

## CASE REPORT

# Avoiding misdiagnosis: cystic calcified brain metastases of uterine cervical cancer mimicking neurocysticercosis

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## SUMMARY

The radiological finding of multiple calcified brain lesions is atypical for brain metastases and in absence of a clear evidence of disseminated neoplastic disease the differential diagnosis may be difficult. Calcified brain metastases (CBM) are rarely encountered in clinical practice and they mostly arise from lung, breast and gastrointestinal primitive tumours. Only one case of uterine cervical carcinoma (UCC) with CBM has been reported so far. We describe the case of a 41-year-old Caucasian woman with a history of hysterectomy and bilateral salpingo-oophorectomy for UCC 3 years prior to observation and no evidence of neoplastic recurrence that developed cystic CBM. Owing to their peculiar radiological appearance, lesions were initially misidentified as neurocysticercosis, the most common parasitic infection of the central nervous system. We offer the reader some important teaching points for the differential diagnosis and discuss the rarity of our case.

## BACKGROUND

Neurocysticercosis (NC) is the most common parasitic infection of the central nervous system (CNS) and it is a well-known mimicker of a variety of neurological conditions.<sup>1</sup>

Diagnosing NC can be a challenge in non-endemic countries, given the rarity of the disease and the multifaceted presentation.<sup>1 2</sup>

In this article we present the second case of calcified brain metastases (CBM) arising from a primary uterine cervical carcinoma (UCC) that were initially misdiagnosed as NC.

## CASE PRESENTATION

We report the case of a 41-year-old Caucasian woman with a history of UCC (stage IB G2, International Federation of Gynecology and Obstetrics classification) treated with hysterectomy and bilateral salpingo-oophorectomy and lymphadenectomy 3 years prior to observation and no evidence of neoplastic recurrence. The patient was not on any medical therapy and denied other relevant diseases.

The patient presented in the emergency room after she had experienced left hemibody focal motor seizures with secondary generalisation.

She reported no other symptoms, denied recent travels out of the country and use of illicit drugs. Neurological examination revealed a right superior quadrantopsia. A complete physical examination and chest radiography were normal.

## INVESTIGATIONS

A cerebral CT showed the presence of multiple supratentorial and infratentorial hyperdense lesions, located near the cortical surface and in the deep grey matter, without significant enhancement after contrast administration and no mass effect, the biggest one located on right parietal-occipital parafalcine region ([figure 1](#)).

Brain MRI confirmed more than 10 round-shaped lesions of cystic appearance, hypointense on T2-weighted and diffusion-weighted image sequences, with a thin peripheral rim enhancement after gadolinium administration. Few lesions had a subependymal position in the lateral ventricles. The biggest cyst showed a mixed intensity, suggesting the presence of an air-liquid interface. There were no signs of perilesional oedema or mass effect ([figure 2](#)).

Laboratory test showed normal blood cell count, normal acute phase proteins levels and the analysis of the T-cell subsets showed no clonal abnormalities. The patient had no signs of immunodepression and testing for tuberculosis and HIV were negative. Other tests for parasitic disease including cryptococcal antigen, toxoplasma gondii antibodies and specific enzyme-linked immunoelectrotransfer blot (ETIB) assays for NC were normal. Cerebrospinal fluid (CSF) examination, including cytology, cultural tests, PCR for neurotropic viruses and ELISA for NC were negative. Neoplastic markers showed an increase in tissue polypeptide antigen (304 U/L), and a mild increase of neuron-specific enolase. An ophthalmological examination was normal.

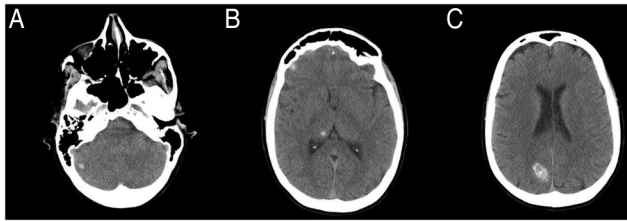
CT of the chest revealed millimetric scattered nodules the biggest (12 mm diameter) located at the right hilum and some isolated mediastinal lymph nodes of increased size without pleural effusion. CT of the abdomen showed no metastatic lesions.

In a follow-up MRI performed 7 weeks later, new lesions were seen and some of the previously described ones were increased in volume ([figure 3](#)). One and a half months later a wedge lung resection performed by minimally invasive video-assisted thoracoscopy was performed to remove a small portion of the lung containing the suspicious nodules without removing a complete lung lobe. Histology revealed a moderately differentiated squamous cell carcinoma with necrotic aspects and it was compatible with the diagnosis of UCC metastases.



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**Figure 1** Non-enhanced CT scan. Hyperdense lesions on (A) right cerebellar hemisphere, (B) right posterior hypothalamus and right frontal lobe and (C) right parieto-occipital lobe.

**OUTCOME AND FOLLOW-UP**

The patient received whole brain radiotherapy (WBRT) and systemic chemotherapy and survived for 18 months. Postmortem examination of brain lesions confirmed the diagnosis of CBM.

