**CASE REPORT**

**A rare case of malignant meningitis from a likely bronchogenic melanoma primary cancer**

Jessica Little¹,*, Christopher Rajkumar² and Waqar Saleem¹

¹Department of Oncology, Imperial College Healthcare NHS Trust, Charring Cross Hospital, Fulham Palace Road, London W6 8RF, UK, and ²Department of Endocrinology, Imperial College Healthcare NHS Trust, St Mary’s Hospital, Praed Street, London W2 1NY, UK

*Correspondence address. Department of Oncology, Charring Cross Hospital, Fulham Palace Road, London W6 8RF, UK. Tel: +44-020-3311-1234 × 18427; E-mail: jessica.little2@nhs.net

**Abstract**

Malignant meningitis is a rare condition with varied clinical presentations, often mimicking other neurological conditions. Here we report a rare case of malignant meningitis from primary bronchogenic melanoma. The patient initially presented with vomiting and headache. Over the next 12 days she developed rapidly progressive neurology: losing mental faculties, vision, hearing and limb power. Lumbar puncture results revealed malignant cells. Computer tomography of the chest found an endobronchial lesion which was later biopsied and histology revealed a melanoma. This condition is very rare and diagnosis was difficult. We discuss ideas to help expedite diagnosis and management of such cases in the future.

**INTRODUCTION**

Malignant meningitis is a rare condition that occurs when malignant cells infiltrate the leptomeninges and disseminate within the cerebro-spinal-fluid (CSF) [1, 2]. The most common primary tumours are breast, lung, melanoma and haematological malignancies [1, 3, 4]. The condition results in a variety of presentations and mimics other neurological conditions [1, 5]. Diagnosis is difficult and confirmed by malignant cells on CSF analysis and characteristic signs on MRI [1]. CSF protein and lactate are usually raised [3]. After tissue diagnosis, management options include radiotherapy and chemotherapy. Prognosis remains poor since presentation is usually late and disease rapidly progressive [6–8].

**CASE REPORT**

**Day 1**

A 51-year-old Portuguese female visited A&E with a headache and vomiting. She had a transurethral resection for superficial bladder cancer 2 years ago and a pacemaker for mobitz-type-2 heartblock. She had a 35-pack-year smoking history and drank 10 units of alcohol per week. Over the preceding 3 weeks she had several hospital attendances with epigastric pain and vomiting. Investigations had been normal—she was diagnosed with gastroenteritis and discharged.

This occasion, she reported ongoing epigastric pain, vomiting and new postural headaches associated with neck pain and photophobia. She had noticed progressive vision loss and unsteady gait. She denied fevers or weight-loss. On examination her GCS was 15, she had bilateral papilloedema and visual acuity reduced to hand-movement on the left. The rest of the cranial nerves III–XII and peripheral neurological examination were unremarkable, apart from an ataxic gait. She had normal observations, blood tests and x-rays. CT head and lumbar puncture were performed and she was commenced on antibiotics and antivirals to cover infective meningitis.

CT head revealed a contrast-enhancing lesion in the left pre-pontine region, likely to be a trigeminal schwannoma or metastatic deposit (Fig. 1). Lumbar puncture found clear CSF,
normal opening pressures, WCC 4, raised protein 2.51 and low glucose 0.3.

Since the CT findings did not explain the clinical picture, an MRI head was recommended. This had to be performed at another trust since we did not have a pacemaker-compatible scanner.

**Days 2–4**

The patient was reviewed by neurology, infectious-diseases, ophthalmology and microbiology. Differentials included infective (particularly TB and fungal), inflammatory and neoplastic diseases. CT-venography showed no evidence of venous sinus thrombosis. Further tests included: B12/folate, LDH, ESR, hormones, ACE, immunoglobulins, complement, autoimmune and porphyria screen, tumour markers, myeloma-screen, TB ellispot, hepatitis, HIV, CMV, cryptococcal, aspergillus, toxoplasmosis and Borrelia burgdorferi. All results were unremarkable.

Further CSF results revealed no bacterial, acid-fast-bacilli or fungal growth, viral and TB PCR were negative. CSF cytology showed malignant cells (Fig. 2).

CT chest, abdomen and pelvis found a solitary 15 mm par enchymal lung nodule and a 5 mm endobronchial lesion in the right lower lobe.

**Day 5**

In light of these findings; antimicrobials were stopped, dexamethasone plus a proton-pump-inhibitor started and an MRI spine, head and orbits requested. The working diagnosis was malignant meningitis of unknown primary cancer. Bronchoscopy confirmed an endobronchial tumour. The patient was transferred to oncology while awaiting histology.

**Days 6–8**

Further examination found no lymphadenopathy, suspicious skin or ophthalmic lesions. She had left nipple inversion (long-standing), but no breast lumps or skin changes. An urgent breast clinic appointment and mammogram were arranged and ER/PR/HER-2 status requested on CSF.

During this time she deteriorated with confusion (GCS 14) and rapidly progressive neurology: tinnitus, hearing loss and bilateral proximal lower limb weakness (power 3–4/5). She lost 5 kg of weight in 2 weeks.

