Leptomeningeal carcinomatosis as primary manifestation of pancreatic cancer

Victoria T. Trinh [a], Rafael Medina-Flores [b], Muhammad O. Chohan [a,*]

[a] Department of Neurosurgery, University of New Mexico Hospital, MSC 10-5615, 1 University of New Mexico, Albuquerque, NM 87131, USA
[b] Department of Neuropathology, Marshfield Clinic, Marshfield, WI, USA

ARTICLE INFO

Article history:
Received 6 October 2015
Accepted 12 December 2015

Keywords:
Leptomeningeal carcinomatosis
Leptomeningeal disease
Pancreatic carcinoma

ABSTRACT

Leptomeningeal carcinomatosis (LMC) is a rare complication of cancer that often presents at an advanced stage after obvious metastasis of a primary cancer or locally advanced disease. We present an uncommon case of LMC secondary to pancreatic carcinoma presenting with headache, unilateral VII nerve palsy, and lower extremity weakness. Initial cerebrospinal fluid (CSF) studies were concerning for chronic aseptic meningitis but negative for malignant cells; the diagnosis of tuberculous meningitis was erroneously evoked. Three lumbar punctures were required to capture malignant cells. The diagnosis of LMC was based on CSF examination with cytology/immunohistochemistry and leptomeningeal enhancement on MRI. *Post mortem* autopsy revealed advanced and diffusely metastatic pancreatic adenocarcinoma. This patient demonstrates that solid tumors can present with leptomeningeal spread that often confuses the treating physician. Fungal or tuberculous meningitis can mimic LMC in the absence of neoplastic signs and negative CSF cytology. This event is exceedingly rare in pancreatic cancer. If the index of suspicion is high, repeat CSF sampling can increase the sensitivity of detection of malignant cells and thus result in the correct diagnosis.

1. Introduction

Leptomeningeal carcinomatosis (LMC) refers to spread of cancer cells to the leptomeninges and cerebrospinal fluid (CSF) and occurs in 5–8% of all cancer patients, with the most common cancers being lung, breast, melanoma and lymphoma [1]. Brain metastasis from pancreatic adenocarcinoma is an exceedingly rare event carrying an incidence of 0.33% [2], with only 20 cases reported in the literature to our knowledge [3]. LMC from pancreatic cancer is even rarer, with only seven reported cases [4–10]. We present a patient with pancreatic cancer, which manifested itself as LMC, and the primary site was only diagnosed *post mortem*.

2. Case report

A 58-year-old man presented with worsening headache, paraparesis, and unilateral VII nerve palsy. Brain CT scan showed moderate ventriculomegaly, while lumbar puncture (LP) revealed elevated protein, low glucose, and leukocytosis with reactive monocytes. Differential included aseptic and carcinomatous meningitis. MRI of the spine revealed diffuse enhancement along the meningeal lining of the cervico-thoracic spine (Fig. 1a) and an abdominal CT scan showed no obvious mass (Fig. 1b). He was treated for suspected tuberculous meningitis based on his travel history but continued to deteriorate. Repeat LP showed pleomorphic cells with nuclear atypia, and abnormal mitosis (Fig. 1c). The patient opted for palliative care. Time from initial presentation to death was 34 days.

3. Pathology

CSF was immunoreactive for pankeratin, cytokeratin 7 (CK7) (Fig.1d, e), and CK20 (Fig. 1f). Hematolymphoid markers CD45 and CD30 (Fig. 1g, h) were also positive. On autopsy, the pancreas was replaced by malignant cells invading the stroma (Fig. 2a) with fatty infiltration and peripheral mucin (Fig. 2b). Dense sheets of pleomorphic, spindle-shaped cells with melanin were present in the Virchow–Robin spaces (Fig. 2c). The cerebral gyri were flattened, with narrow sulci (Fig. 2d). Autopsy of the thoracolumbar cord revealed thickened dorsal spinal roots and dorsal root ganglia (Fig. 2e).

4. Discussion

For most solid tumors, the development of LMC occurs late in the course, but in our patient, leptomeningeal disease was the initial manifestation of pancreatic tumor without the usual symptoms of jaundice or cholestasis. In addition, our patient presented a diagnostic dilemma, as in the absence of cancer cells after repeat LP, the diagnosis of tuberculous meningitis was erroneously evoked. The primary cancer was not identified until a *post mortem* examination.

Of the seven reported cases of LMC in the literature [4–10] (Table 1), LMC was a late event in six patients. We believe that this is the first case in which LMC alone (and not solid brain metastasis) was the primary manifestation of pancreatic cancer. Including the current patient, all but one were male, aged between 45–72 years and with normal initial brain radiology.

Demonstration of malignant cells in the CSF by cytological analysis is the diagnostic gold standard for LMC. Shedding of malignant cells in the CSF occurs intermittently, requiring multiple taps to acquire malignant cells. Sensitivity of LP increases from an estimated 45–55% after the first tap to 90% with the third tap [11], thus highlighting the importance of repeat CSF sampling.

In the absence of a clinically known or suspected primary site, immunocytochemistry of CSF can be helpful in determining tumor lineage [12]. Our patient demonstrated immunoreactivity for adenocarcinoma markers pankeratin, cytokeratin (CK7), and CK20. Other CSF abnormalities such as a high opening pressure,

* Corresponding author. Tel.: +1 505 272 24280; fax: +1 505 272 6091.
E-mail address: mchohan@salud.unm.edu (M.O. Chohan).

