CASE REPORT

An unusual case of leptomeningeal carcinomatosis in a patient with primary adenocarcinoma of the lung

Nadina Tinsley,¹ Nikitha Yemula,² Satheesh Ramalingam,³ Shyam Madathil⁴

¹Department of Oncology, Christie NHS Foundation Trust, Manchester, UK

²Department of Paediatrics, Heart of England NHS Foundation Trust, Birmingham, UK

³Department of Radiology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK

⁴Department of Respiratory, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK

Correspondence to
Dr Nadina Tinsley,
nadina.tinsley@nhs.net

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SUMMARY

A 72-year-old man was brought to the emergency department with acute onset confusion and haemoptysis. Chest X-ray showed a possible lung mass, while CT head showed a fluid-filled, space-occupying lesion (SOL) in the right frontal lobe of the brain. MRI head indicated that this SOL had spilt its contents into the subarachnoid and intraventricular spaces. Due to a fluctuating Glasgow Coma Scale (GCS), the patient underwent emergency debulking. Macroscopically, a frail-walled cystic tumour filled with straw-coloured fluid was noted; histology confirmed metastasis from a primary lung adenocarcinoma. Whole brain radiotherapy was given, with a view to commence systemic therapy. The patient, however, deteriorated and unfortunately passed away a few weeks after completing radiotherapy. This patient presented with leptomeningeal metastasis as the first presentation of a lung adenocarcinoma, and had a highly unusual mechanism by which leptomeningeal spread had occurred, with metastatic brain tumour spilling its contents into the meningeal spaces.

BACKGROUND

Spread of cancerous cells to the leptomeninges, otherwise known as 'leptomeningeal carcinomatosis' (LC), 'leptomeningeal metastasis', 'carcinomatous meningitis' or 'meningeal carcinomatosis', is a rare but recognised site of metastasis from extracranial primary brain tumours, haematological cancers and solid tumours.¹ It is formally diagnosed with a combination of MRI head (with intravenous contrast), lumbar puncture and cytology.² The exact mechanism/s by which LC occurs is/are not well understood; however, several theories have been described, including direct and haematological spread, and seeding from the neurosurgical removal of primary brain tumours.^{3,4} Here, we describe an unusual case of a male patient who presented with leptomeningeal metastasis as the first presentation of lung cancer and was found to have a unique mechanism by which the leptomeninges were infiltrated.

CASE PRESENTATION

A 72-year-old man, with a 60-pack-year history of smoking, was brought to the accident and emergency department with acute onset confusion and haemoptysis. History was primarily collateral, with his daughter reporting a 1-day history of acute confusion and 2–3 days of reduced appetite, fatigue and haemoptysis. Medical history included

ischaemic heart disease, previous alcohol excess and, of note, a fall with a head injury 1 month ago. Medication history included aspirin, lisinopril, metoprolol and simvastatin. Social history revealed that the patient lived with his daughter, but was fully independent with activities of daily living. Physical examination revealed equal intensity breath sounds throughout both lungs, and an unremarkable cardiac, abdominal and limb examination. Neurological examination was challenging as the patient was not cooperative; GCS on admission was 14/15 (confusion) and power in all four limbs was 5/5. A further detailed neurological examination was not possible.

INVESTIGATIONS

Laboratory bloods were unremarkable. A chest X-ray (figure 1) showed an ill-defined opacification in the right lower zone with a probable air-fluid level within it. A CT thorax, abdomen and pelvis showed a 5.6×4.7 cm cavitating, abscess-like mass in the right lower lobe with an air-fluid level; a couple of much smaller cavitating lesions were also seen in the right apex. To investigate the confusion, a CT head was requested (figure 2A,B); this revealed a large (approximately 5.6×4.3 cm) cavitating, fluid-filled space-occupying lesion (SOL) in the right frontal lobe. Further layering of hyperdense material was seen within the occipital horns of both lateral ventricles. For more detailed imaging, the patient underwent an MRI head, which showed that this SOL had indeed spilled/haemorrhaged its contents into the intraventricular and subarachnoid compartments (figure 3A,B,C,D) with diffuse leptomeningeal involvement. As part of the lung cancer workup, the patient also underwent bronchoscopy. Bronchoalveolar samples were, however, largely inconclusive, although ruling out TB of the lung.

