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Breast carcinoma metastasis to intracranial meningioma

Jui-Wei Lin^a, Feng-Wen Su^b, Hung-Cheng Wang^b, Tao-Chen Lee^b, Jih-Tsun Ho^b, Chiu-Hsien Lin^c, Yu-Jun Lin^{b,*}^a Department of Pathology, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Chang Gung University College of Medicine, Kaohsiung, Taiwan^b Department of Neurosurgery, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Chang Gung University College of Medicine, No. 123, Ta Pei Road, Niao Sung Hsiang, Kaohsiung County, 83301, Taiwan^c Department of Family Medicine, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Chang Gung University College of Medicine, Kaohsiung, Taiwan

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ABSTRACT

Meningiomas and breast cancers are common tumors among women in the fifth to seventh decade. However, metastasis from breast cancer to an intracranial meningioma is rare. A 63-year-old woman presented with headache, nausea and vomiting, and progressive right hemiparesis for one month. She had undergone a right modified radical mastectomy in another hospital 10 years prior. At that time, the pathological diagnosis was infiltrating ductal carcinoma. She required adjuvant radiotherapy and chemotherapy for a local recurrence 7 years later. On admission to our hospital, cranial CT scans showed a brightly enhancing, irregularly shaped lesion over the left high parietal lobe with surrounding parenchymal edema. Histopathological examination of the lesion revealed two distinct tumor types, meningioma and metastatic carcinoma of breast tissue origin. Although meningiomas have well-known radiological features, other tumors, including metastases from breast cancers may simulate them. In the clinical setting of previously diagnosed breast cancer, prompt craniotomy for removal of meningioma-like intracranial lesions is recommended to avoid missing the diagnosis of breast cancer metastasis which carries a poorer prognosis than meningioma and requires a different treatment strategy.

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1. Introduction

The simultaneous occurrence of meningioma and breast cancer with brain metastasis is an unusual, but known event.^{1,2} Breast cancers have also rarely been reported to metastasize to meningiomas (tumor-to-tumor phenomenon).^{3–7} There are several hypotheses for this phenomenon;⁸ however, the exact mechanism remains obscure. The occurrence of metastasis into a primary brain tumor might be simply chance, but it is also possible that a combination of factors such as the vascularity of the “recipient” tumor, its cell surface, and its metabolic and immunologic properties are responsible for the metastatic affinity of some tumors.^{3,9–12} We report a rare case of breast cancer metastasizing to an intracranial meningioma.

2. Case report

A 63-year-old woman presented with headache, nausea and vomiting and progressive right hemiparesis for one month. Ten years prior, she had undergone a right modified radical mastectomy for a breast carcinoma at another institution. The pathological diagnosis was infiltrative ductal carcinoma. The tumor was progesterone receptor (PR)-positive using immunohistochemical staining, and estrogen receptor (ER)-negative and HER-2/neu-negative. She required irradiation and chemotherapy 7 years later due to local recurrence and axillary lymph node metastasis.

On admission to our hospital, a right mastectomy incision scar was observed. Neurological examination revealed disorientation to time and place and right hemiparesis. Neuro-ophthalmological examination revealed bilateral papilledema. However, other neurological and physical examinations were normal. A cranial CT scan without contrast enhancement revealed a left high parietal

* Corresponding author. Tel.: +886 7 7317123x8011; fax: +886 7 7317562.
E-mail address: lin-yu-jun@yahoo.com.tw (Y.-J. Lin)