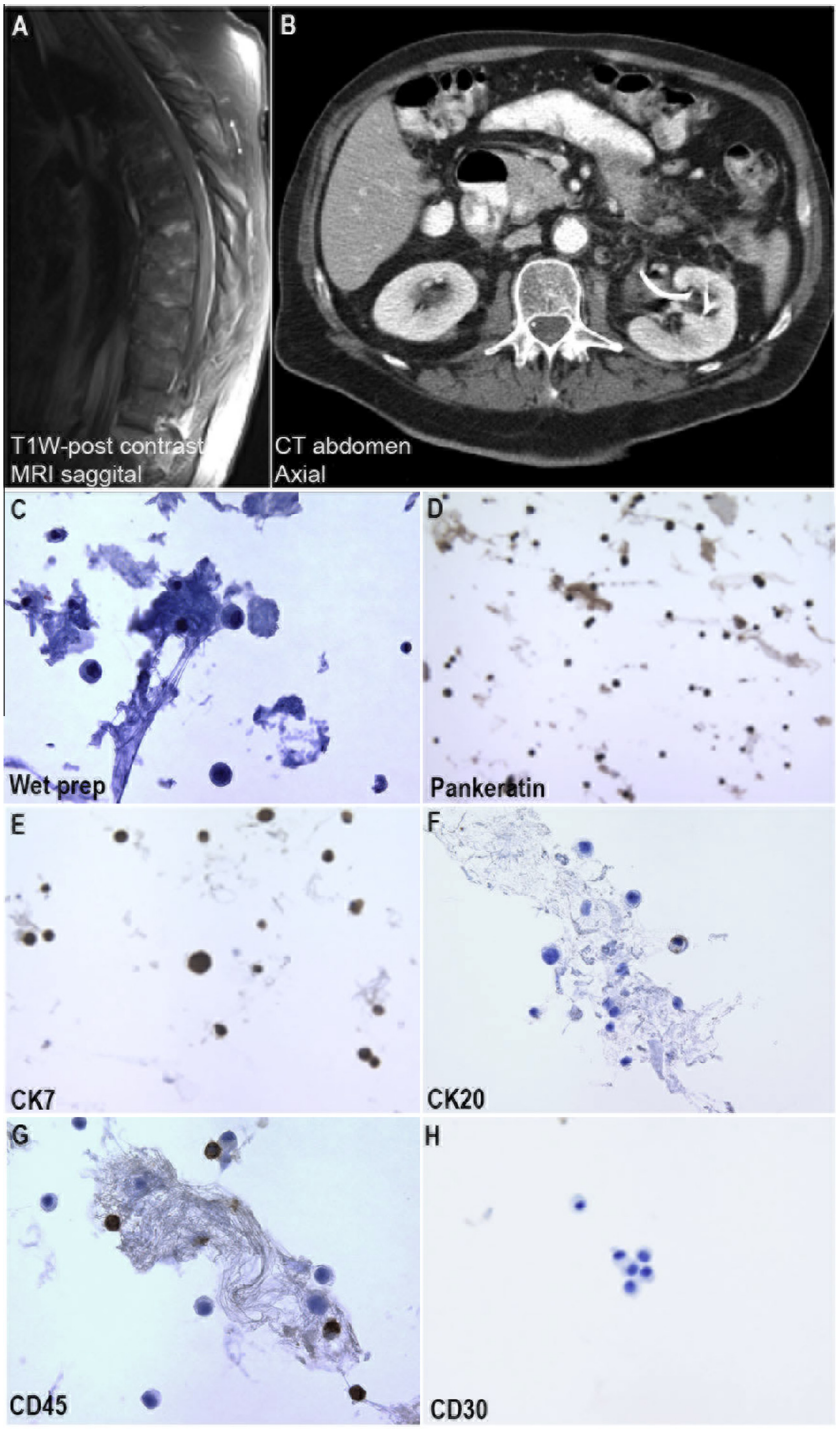

Fig. 1. Radiographic and pathology findings. Sagittal gadolinium-enhanced T1-weighted MRI (A) of the spine reveals diffuse enhancement of the leptomeninges lining the cervicothoracic spine. Axial CT scan of the abdomen (B) reveals extensive retroperitoneal stranding which extends into the perinephric, pancreatic tail and splenic hilar regions. (C) Wet preparation of the cerebrospinal fluid showing pleomorphic cells with nuclear atypia and abnormal mitoses (original magnification × 40). Pankeratin (D, original magnification × 10), CK7 (E, original magnification × 40), and CK20 (F, original magnification × 20) immunostains are positive, consistent with adenocarcinoma and epithelial differentiation. Hematolymphoid markers LCA (G, original magnification × 40) and CD30 (H, original magnification × 20) are positive as well, demonstrating that most tumor markers can react variably across different tumor types. T1W = T1-weighted, CK = cytokeratin, CLA = cutaneous lymphocyte-associated antigen.

leukocytosis, and high protein, can be present but may confuse the diagnosis for aseptic meningitis [11].

Leptomeningeal involvement similar to LMC can be seen on MRI in fungal and tuberculous meningitis, intracranial fibromatosis, lymphoma and sarcoidosis [13]. Our patient exemplifies the fact that solid tumors may manifest with LMC even in the absence of systemic disease, and alerts the neurosurgeon to considering the diagnosis with proper clinical context.