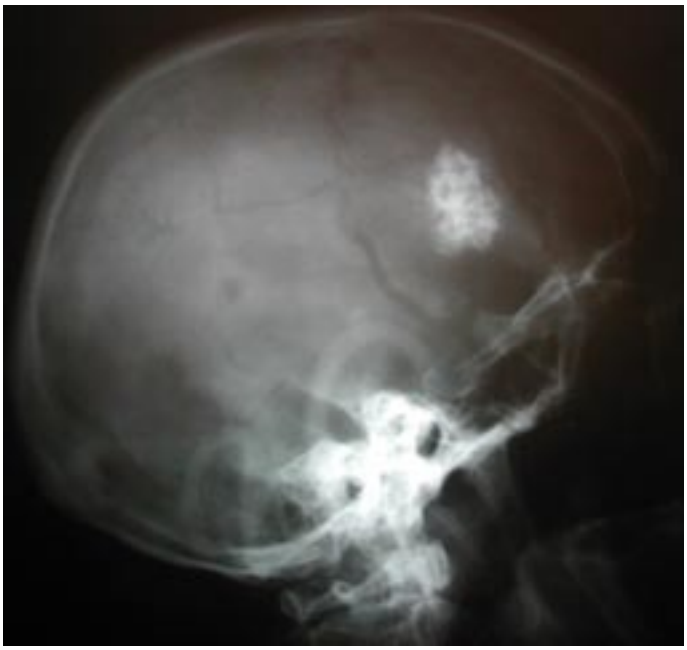

Figure 1. Cranial X-ray shows a frontal calcified lesion.

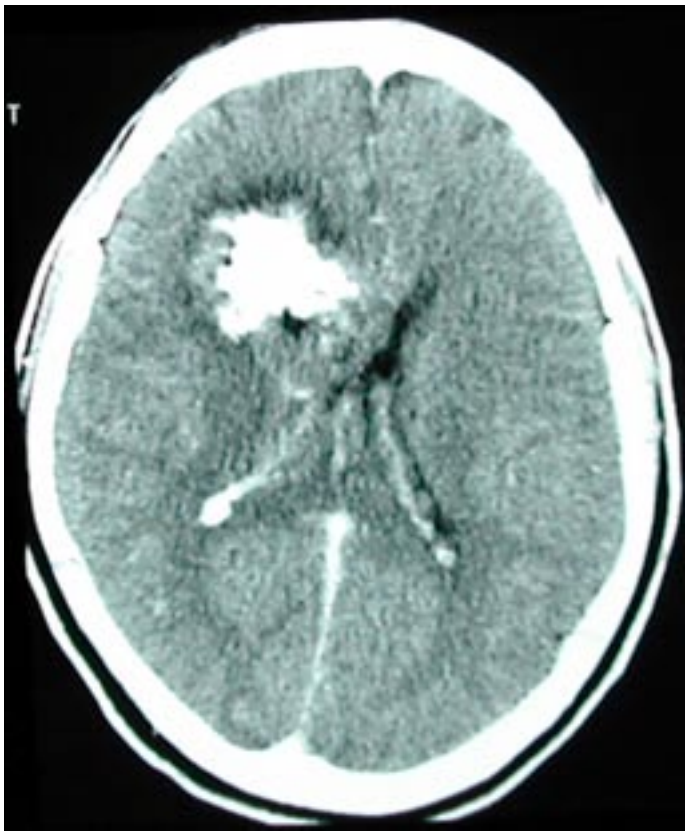

Figure 2. Cranial CT shows a calcified 4x5x5 cm mass lesion in right frontal lobe.