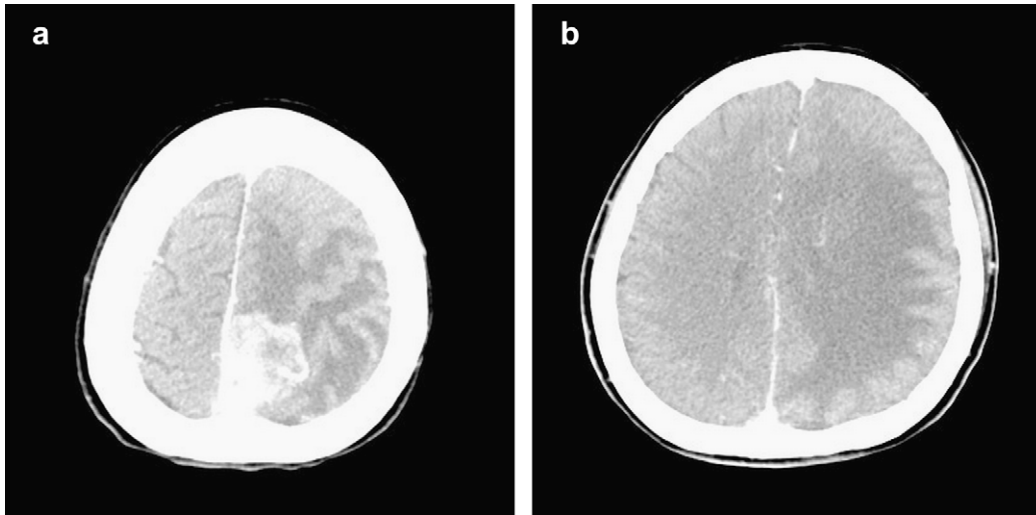


Fig. 1. Contrast-enhanced axial CT scan of the brain showing (a) a brightly enhancing lesion over the left high parietal lobe with adjacent falx cerebri thickening and a central hypodense area; and (b) perilesional parenchyma edema and midline deviation to the right.

lesion with thickening of the adjacent falx cerebri and perilesional edema. A contrast-enhanced cranial CT scan showed homogenous enhancement of the tumor with a central hypodense area (Fig. 1).

The patient underwent left parietal craniotomy for tumor removal. A well circumscribed, grayish yellow solid tumor, measuring 4.0 cm × 3.0 cm × 3.5 cm, was found firmly attached to the superior sagittal sinus. The perioperative diagnosis was meningioma, and gross total removal of the tumor was performed. The postoperative course was uneventful.

2.1. Histological examination

The surgical specimen was immediately fixed in 10% formalin for examination by light microscopy. Selected samples from the tumor were routinely embedded in paraffin. Sections 2 μm thick were cut and stained with hematoxylin and eosin.

The sample was composed mainly of sheets of neoplastic meningothelial cells, featuring abundant intranuclear inclusions.

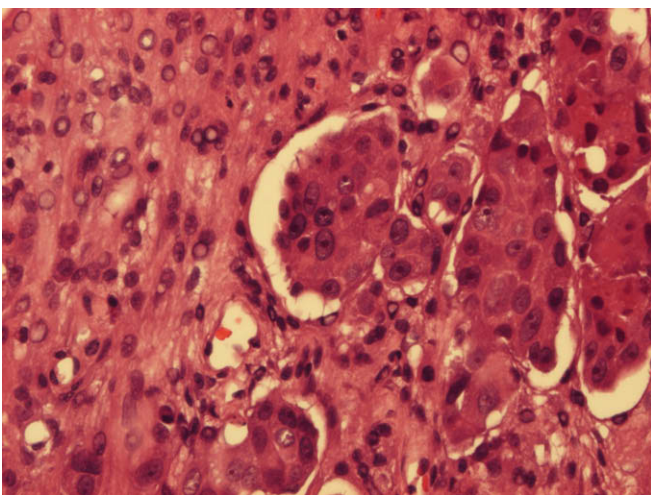


Fig. 2. The meningioma component (left side) shows sheets of neoplastic meningothelial cells, featuring abundant intranuclear inclusions. The carcinoma component (right side) shows clusters of polygonal neoplastic cells with pleomorphic, hyperchromatic nuclei and prominent nucleoli (hematoxylin and eosin stain, original magnification, ×200).

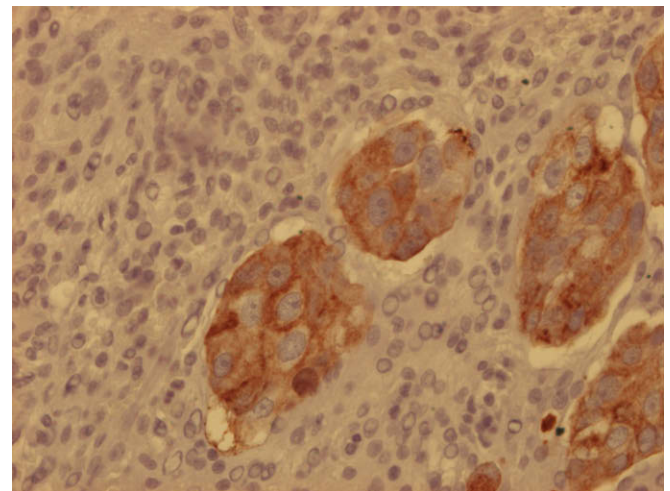


Fig. 3. The carcinoma component shows positive staining for low molecular weight cytokeratin, while the meningioma component is negative (immunohistochemistry stains, original magnification, ×200).

Aggregates of lipomatous components were distinct, warranting the diagnosis of metaplastic meningioma, a subtype of WHO grade I meningioma. In addition, there were clusters of polygonal neoplastic cells bearing (i) pleomorphic, hyperchromatic nuclei; (ii) prominent nucleoli; and (iii) a large amount of pinkish cytoplasm located at the periphery, yet within the confinement of the meningioma (Fig. 2). No tumor emboli were noted.

