

Leptomeningeal Metastases in Disguise

隱藏的柔腦脊膜癌症轉移

E Lee, I Kam, WK Tai

李浩銘、金偉嫻、戴詠琪

Abstract

Atypical symptoms sometimes occur in association with organic brain conditions but may be misinterpreted as conversion symptoms. A case in which a 46-year-old woman presented with non-specific episodic dizziness related to leptomeningeal metastases is described. This case highlights the importance of considering organic causes in patients with atypical symptoms and the usefulness of magnetic resonance imaging for investigating possible organic causes.

Key words: Breast neoplasms; Conversion disorder; Dissociative disorders; Hysteria; Neoplasm metastasis

摘要

器質性腦綜合症出現非典型症狀，間中可能被誤診為轉化症狀。本文報告一名46歲女病人因柔腦脊膜癌症轉移出現偶發眩暈。這病例顯示醫護人員應考慮呈不明確症狀的病人是否有器質性病因的重要性，以及利用磁力共振影像診斷的好處。

關鍵詞：乳癌、轉化障礙、分離性障礙、歇斯底里症、癌轉移

Introduction

The term 'hysteria' was coined by Hippocrates and popularised again after Freud's studies on the issue. It was used to describe numerous conditions ranging from a uterine disorder to a variety of physical symptoms caused by unresolved emotional conflicts. In the 19th century, it had become 'a so-called general neurosis' without definite localisation in the nervous system.¹ Nowadays, we use the terms 'dissociative disorders' or 'conversion disorders' as cited in the 10th revision of the International Classification of Diseases² and the Diagnostic and Statistical Manual of Mental Disorders – 4th Edition to describe the condition.³ Reported rates vary widely, ranging from 11/100,000 to 300/100,000 in general population samples.³ It occurs more frequently in women than in men, with reported ratios varying from 2:1 to 10:1.² The onset is generally from late childhood to early adulthood and it rarely occurs before the

age of 10 years or after the age of 35 years.³

Not uncommonly, especially in the consultation-liaison setting, psychiatrists are asked to see patients presenting with physical symptoms without identifiable organic pathology, where it is suspected that the symptoms are generated by psychological mechanisms. Misdiagnosis in these circumstances has been reported to be as high as one-third in early studies.^{4,5} A recent systematic review by Stone et al⁶ suggests a 4% misdiagnosis rate of conversion symptoms. A broad range of neurological conditions, e.g. epilepsy, movement disorders, and multiple sclerosis, may be diagnosed later.⁶

We report a patient who presented with episodic, non-specific dizziness and headaches, and was initially diagnosed with a conversion disorder but turned out to have leptomeningeal metastases. A review of the subject and the importance of considering organic causes in patients with atypical presentation are discussed.

Case Report

A 46-year-old married housewife with no family or personal psychiatric history first presented to our in-patient psychiatric unit in February 2007. She complained of headaches and episodic dizziness for 2 weeks. She was born locally and educated up to secondary school level with a below-average performance. Before admission, she lived with her husband and a 10-year-old daughter. Her pre-morbid personality was described as anxious and sensitive.

Dr Edwin Lee, MSc, MRCPsych, Department of Psychiatry, Tai Po Hospital, Tai Po, Hong Kong, China.

Dr Irene Kam, MRCPsych, FHKAM (Psychiatry), Department of Psychiatry, Tai Po Hospital, Tai Po, Hong Kong, China.

Dr WK Tai, MBChB, Department of Psychiatry, Tai Po Hospital, Tai Po, Hong Kong, China.

Address for correspondence: Dr Edwin Lee, Department of Psychiatry, Tai Po Hospital, Tai Po, Hong Kong, China.

Tel: (852) 2636 7754; Fax: (852) 2647 5321;

E-mail: edwinlee@excite.com

Submitted: 12 March 2007; **Accepted:** 30 April 2007

She enjoyed good health until 2003 when she was discovered to have stage II (T2N1M0) breast carcinoma. Modified radical mastectomy was done, followed by treatment with adjuvant chemotherapy. Her physical state remained satisfactory until 2 weeks prior to the index admission when she attended the emergency department and was admitted to a medical unit for a generalised headache and dizziness. A physical examination and biological investigations, including repeated plain computed tomographic brain scans, a chest X-ray, and blood tests were normal. A preliminary diagnosis of tension headache was made but her symptoms were so distressing that she needed to rest in bed for most of the time and her symptoms got worse whenever the issue of discharge from the medical unit was discussed. Finally, she was discharged from the ward accompanied by her husband and analgesics were prescribed for symptom control.