DIFFERENTIAL DIAGNOSIS

When this patient first presented to our clinical decision unit, the working diagnosis was lung abscess with cerebral spread. The patient was therefore placed on intravenous ceftriaxone, metronidazole and dexamethasone. With the patient's presentation, smoking history and CT thorax findings in mind, an underlying lung cancer with brain metastases was the most likely differential diagnosis. The MRI head findings raised the possibility of leptomeningeal spread from the SOL. Ultimately, a tissue diagnosis was needed.

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Figure 1 Chest X-ray showing an ill-defined mass in the right lower lobe.

TREATMENT

Due to the patient's fluctuating GCS, he underwent emergency debulking. The neurosurgeons noted a frail-walled cystic tumour with straw-coloured fluid inside, in keeping with tumour necrosis and remote haemorrhage. After decompression of the cyst and aspiration of the fluid, a pseudoplane was created between the cyst and the brain. The tumour and cyst were then carefully excised, with samples sent to the laboratory. Histology (figure 4A,B,C,D) confirmed a metastatic adenocarcinomatous

picture. The tumour showed a Programmed Death Ligand 1 (PD-L1) expression of 100% but was negative for mutations in the Epidermal Growth Factor Receptor (EGFR) gene, as well as being negative for Anaplastic Lymphoma Kinase (ALK) rearrangement. The overall morphology and immunohistochemistry favoured a lung primary.

OUTCOME AND FOLLOW-UP

A formal diagnosis of T2b N0 M1b adenocarcinoma of the lung with brain metastases was made. This man's performance status was 1, and as per the agreed standard of surgically resected brain metastases, he underwent adjuvant whole brain radiotherapy (20 Gy in five fractions) with a view to proceed to systemic therapy.⁵ Postradiotherapy, however, his condition quickly deteriorated, wherein he became wheelchair user, fatigued and doubly incontinent. Barely weeks after radiotherapy, he represented with a community acquired pneumonia and was started on intravenous antibiotics. A repeat CT head showed an acute intraparenchymal haemorrhage in the right frontal lobe. Within a week of admission, this man unfortunately passed away. The cause of death placed on his death certificate was metastatic adenocarcinoma of the lung.

DISCUSSION

Our patient was diagnosed with LC at first presentation. Brain metastases from his primary lung adenocarcinoma caused direct leptomeningeal infiltration through spillage of tumour contents. Using 'PubMed' and 'Google Scholar', we conducted an extensive literature search, and to the best of our knowledge, this patient is the first reported example of such a mechanism.

As in our patient, we have found a handful of case reports where LC was the first presentation of lung adenocarcinoma.⁶⁻⁹

Figure 2 (A) Non-enhanced CT head shows a well-defined cystic lesion with sedimentation of cellular debris and hyperdense material within the lateral ventricles. (B) A contrast-enhanced CT head illustrates minor cyst wall enhancement.

Figure 3 (A) Axial contrast-enhanced T1-weighted image shows a ring-enhancing lesion in the left frontal region with perilesional oedema, while (B) the axial Fluid-attenuated inversion recovery (FLAIR) image shows hyperintense (exudative) fluid within the lateral ventricles and in the subarachnoid spaces; the fluid signal intensity is similar to the fluid within the cystic lesion. The fluid within the cystic lesion shows low signal intensity on the diffusion-weighted image (C) as well as high apparent diffusion coefficient values (D), indicating free diffusivity.