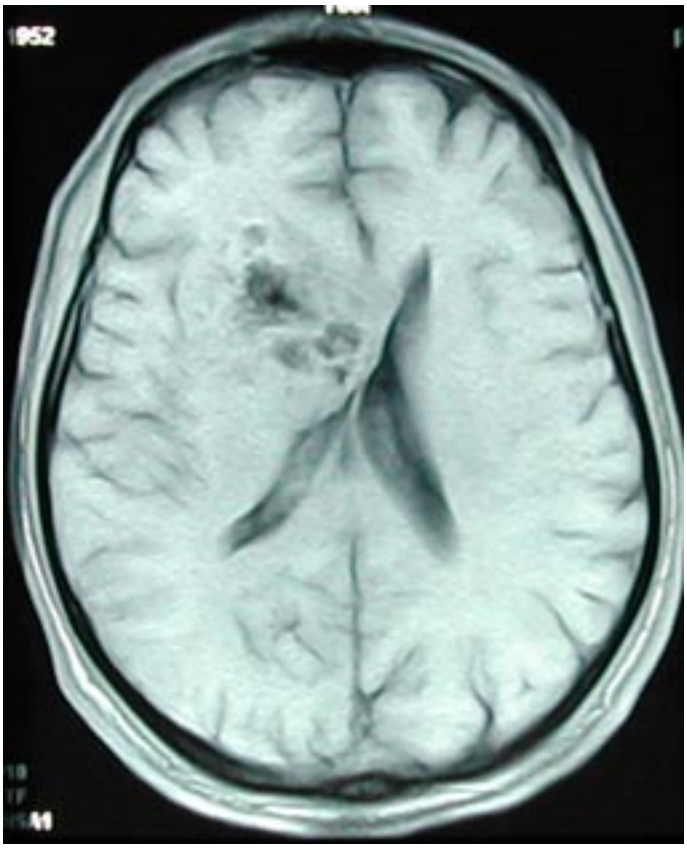

Figure 3. MRI shows mixed signal intensity on T1-weighted image.

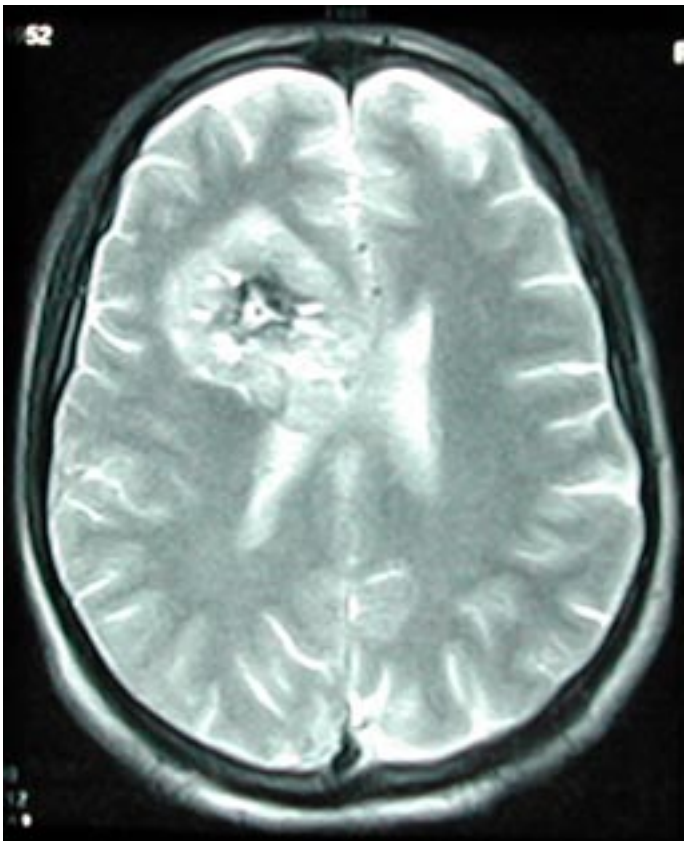

Figure 4. MRI shows high signal intensity on T2-weighted image.

differentiated the tumour from ganglioglioma (figure 5). On immunohistochemical study on resected specimen there was positive reaction to synaptophysin antibody (Figure 6).

DISCUSSION

Gangliocytoma is a rare tumour of the central nervous system (CNS). It belongs to the sub-group of the neuroepithelial tumours classed as the "neuronal and mixed neuronal-glial" tumours (4). Gangliocytomas are composed purely of ganglion cell-like neuronal elements and lack a glial component (6, 8). According to the World Health Organization (WHO) system of grading, it is a grade I tumour (4).

Our patient with gangliocytoma was fifty-two years of age. Gangliocytomas are extremely rare, with a reported frequency of only 0.1% (3, 7) and most of them occur in children and adults under the age of thirty years (3, 10). However occurance of this tumour in older patients have been reported (9).

The gangliocytoma in our patient was asymptomatic. Generally they grow very slowly and are of benign nature. These tumours have distinct margins. A common location is in the temporal lobes, but sellar, pineal, third ventricle and frontal locations have also been reported (3, 11, 12). The usual presenting symptom is refractory epilepsy, thus they are usually detected radiologically during etiological investigations for seizures (1). Altman (1) reported three children who had surgery to remove gangliocytomas in order to control seizures that were refractory to medical treatment. Other rare manifestations are raised intracranial pressure due to third ventricle location or mass effect (13), endocrine disorders (those located in sellar region) and focal signs (2, 11, 14).