**DISCUSSION**

The presence of multiple calcified cystic lesions, the absence of oedema or mass effect and the involvement of the subependymal space are atypical for brain metastases and suggested the hypothesis of NC, a CNS infection by tapeworm *Taenia solium* at the larval stage.<sup>3</sup>

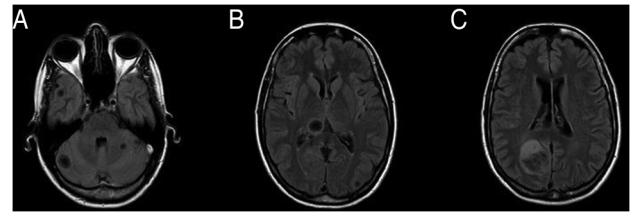
NC is endemic in many low-income countries of Latin America, sub-Saharan Africa and Asia and the infection usually occurs after the ingestion of undercooked pork meat.<sup>1-4</sup> Although our patient denied recent travels and was not immunodepressed, NC may be asymptomatic for years and affect immunocompetent people.<sup>1</sup>

The evolution of NC lesions can be summarised by neuroimaging studies: in the earlier vesicular-colloidal stages, lesions have cystic appearance and may show a peripheral enhancement. In the granular and nodular stages, the cysts tend to retract and can be surrounded by oedema, then evolving in calcified remnants in the later phases.<sup>1</sup>

Two main radiological features can help in the diagnosis of NC: the first is the recognition of the scolex, which presents as an eccentric focus of enhancement attached to the cystic wall; the second is the demonstration of lesions in different stages of evolution.<sup>5</sup>

However, the scolex—whose finding has a pathognomonic value—was not visible on MRI and the presence of lesions of different sizes was not sufficient to outline different evolutive stages. In fact, the MRI characteristics of our patients' CT hyperdense lesions mimicked NC at the vesicular-colloidal stage, when they are usually not calcified.

The negativity of serology and CSF assays for NC confirmed this theory. The sensitivity of ETIB assays approaches 98% in



**Figure 3** T2-weighted fluid-attenuated inversion recovery MRI. Multiple hypointense lesions on (A) bilateral cerebellar hemispheres and right temporal pole. (B) enlarged cyst on right posterior hypothalamus and on (C) right parieto-occipital cortex with fluid level (see figure 1C and figure 2C).

patients with two or more live parasites and therefore negative results in patients with multiple viable cysts are virtually impossible.<sup>5,6</sup>

A previous history of UCC raised our suspicion for metastases despite the apparent disease remission and negative general examination and chest X-ray.

We documented the second case of CBM secondary to UCC.<sup>7</sup> The rarity of our finding is magnified by the low incidence of UCC cerebral metastases (0.6%),<sup>8</sup> and the few available descriptions of CBM from other sites.<sup>9</sup> Brain can rarely be the first localisation of metastatic UCC being involvement of other distant sites (eg, lungs) more common.<sup>10</sup> On the contrary, pulmonary localisations of NC are exceptional and occur only after widespread dissemination to CNS, muscle and eye.<sup>1</sup>

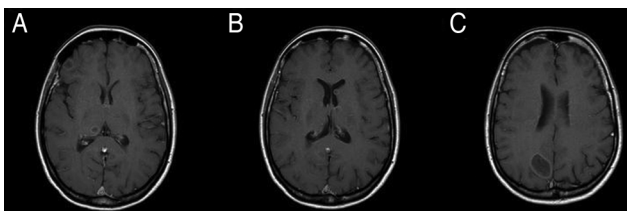
Similarly to the previous report the histology revealed squamocellular carcinoma and the patient had a relatively long survival, confirming a milder prognosis for CBM compared with non-calcified brain metastases.<sup>7,8</sup>

WBRT alone or with chemotherapy appears a reasonable option for multiple CBM but no standardised approach exists.

We must acknowledge that a brain biopsy could be considered to exclude the presence of two concomitant diagnoses (eg, pulmonary metastatic disease and parasitic cerebral involvement). In accordance with the patient preference we avoided another unpleasant invasive procedure and in line with our expectations the postmortem examination of brain lesions confirmed the diagnosis of CBM.

Diagnosis of NC should rely on published guidelines and empirical antiparasitic treatments should not be used to bypass clinical reasoning.

CBM are rare and can originate from UCC and mimic NC. An accurate differential diagnosis is mandatory in order to avoid treatment delays and unnecessary interventions.



**Figure 2** Gadolinium-enhanced T1-weighted MRI. Cystic lesions are seen on (A) right posterior hypothalamus and right frontal lobe (see figure 1B), (B) subependymal space of the left lateral ventricle, (C) right parieto-occipital cortex (see figure 1C).

**Learning points**

- ▶ We presented the second case of calcified brain metastases of uterine cervical cancer.
- ▶ Calcified brain metastases might have cystic appearance and mimic neurocysticercosis, the most common parasitic infection of the central nervous system.
- ▶ Important clues for the diagnosis of neurocysticercosis are the radiological identification of the scolex and the demonstration of lesions at different evolutive time points.
- ▶ A negative serology in a patient with multiple cysts almost always excludes the diagnosis of neurocysticercosis.
- ▶ Calcified brain metastases tend to have a slow progression.

**Contributors** JF acquired the data. JF and AS participated in the conception and design of the paper and drafted the manuscript. JF, AS and PM interpreted the data, revised the manuscript for intellectual content and approved the final version of the manuscript.

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**Patient consent** Obtained.

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