The main presenting clinical features were headache, dizziness, nausea, vomiting, deafness, meningeal irritation and cranial nerve pathologies. A study in Taiwan reviewed 34 cases of

cytologically proven LC from lung cancer.¹⁰ These data showed that leptomeningeal spread occurred only in 0.7% of their total lung cancer diagnoses, with 32 out of 34 reports of LC being

Figure 4 (A) Cytological findings reveal a neoplasm within the brain tissue, arranged in sheets or a pseudopapillary pattern (marked with two arrows), which is focally discohesive in areas. (C) Intracytoplasmic vacuolation is also demonstrated (marked with an arrow). (B) Immunohistochemistry findings showed that Cytokeratin CAM52 (pancytokeratic) was strongly positive, suggestive of an adenocarcinomatous cell line, while (D) Thyroid transcription factor (TTF-1) was also strongly staining, narrowing the primary to either the lung or thyroid. Overall, the appearances are those of a metastatic adenocarcinoma of the lung.

of an adenocarcinomatous origin. Sudo *et al* also demonstrated adenocarcinoma to be the most common histological subtype (70% of LC cases).¹¹ In addition, the analysis of clinicopathological features for leptomeningeal metastases in three patients with non-small cell lung cancer all revealed both tissue and Cerebrospinal fluid (CSF) confirmation of adenocarcinoma.⁹ An autopsy case report of a 59-year-old woman noted ‘signet ring cells’ (a rare but recognised cytological feature of lung adenocarcinoma) in both the lung mass and leptomeninges.⁸

The general mechanisms of LC are not well understood. Using their case of signet ring colorectal adenocarcinoma, Assi and colleagues postulated four distinct routes of metastasis to the leptomeninges³:

1. Haematological pathway: spread of malignant cells to the subarachnoid compartment through portal and paravertebral arteries and veins is the most common way of LC in haematological cancers.
2. Neural spread: metastatic travel via long peripheral or cranial nerves to the subarachnoid using endoneural, perineural or lymphatic trajectories of nerve roots.

3. Skull bone marrow micrometastases resulting in perivenous spread into the meningeal spaces.

4. Direct extension from subdural or extradural tumours.

In this report, there was no postulation of leptomeningeal spread through necrotic tumour material spilling and causing meningitis. Indeed, we have found only one study where this was discussed as a concept—a report on metastatic craniopharyngioma in children; it was not, however, recognised in their own patient.¹² Jun Hyong Ahn and group described the likelihood of surgical spillage of malignant cells into the leptomeninges during the neurosurgical resection of brain metastases.⁴ It was found that the resection method (en bloc or piecemeal) as well as the proximity of the tumour to the CSF pathway all affected this risk, a pivotal reason why adjuvant whole brain radiotherapy after surgical resection of solitary brain metastases is now the agreed standard.^{4,5}

A separate specific search for LC appearance on brain imaging was also undertaken. A relevant clinical analysis of 42 cases of meningeal carcinomatosis from solid tumours illustrated numerous CT brain findings: hydrocephalus 62%, contrast

enhancement in cerebral sulci or basal cisterns 31%, concomitant parenchymal metastases in 15% and normal scan in 18%.¹³ Another study which correlated MRI findings in leptomeningeal metastases classified patients into four groups as per gadolinium-enhanced MRI appearances: diffuse enhancement of the subarachnoid space (including the cisterns around the midbrain, the Sylvian fissures or the cerebellar and cerebral sulci), diffuse, thick partially nodular enhancement of the dura matter, nodular masses in the spinal canal or normal scan.¹⁴ Four further studies were found, all of which had non-specific meningeal enhancement on MRI but no separate brain lesion.^{8 15–17}

Learning points

- ▶ Leptomeningeal carcinomatosis from lung cancer as a first presentation remains relatively uncommon but is one to be aware of.
- ▶ Leptomeningeal metastases from a lung primary seem to occur more frequently with adenocarcinomas, compared with small cell or squamous cell lung cancer.
- ▶ We found no reported cases of lung adenocarcinoma causing leptomeningeal infiltration through direct tumour material spilling into the subarachnoid or intraventricular spaces. Though unusual, we feel this mode of disease spread is an important differential to consider in future patients with similar investigative findings.

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