A panel of immunohistochemical stains was applied. The meningioma component was positive for epithelial membrane antigen, vimentin and PR, and displayed a low proliferative index (2%). The carcinoma component was positive for low molecular weight (LMW) cytokeratin and PR, and displayed a high proliferative index (70%, Fig. 3).

3. Discussion

The possible association of breast cancers with meningiomas in women has been explained in many ways.¹³ The preponderance of intracranial meningiomas as recipients of other tumors deserves

some comment. First, meningiomas, with few exceptions, are benign and slow-growing tumors. This offers a long time for metastases to take root and develop. According to Richardson and Katayama,¹⁴ a benign tumor is more inclined to receive metastases than a malignant tumor. Second, most meningiomas are highly vascular tumors, which may enhance the chances of receiving hematogenous metastases.^{15,16} Third, epidemiological studies show a high frequency of the simultaneous occurrence of breast cancer and meningioma.^{5,17,18}

The association between breast carcinoma and meningioma may be related to hormonal factors.^{8,11,18–20} ERs and PRs have been found in meningioma cells.²¹ This observation implies that meningioma may provide a favorable environment for the implantation of a metastasis from a breast carcinoma. In the present patient, we found a high concentration of PRs in both neoplasms. In addition, breast cancers and meningiomas have some characteristics that might account for their association. Both tumors occur predominantly in women in the fifth to seventh decades of their lives and the tumors tend to grow during pregnancy.^{5,22} These features give further support to the hypothesis that there is a hormonal relationship. Furthermore, the over-expression of the c-myc oncogene in both tumors might have a role in their development.²³

Four criteria for tumor-to-tumor metastasis to be diagnosed were proposed by Campbell et al.²⁴ They are: (i) at least two primary tumors must exist; (ii) the recipient tumor must be a true neoplasm; (iii) the metastatic neoplasm should show established growth in the recipient tumor, not the result of contiguous growth from an adjacent tumor, collision tumor or tumor emboli; and (iv) tumors that have metastasized to the lymph nodes where lymphoreticular malignant tumors already exist are excluded. Pamphlett²⁵ proposed two criteria for the diagnosis of “true” tumor-to-meningioma metastasis: (i) the metastatic focus must at least be partially enclosed by a rim of histologically distinct host tumor tissue; and (ii) the existence of the metastasizing primary carcinoma must be proven and compatible with the metastasis. Our present patient fulfils these criteria.

Other types of carcinomas metastasize to meningiomas. The most common sources of metastases to intracranial meningiomas are breast cancers, followed by lung cancers.⁴ Breast cancer is the most common cancer in female adults and lung cancer is the second most common cancer in male adults. Based on this observation, the frequency of breast cancers metastasizing to meningiomas may be largely due to the common occurrence of breast cancer rather than the coexistence of ERs or PRs or any other factors in both tumor types.

Regarding the tumor-to-tumor phenomenon, the rich vascular network of meningiomas has been suggested to act as a tumor filter.²⁶ Metastatic tumor cells may be preferentially filtered and adhere to the recipient tissue bed, which is abundant in blood vessels. A high E-cadherin expression has also been proposed to promote the adhesion of metastatic cells, if it is also expressed by the recipient cells.²⁶

It is very difficult to tell if a meningioma contains metastatic tumor before histological examination. Hypodense areas within a hyperdense, well demarcated, and enhancing mass on CT scan have been described in some patients with meningioma containing metastatic breast carcinoma.^{8,22} However, these hypodense areas within a meningioma more commonly represent only necrotic foci, cystic degeneration, or hemorrhage. MRI features of metastases into a primary brain tumor have been reported in only a few patients. Lee et al.²⁷ reported areas of marked enhancement in a background of moderate enhancement in MRIs of breast carcinomas metastasizing to meningioma. Elmaci et al. described marked enhancement surrounded by a moderately enhancing

halo compared to the usual homogeneous enhancement of meningioma.⁸ The radiologic diagnosis of metastasis within primary brain tumors will probably become easier with more frequent use of magnetic resonance (MR) spectroscopy. MR spectroscopy has been proposed as a useful diagnostic tool in the preoperative imaging assessment of patients with brain tumors. This technique provides more information concerning tissue characterization than MRI alone. In a breast cancer metastasis into an intracranial meningioma, Watanabe et al. found a high choline to creatine ratio and lactate to lipid peak on proton MR spectroscopy.⁶ This finding suggested malignancy in the meningioma. One should consider this imaging modality as it may offer relevant information.^{22,28}

4. Conclusion

In women with a history of breast cancer and presenting with an intracranial mass, the differential diagnosis of the brain tumor between metastatic and primary tumors is of grave diagnostic and prognostic importance. There is chance that the mass is a potentially curable meningioma, but a diagnosis of metastatic breast cancer would require different treatment strategies. MR spectroscopy may provide valuable radiological information. The possible association of breast cancers with meningiomas in women can be explained in many ways. Knowledge about the behavior of metastatic tumor cells may help in reaching accurate diagnosis, even preoperatively.

