Subliminal and Trigeminal - A Case of Trigeminal Neuralgia as the Initial Manifestation of Leptomeningeal Carcinomatosis

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LEARNING OBJECTIVES

- To understand the clinical features of leptomeningeal carcinomatosis
- To recognize the importance of a broad differential diagnosis in those presenting with trigeminal neuralgia

INTRODUCTION

Leptomeningeal carcinomatosis (LMC) is an uncommon form of solid tumor metastasis most associated with lung and breast cancer. Rarely is LMC the initial manifestation of these cancers, and due to the non-specific symptoms can make diagnosis challenging. Presented here is a case of trigeminal neuralgia due to LMC as the initial manifestation of non-small-cell lung cancer (NSCLC).

CASE PRESENTATION

- A 53 year old woman never-smoker presented to her dentist with left maxillary pain and underwent second left maxillary molar removal.
- Her symptoms persisted which led to ENT and neurosurgery evaluation, prompting brain MRI which revealed a likely left frontal vascular malformation, but no other abnormalities.
- Over several months, her facial pain became intractable and ultimately led to a seizure, for which she was admitted at an outside hospital.
- Repeat MRI showed new extensive nodular leptomeningeal enhancement (figure 1), however CSF studies from lumbar puncture were unremarkable.
- Further imaging revealed a PET-avid spiculated left lower lobe mass with no other lesions. CT-guided biopsy of the lung mass was non-diagnostic.
- She was transferred to our hospital for further work-up of what was felt to be primary malignancy of the lung with LMC.
- Her exam upon arrival was non-focal except for diplopia with downward gaze and pain in left cranial nerve V2/V3 distribution (figure 2), consistent with trigeminal neuralgia which was responsive to carbamazepine. Repeat LP was again unremarkable.
- After presentation at lung tumor board, decision was made to pursue open craniotomy for appropriate staging. Cerebellar and dural biopsies as well as CSF analysis all revealed metastatic adenocarcinoma likely of lung origin, thus confirming stage IV NSCLC.
- Because of her lack of smoking history and relatively young age, tissue was sent for genetic analysis and found to be EGFR positive.
- Because of her poor performance status, she was felt to be a poor candidate for treatment, and she was discharged with plans for hospice.

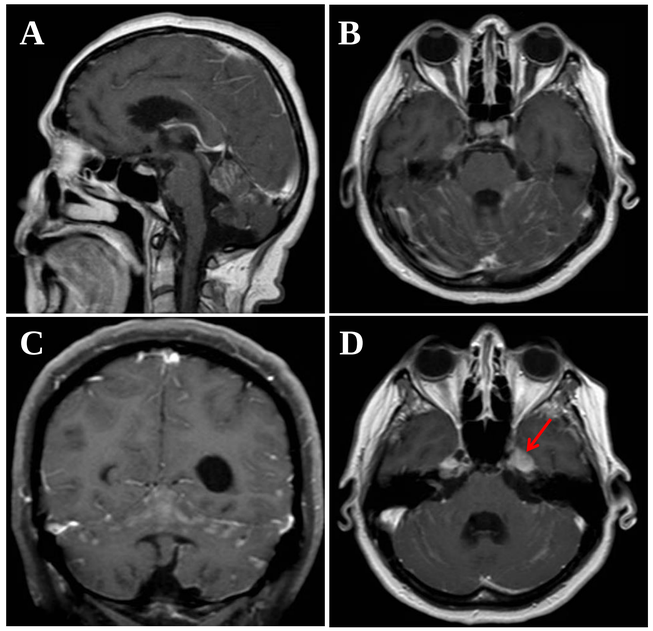

Figure 1: T1-weighted gadolinium-enhanced MRI findings. A) Sagittal view showing nodular leptomeningeal enhancement overlying the cerebral hemispheres, most prominently in the posterior fossa. B) Axial and C) Coronal views showing enhancement along the cerebellar fovea and vermis. D) Axial view showing mass-like enlargement filling both Meckel's caves, more prominent on the left (red arrow), and likely responsible for this patient's trigeminal neuralgia.