**DISCUSSION**

We have presented a rare case of malignant meningitis from a primary melanoma. In the absence of disease elsewhere and a discrete lung mass with corresponding histology shown on CT, this may represent a case of bronchogenic melanoma [9].

Primary malignant melanoma originating from an extracutaneous site is rare—and primary bronchogenic melanoma is one of the rarest visceral manifestations (0.01% of all primary lung tumours) [10]. There are only 41 reported cases in English literature—at least 8 of these had brain metastases at diagnosis [10]. Prognosis is extremely poor with a minority of patients surviving greater than 18 months [10].

Systemic therapy cannot be given until histological confirmation of diagnosis. A potential treatment option is tyrosine-kinase inhibitors. In our case, even if histology had been known earlier, it is unlikely the outcome would have changed since the patient deteriorated so quickly. Never-the-less we have highlighted a number of learning points to help expedite diagnosis and management of such cases.

**Learning points**

This patient had three previous visits to A&E with similar symptoms before she was admitted. This highlights the
importance of asking about headaches when someone presents with vomiting and having a high index of suspicion—particularly with a previous history of cancer.

At Imperial NHS Trust, we are fortunate to benefit from readily available expert opinions and reviews from multiple specialties when diagnosis is uncertain. Multiple opinions, however, led to numerous investigations being performed. These took up time, resources and on the whole did not help with diagnosis—especially once malignant cells had been identified. Lumbar puncture and imaging are the investigations that should be prioritized. In the case presented, since the pacemaker created difficulties obtaining an MRI, CSF cytological examination was the most important investigation and should have been expedited.

This case highlighted the need for a specialized leptomeningeal service that Imperial are currently in the process of developing. This service should be able to organize the necessary investigations (including MRI) and facilitate treatment quicker and more efficiently in the future.

ACKNOWLEDGEMENTS
None.

CONFLICT OF INTEREST STATEMENT
No conflicts of interest.

FUNDING
No sources of funding.

ETHICAL APPROVAL
No ethical approval required.

CONSENT
Verbal informed consent was obtained from the patient’s next of kin to write a case report and documented in patient’s medical notes. Patient’s family live in Portugal and we are unable to get written consent.

No patient identifiable information has been included in this case report. We have anonymised all information.

GUARANTOR
Drs Jessica Little and Waqar Saleem.

REFERENCES
1. Rigakos G, Liakou C, Felipe N, Orkoulas-Razis D, Razis E. Clinical presentation, diagnosis, and radiological findings of neoplastic meningitis. Cancer Control 2017;24:9–21. URL https://www.ncbi.nlm.nih.gov/pubmed/28178708.
2. Sim K, Nam K, Lee H, Park J, Ryu G, Chang J, et al. Chest wall pain as the presenting symptom of leptomeningeal carcinomatosis. Ann Rehabil Med 2014;38:861–4. URL http://pdf.medrang.co.kr/paper/pdf/Jkarm/Jkarm038-06-21.pdf.
3. Djukic M, Trimmel R, Nagel I, Speer A, Lange P, Standelmann C, et al. Cerebrospinal fluid abnormalities in meningosis neoplastica: a retrospective 12-year analysis. Fluids Barriers CNS 2017;14:7. URL https://www.ncbi.nlm.nih.gov/pubmed/28351400.
4. Brower J, Saha S, Rosenberg S, Hullett C, Ian Robins H. Management of leptomeningeal metastases: prognostic factors and associated outcomes. J Clin Neurosci 2016;27:130–7. URL https://www.ncbi.nlm.nih.gov/pubmed/26778048.
5. Zadro I, Brinar V, Barun B, Ozretic D, Pazanin L, Grahovac G, et al. Primary diffuse meningeal melanomatosis. Neurologist 2010;16:117–9. URL https://www.ncbi.nlm.nih.gov/pubmed/20220448.

6. Roth P, Weller M. Management of neoplastic meningitis. Chin Clin Oncol 2015;4:26. URL https://www.ncbi.nlm.nih.gov/pubmed/26112812.

7. Teyssonneau D, Daste A, Dousset V, Hoepffner J, Ravaud A, Gross-Goupil M. Metastatic non-muscle invasive bladder cancer with meningeal carcinomatosis: case report of an unexpected response. BMC Cancer 2017;17:323. URL https://www.ncbi.nlm.nih.gov/pubmed/28494780.

8. Glitza I, Haymaker C, Bernatchez C, Vence L, Rohlf M, Richard J, et al. Intrathecal administration of tumor-infiltrating lymphocytes is well tolerated in a patient with leptomeningeal disease from metastatic melanoma: a case report. Cancer Immunol Res 2015;3:1201–6. URL https://www.ncbi.nlm.nih.gov/pubmed/26216147.

9. Katz KA, Jonasch E, Hodi FS, Soiffer R, Kwitkiowski K, Sober AJ, et al. Melanoma of unknown primary: experience at Massachusetts General Hospital and Dana-Faber Cancer Institute. Melanoma Res 2005;15:77–82.

10. Kyriakopoulos C, Zarkavelis G, Andrianopoulou A, Papoudou-Bai A, Stefanou D, Boussios S, et al. Primary pulmonary malignant melanoma: report of an important entity and literature review. Case Rep Oncol Med 2017;2017:8654326. URL https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5352873/.