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Axonal effects of camphor poisoning

Stacey Jankelowitz*, Armin Mohamed, David Burke

Institute of Clinical Neurosciences, Level 8, Royal Prince Alfred Hospital, Missenden Road, Camperdown 2050, New South Wales, Australia
Institute of Clinical Neurosciences, The University of Sydney, Sydney, New South Wales, Australia

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ABSTRACT

This report documents changes to axonal excitability in motor nerves in acute camphor toxicity. Although there were no changes to indicate an alteration in resting membrane potential, there was an exaggerated response to hyperpolarising currents in both threshold electrotonus and the current–threshold relationship. These findings suggest a transient decrease in the hyperpolarisation-activated conductance (I_H). This report demonstrates that recently developed techniques for measuring axonal excitability are readily applied in the acute care setting and can document subclinical abnormalities that could be relevant to the underlying pathophysiology.

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1. Case report

A 39-year-old female was transferred by ambulance from a psychiatric hospital to the general hospital, having been found unresponsive in her room. Her breath smelt of camphor and she had a box of mothballs in her hand. She suffered four generalised seizures prior to reaching the hospital. She experienced further generalised seizures and myoclonic jerks while in the emergency department. She was intubated and ventilated, sedated with benzodiazepines and administered phenytoin intravenously; the seizures ceased. Investigations revealed a metabolic acidosis; her liver function tests were mildly deranged. Pharmacodynamic studies to determine camphor levels were not performed. She required continuous venovenous hemodialysis for 5 days to treat the acidosis, and her liver function abnormalities resolved over this time. Activated charcoal lavage was also performed after 2 days in the intensive care unit (ICU), because of the persistent metabolic acidosis. The electroencephalogram showed generalised beta activity and left frontotemporal slowing. Routine nerve conduction studies were normal. The patient was ventilated for 5 days and experienced mild respiratory acidosis after extubation. Haemodialysis was continued for a further 4 days. One week prior to this admission, the patient had overdosed on a combination of temazepam, citalopram, paracetamol and codeine, prompting her admission to the psychiatric hospital. She had a history of depression but had not demonstrated suicidal tendencies until the time of the overdose. There was no other medical history of note.

Nerve excitability studies were performed when the acid base status and serum potassium were within normal limits.¹ At this time the patient was alert and was mobilising with assistance; she gave informed consent to the studies, but was still housed in

the ICU. Nerve excitability studies were repeated 15 days after the initial assessment, and then again 21 days later. The patient had no peripheral nerve symptoms at any time, had normal nerve conduction studies and did not have any abnormalities on clinical neurological examination.

In all three excitability studies there were no significant changes in the refractory, supernormal or late subnormal periods of the recovery cycle (Fig. 1A), suggesting that there was no significant alteration in axonal membrane potential. However, the initial two excitability studies showed an excessive response to hyperpolarising currents in the threshold electrotonus (Fig. 1B). A similar response to hyperpolarising currents was observed in the current–threshold relationship, and the slope of the relationship in the hyperpolarising direction was reduced (Fig. 1C). These changes had almost resolved 6 weeks from the time of admission. These findings indicate a transient decrease in the hyperpolarisation-activated conductance (I_H , mediated by the HCN channel family). Thus, despite the marked central hyperexcitability induced by camphor poisoning, peripheral nerve axons are not depolarised. However, there is evidence for impairment of a specific ion channel (I_H).

2. Discussion

Nerve excitability studies were performed in this patient because the exact mechanism of action of camphor toxicity is not well understood. It was conceivable that the hyperexcitability of the central nervous system, manifested as epilepsy, might be accompanied by comparable hyperexcitability of the peripheral nerve axons. This prospect is supported by reports of peripheral nerve abnormalities in those who experience stroke,² spinal cord injury³ or multiple sclerosis,⁴ as well as in those who have an inherited epilepsy syndrome.⁵

* Corresponding author. Tel.: +61 2 9036 3091; fax: +61 2 9036 3092.

E-mail address: sjankelowitz@med.usyd.edu.au (S. Jankelowitz)