The case we presented had large calcifications in his cranial X-ray, which had led to suspicion of an intracranial tumour. Even if this occurs on rare occasions, this case reminds the usefulness of simple cranial X-ray for suspecting intracranial tumours.

In our patient the CT of head also demonstrated presence of calcification within the gangliocytoma. CT findings of gangliocytomas are variable (1, 13, 15). Presence of calcification and cystic components are common (13). Solitary intracranial calcification could be physiological or due to infection, vascular condition or neoplasm (5). Among neoplasms there is a propensity for calcification in gangliogliomas, oligodendrogliomas, fibrillary astrocytomas, ependymomas (16) and these tumours must be considered in the differential diagnosis of right frontal intracranial calcified lesion.

On MRI of head of our patient the appearance of gangliocytoma was of mixed intensity on T1-weighted images and no significant contrast enhancement and hyperintense on T2 weighted

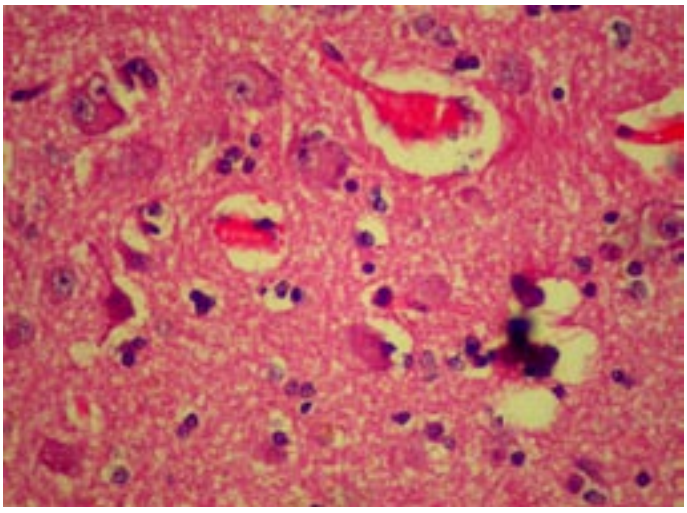

Figure 5. Tumour tissue consisting of mature ganglion cells in a neurofibrillary background with minor atypical features like binucleation (upper left corner) and differences in size and shape (H. E. x 200).

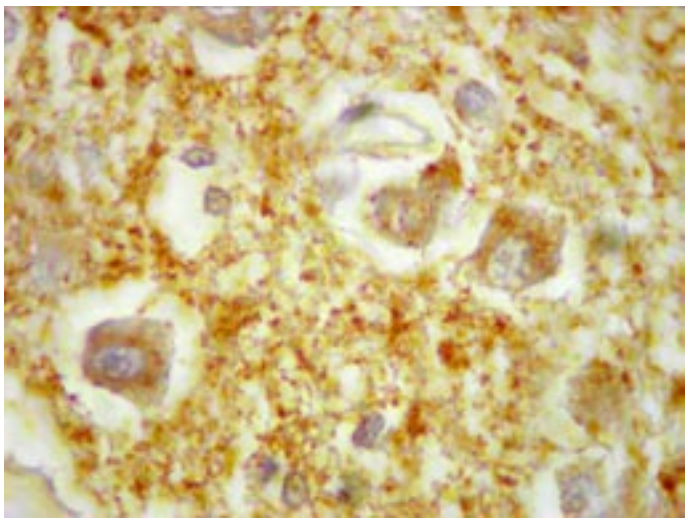

Figure 6. Punctuated synaptophysin positivity in cytoplasm of tumoral ganglion cells (DAB x 400).

images. This is consistent with other publications on the MRI appearances of gangliocytoma (13). However, the MRI appearances of gangliocytomas can be variable including hypointense on T2 weighted images (1, 15) and may enhance with contrast (13).

Since the MR and CT findings of gangliocytomas show significant overlap with those of gangliogliomas, differentiation between them usually relies on histopathological examination (8, 10).

On microscopy gangliocytomas exhibit mature neuronal elements without a glial component. The absence of the glial component differentiates this tumour from gangliogliomas. Immunohistochemistry demonstrates positive staining of the cytoplasm with synaptophysin, which verifies neuronal component (7, 8, 12). The case we presented had typical histopathological features of a gangliocytoma: mature neuronal cell bodies with minor atypical features and lack of glial component and, a positive staining for synaptophysin on immunohistochemistry.