She was referred to the psychiatric clinic for psychological assessment of 'anxiety with multiple somatic complaints'. After she went home, she had to stay in bed for most of the time and could not perform housework. Her condition did not improve and she consulted a psychiatrist in private practice. Depressive symptoms and some underlying psychosocial stressors were identified and she was referred to the emergency department for psychiatric admission, with a provisional diagnosis of 'hysteria'. A mental state examination upon admission revealed a calm and cooperative lady with relevant and coherent speech. Her mood was euthymic with congruent affect. She expressed feelings of guilt and worthlessness. There were no other anxiety symptoms. No psychotic symptoms or suicidal ideas could be elicited. Her cognitive function was intact. She was apparently well, walked unaided, and remained attentive through the interview.

Enquiry about her social situation revealed a long-standing marital discord. The couple gave limited psychological support to each other. Her husband often criticised her and the patient tended to bottle up her feelings. She disclosed relationship problems with her husband and friends with recent on-going conflicts.

As she elaborated on the marital discord, she developed a state of marked anxiety and started to complain of dizziness. She closed her eyes at that juncture and appeared very tense with clenching of fists, muscle twitching, and an increased pulse rate. She remained conscious throughout and responded to direct suggestions for relaxation and fully recovered after 10 minutes. As the conversation went on and the issue of her marital problems came up, she developed a similar anxiety state associated with a subjective complaint of severe dizziness.

During hospitalisation, she had repeated episodes of similar dizzy spells, especially when discussing her husband. Serial physical examinations showed that she was afebrile with normal vital signs. A neurological examination revealed no focal neurological deficit or cerebellar signs. Fundoscopy findings were normal. In view of the negative physical findings and ongoing social problems, underlying psychological conflict and suppressed emotions

manifesting as symptoms that worsened upon attempts to explore the conflict were suspected. The symptoms seemed to symbolise her need for dependence on others and the apparent 'secondary gain' of being ill was perpetuated by her husband who spent more time with her. Further psychological exploration and abreaction was planned, but her symptoms increased in severity over the next few days. She was observed to have more frequent dizzy spells and had to stay in bed for longer periods. On one occasion, she developed urinary incontinence in the ward. These unusual symptoms suggested organic pathology and it was decided that further investigation of the brain was needed. Magnetic resonance imaging was arranged and the scan with contrast showed an increase in leptomeningeal enhancement in the cerebellar hemispheres, suggesting leptomeningeal metastases. She was subsequently transferred to the medical unit and a cerebrospinal fluid (CSF) cytological examination revealed carcinoma cells. She developed dysphagia and had poor oral intake and died from her illness within 2 weeks of the correct diagnosis being made.

Discussion

Breast cancer is the second most common source of brain metastases, making up 10 to 20%.⁷⁻⁹ It is the most likely solid tumour to exhibit leptomeningeal colonisation.¹⁰ The estimated frequencies of leptomeningeal metastases in clinical and autopsy series of patients with breast cancer are 2 to 5% and 3 to 6%, respectively.¹¹ The occurrence of leptomeningeal metastases can range from weeks to more than 15 years from the initial breast cancer diagnosis.^{12,13} Patients with breast cancer may develop leptomeningeal metastases even when systemic disease is under control or absent.¹⁴

Leptomeningeal metastases arise on the pia and the arachnoid or in the subarachnoid space.¹⁵ Spread to the leptomeninges may occur via multiple routes including haematogenous, direct extension, transport through the venous plexus, and extension along nerves or perineural lymphatics.¹⁰ The location of the tumour determines signs and symptoms. The most frequent presentation is with spinal symptoms, e.g. leg weakness and paraesthesia. The obstruction of CSF flow can lead to headaches, nausea, vomiting, lethargy, confusion, memory loss, ataxia and, rarely, seizures. Cerebral dysfunction can lead to a change in mental status.^{16,17} Our patient's symptoms might be explained by the location of the metastases but the role of psychological stress in modulating her symptoms was difficult to determine. The possibility of epileptic attacks could not be confirmed as the patient died before electroencephalography could be performed but the clinical presentation made this less likely. Demonstration of malignant cells in the CSF is the definitive method of diagnosing leptomeningeal metastases. An elevated CSF protein level and a mononuclear pleocytosis are commonly present. Less frequently, a pathologically abnormal CSF glucose level of less than 70% of the serum glucose level is

discovered.¹⁸

Somatic complaints with normal investigations are common reasons for referral for psychiatric assessment. The absence of expected physical findings and the presence of psychological stress may suggest the possibility of a conversion disorder. The exact mechanism of symptom generation in conversion disorders is still unknown but neurobiological correlates are illustrated by recent functional imaging studies.¹⁹