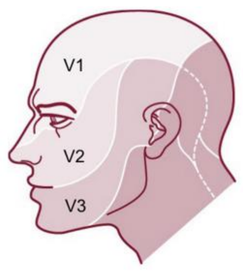

Figure 2: Representation of dermatomes corresponding to the three trigeminal nerve branches: V1, V2, and V3. [8]

Sign/Symptom	Incidence (%)
Cranial nerve palsies	75
Headache	66
Mental status changes	45
Limb weakness	44
Difficulty walking	33
Meningismus	21
Nausea-vomiting	20
Seizures	10
Dizziness	9

Table 1: Incidence of clinical signs and symptoms of leptomeningeal carcinomatosis, as reported by Francolini et al[2].

System	Pathology
Trauma	Accidental, dental, iatrogenic
Inflammatory	Scleroderma Sjogren's syndrome Sarcoidosis Multiple sclerosis
Vascular	Pontomedullary ischemia Vascular malformation
Neoplastic	Intra- or extracranial compression Perineural spread Metastasis (lung, breast, melanoma) Leptomeningeal carcinomatosis
Infectious	Viruses (VZV, HSV) Syphilis Lyme disease
Toxic-metabolic	Oxaliplatin Diabetes mellitus

Table 2: Differential diagnosis of trigeminal neuralgia[5]. VZV = varicella zoster virus; HSV = herpes simplex virus

DISCUSSION

- The vast majority of patients with LMC have a prior cancer diagnosis. Symptoms often manifest late in disease course after having undergone systemic treatment.
- It is rare for LMC to be the initial manifestation of malignancy, occurring in only ~5% of cases[1].
- As seen in this patient, LMC often presents with cranial nerve palsies[2] (Table 1), the most commonly involved being cranial nerves III, IV, VI, and VII[3].
- Although imaging may show signs consistent with LMC, diagnosis is definitively made by CSF examination. While cytologic studies carry 50% sensitivity for detecting LMC on initial lumbar puncture, sensitivity increases to 85% after three lumbar punctures[4].
- Leptomeningeal involvement similar to LMC can be seen on MRI in fungal and tuberculous meningitis, intracranial fibromatosis, lymphoma, and sarcoidosis[5]. Therefore, particularly in the absence of systemic metastases (as seen in this patient), the clinical context must be considered.
- Because this patient lacked other systemic metastases, the confirmation of her leptomeningeal lesions as LMC was critical, as a negative CNS biopsy would indicate stage I disease that would be potentially curative.
- While it can be due to a variety of secondary causes[6] (Table 2), trigeminal neuralgia is most often caused by nerve compression by an aberrant artery or vein, and therefore a high index of suspicion is required to pursue further work-up of neoplastic etiology.
- While tyrosine-kinase inhibitors are the first-line treatment for NSCLC with EGFR mutations, there is no consensus for those who also have LMC, although some data suggest a survival benefit[7].

REFERENCES

1) Gleissner B, Chamberlain MC. Neoplastic meningitis. Lancet Neurol. 2006;5(5):443-52.
2) Francolini M, Sicurella L, Rizzuto N. Leptomeningeal carcinomatosis mimicking Creutzfeldt-Jakob disease: clinical features, laboratory tests, MRI images, EEG findings in an autopsy-proven case. Neurol Sci. 2013;34(4):441-4.
3) Kato Y, Takeda H, Dembo T, Fukuoka T, Tanahashi N. Progressive multiple cranial nerve palsies as the presenting symptom of meningeal carcinomatosis from occult colon adenocarcinoma. Intern Med. 2012;51(7):795-7.
4) Grossman SA, Krabak MJ. Leptomeningeal carcinomatosis. Cancer Treat Rev. 1999;25(2):103-19.
5) Trinh VT, Medina-flores R, Chohan MO. Leptomeningeal carcinomatosis as primary manifestation of pancreatic cancer. J Clin Neurosci. 2016;30:124-7.
6) Smith JH, Cutrer FM. Numbness matters: a clinical review of trigeminal neuropathy. Cephalalgia. 2011;31(10):1131-44.
7) Li YS, Jiang BY, Yang JJ, et al. Leptomeningeal Metastases in Patients with NSCLC with EGFR Mutations. J Thorac Oncol. 2016;11(11):1962-1969.
8) Leclercq D, Thiebaut JB, Héran F. Trigeminal neuralgia. Diagn Interv Imaging. 2013;94(10):993-1001.