In our patient we undertook right frontal craniotomy and complete resection of what turned out to be a gangliocytoma. The patient was very anxious to have this. Other alternative methods of management of this asymptomatic benign lesion would be: repeat CT of head after a period to check for any change or stereotactic biopsy and resect if the patient becomes symptomatic or if there was adverse change on repeat CT of head.

CONCLUSION

Gangliocytoma is a very rare benign neuronal tumour that usually presents with seizures in children and young adults. It can, however, as we report here, be incidentally diagnosed and can occur in middle-age patients. Also in this group of patients gangliocytoma can be a rare cause of intracranial calcification. Plain X-ray studies of skull can on occasions yield troubling incidental findings.

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COMMENTS

Mirzai *et al.*, document the management of an asymptomatic gangliocytoma in an adult patient. Gangliocytomas are extremely rare central nervous system tumors that account for less than 1% of all brain tumors. These tumors typically present in young adulthood with symptoms referable to the location. The majority of tumors are associated with seizures. As evidenced by this report these tumors have characteristic features, typically calcifications on CT images and hypointense on T1 MRI scans. These tumors similar to the report are typically indolent and benign. Surgery alone results in a long progression free survival. I commend the authors on the fine discussion of this rare entity.

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This is an excellent clinicopathological study of a rare tumor that occurred in even more rare age group. Obviously, two other, more commonly observed, locations of this histological entity – the cerebellum (in Lhermitte-Duclos syndrome) and sellar area (when gangliocytomas may mimic or be associated with pituitary adenomas) – are better known to neurosurgeons, but supratentorial gangliocytomas have also been described. Most recently, for example, such tumors were reported mimicking extra-axial neoplasms by Kim et al (authors' ref. 5, http://www.kjronline.org/abstract/files/v02n02108.pdf); one of those cases was also seen in a person in her fifties and had calcifications within the tumor tissue.

It is very interesting to speculate on the source of neurons that undergo neoplastic transformation. In peripherally located tumors, the cortical neurons are thought to be a source of tumor, but in the case described here the ganglion cells from which the tumor originated were either in subcortical white matter (representing some type of dystopia) or in the caudate nucleus.

Also, although there is not enough material to generalize, it does appear that ganglliocytomas in adults over 30 include different degree of calcification. Eventually, this may become a diagnostic criterion for histological differentiation of these tumors.

There are two points related to this case, however, that are worth discussing. First of all, there is once again a value in using plan skull radiographs as a diagnostic modality. In addition to being an excellent tool for diagnosis of skull fractures, it may give some idea about midline shift, presence of elevated intracranial pressure, and, sometimes, show some other abnormalities such as calcifications that lead to further workup in the presented case. In those cases when more sophisticated imaging (CT, MRI, etc.) is not readily available, the usefulness of plain radiographs should not be underestimated.

Second point, however, may cause some disagreement among neurosurgeons (and therefore is even more worth discussing). This concerns operating on asymptomatic patients with potentially stable radiographic abnormalities. I would strongly discourage our colleagues worldwide from repeating the authors' approach in cases like this one – although the authors should be congratulated with excellent outcome, we, most likely, would have never heard of this case should the patient have developed devastating hemiparesis or severe frontal dysfunction after this unnecessary operation. To state that "patient was very anxious" to have this lesion resected is not enough to justify surgery. After all, the

only reason these patients come to us in the first place is to get our advice on appropriate course of action. The neurosurgeon's approach in this case, therefore, should be to explain to the patient that most often calcification is a sign of benign nature, and that no intervention is needed unless the patient develops symptoms or the lesion gets larger on serial imaging.

The case would make an excellent point for discussion at a journal club with residents and trainees – not only that some tumors "do not read the book" and occur in wrong location and wrong age group (showing the importance of keeping wide differential diagnosis), but also that in some cases the common sense should prevail and suppress our desire to operate doesn't matter what! The risk of cutting through the normal brain to remove deep and dangerously located calcified lesion is not justified by the patient's anxiety. This is, therefore, one of those rare cases where approach is rather straight forward – the right thing to do is to repeat imaging in 3, 6, or 12 months (depending on the level of patient's anxiety) to document the lesion's stable appearance, and then save this person from unnecessary surgical risks by watchful observation.

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