In our daily clinical practice, it is sometimes difficult to ascertain the diagnosis of conversion disorder. The pitfall was clearly illustrated in our case — the patient's history suggested an underlying psychological conflict with suppressed emotions; worsening of symptoms upon attempts to explore the conflict; and an apparent 'secondary gain' from her illness forcing her husband to spend more time with her. All these features wrongly pointed case management towards a psychological approach. A multi-dimensional psychiatric assessment can help to give a complete picture of a patient with consideration of bio-psycho-social factors. In fact, much emphasis has been put on detecting the 'primary gain', 'secondary gain', and features like 'la belle indifference' when considering the diagnosis of hysteria in the past. The reliability of such features has since been questioned. Stone et al²⁰ did a systematic review on the clinical features of 'la belle indifference' as a means of differentiating between conversion symptoms and symptoms of organic disease. Their results suggested that this clinical sign should be abandoned until both its definition and utility had been clarified. Conventionally, conversion disorders have been reportedly more common in rural populations, individuals of lower socio-economic status, and individuals less knowledgeable about medical and psychological concepts. Individual conversion symptoms are generally self-limited and do not lead to physical changes or disabilities. In our case, the alarming signs were urinary incontinence, the deteriorating course of the symptoms, and the lack of a clear temporal relationship between the onset of symptoms and the stress. The presence of past physical illness, like a history of breast carcinoma in this case, should raise awareness of a possible organic cause. Concurrent social problems and the underlying personality can shape the way in which symptoms present. It is thus important to consider the possibility of underlying organic pathology by performing adequate investigations in cases where doubt exists.

References

1. Hirschmuller A. The life and work of Josef Breuer: physiology and psychoanalysis. New York: New York University Press; 1989.
2. The ICD-10 classification of mental and behavioural disorders: diagnostic criteria for research. Geneva: World Health Organization; 1992.
3. Diagnostic and statistical manual of mental disorders. 4th ed. Washington DC: American Psychiatric Association; 1994.
4. Slater ET, Glithero E. A follow-up of patients diagnosed as suffering from "hysteria." *J Psychosom Res* 1965;9:9-13.
5. Reed JL. The diagnosis of 'hysteria'. *Psychol Med* 1975;5:13-7.
6. Stone J, Smyth R, Carson A, Lewis S, Prescott R, Warlow C, et al. Systematic review of misdiagnosis of conversion symptoms and "hysteria". *BMJ* 2005;331:989-94.
7. Lee YT. Breast carcinoma: pattern of metastasis at autopsy. *J Surg Oncol* 1983;23:175-80.
8. DiStefano A, Yong Yap Y, Hortobagyi GN, Blumenschein GR. The natural history of breast cancer patients with brain metastases. *Cancer* 1979;44:1913-8.
9. Posner JB. Back pain and epidural spinal cord compression. *Med Clin North Am* 1987;71:185-205.
10. Kesari S, Batchelor TT. Leptomeningeal metastases. *Neurol Clin* 2003;21:25-66.
11. Deangelis L, Rogers L, Foley KM. Leptomeningeal metastasis. In: Harris JR, editor. *Diseases of the breast*. Philadelphia: Lippincott Williams & Wilkins; 2000:867-74.
12. Harris M, Howell A, Chrissohou M, Swindell RI, Hudson M, Sellwood RA. A comparison of the metastatic pattern of infiltrating lobular carcinoma and infiltrating duct carcinoma of the breast. *Br J Cancer* 1984;50:23-30.
13. Smith DB, Howell A, Harris M, Bramwell VH, Sellwood RA. Carcinomatous meningitis associated with infiltrating lobular carcinoma of the breast. *Eur J Surg Oncol* 1985;11:33-6.
14. Yap HY, Yap BS, Rasmussen S, Levens ME, Hortobagyi GN, Blumenschein GR. Treatment for meningeal carcinomatosis in breast cancer. *Cancer* 1982;50:219-22.
15. Lassman AB, DeAngelis LM. Brain metastases. *Neurol Clin* 2003;21:1-23.
16. Ongerboer de Visser BW, Somers R, Nooyen WH, van Heerde P, Hart AA, McVie JG. Intraventricular methotrexate therapy of leptomeningeal metastasis from breast carcinoma. *Neurology* 1983;33:1565-72.
17. Wasserstrom WR, Glass JP, Posner JB. Diagnosis and treatment of leptomeningeal metastases from solid tumors: experience with 90 patients. *Cancer* 1982;49:759-72.
18. Chang EL, Lo S. Diagnosis and management of central nervous system metastases from breast cancer. *Oncologist* 2003;8:398-410.
19. Vuilleumier P, Chicherio C, Assal F, Schwartz S, Slosman D, Landis T. Functional neuroanatomical correlates of hysterical sensorimotor loss. *Brain* 2001;124:1077-90.
20. Stone J, Smyth R, Carson A, Warlow C, Sharpe M. La belle indifference in conversion symptoms and hysteria: systematic review. *Br J Psychiatry* 2006;188:204-9.