JUNE 2015 – CASE 1

55-Year-Old Man with Acute Ascending Paraparesis

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CLINICAL HISTORY

A 55-year-old Brazilian man, with previous history of bariatric surgery developed acute weakness of his lower limbs that started six weeks prior to his admission. He started with paresthesias in lower limbs followed by ascending and asymmetrical paraparesis. He was unable to walk weeks later. He had no pain, no upper limbs weakness and no loss of bowel or bladder control. Physical examination revealed paraparetic gait, and flaccid asymmetric paraparesis (left > right). Deep tendon reflexes were absent in the legs, with indifferent plantar response. Electroneuromyography was consistent with an acute inflammatory demyelinating polyradiculoneuropathy (Guillain-Barré syndrome). MRI of neuro-axis showed diffuse nodular abnormalities of the leptomeninges, more pronounced in dural sac where formed intra-rachidian mass and hemorrhagic extra-axial nodular lesions in posterior fossa, basal cisterns and subarachnoid space of cerebral hemispheres Fig 1a, 1b). A second MRI showed larger lesions and more of them (Figs 1c, 1d). An extensive search for the primary site was negative (chest and abdominal CT, cervical and testicular ultrasonography). Cisternal puncture didn't reveal any neoplastic cells. A biopsy of the lesion (dural sac) was performed.

PATHOLOGY

H&E stains revealed highly infiltrative lesion affecting meninges and nerve bundles, formed of cells with intense pleomorphism, nuclear hyperchromasia, high mitotic index, arranged in both sheets and individually infiltrating cells (Fig 1f and 1g). Histogenesis was determined by IHC that revealed negative immunostaining for cytokeratins, GFAP, EMA, myeloperoxidase, CD3 and CD20. However, S100 and Melan-A (Fig 1e) showed strong positive staining of the tumor cells. No pigmentation was noted. Two weeks later, this patient expired after a large intracranial bleed. Autopsy examination revealed a 1cm black nodular lesion in the stomach, next to the bariatric surgery scar. This tumor had the same immunostaining pattern as the meningeal metastasis. **What is your diagnosis?**

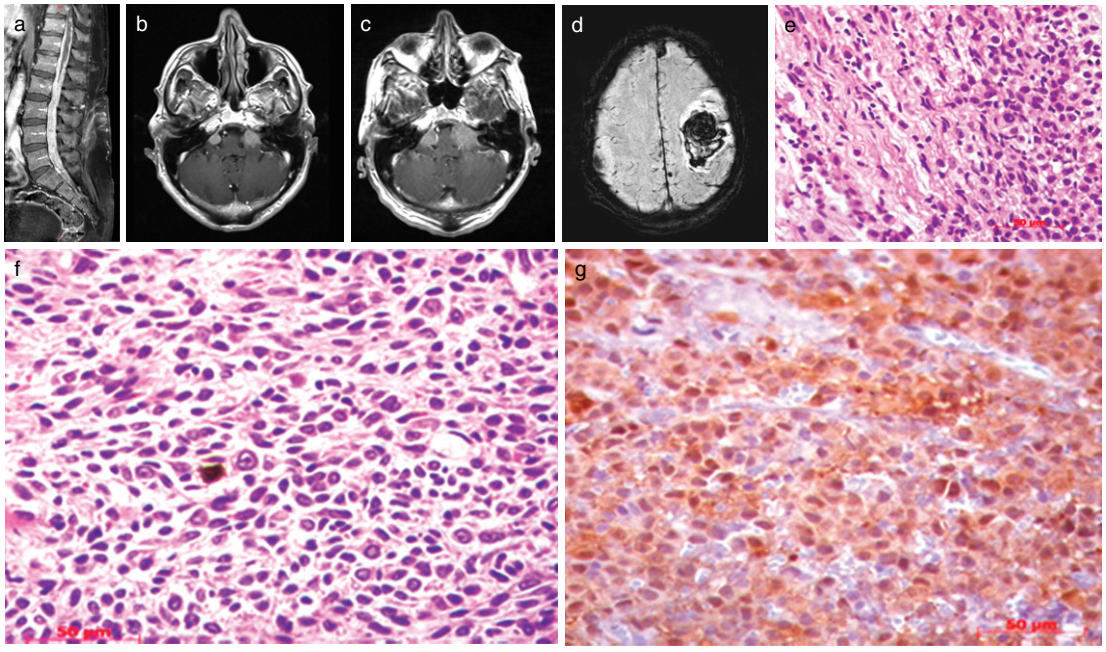

Figure 1.

DIAGNOSIS

Leptomeningeal amelanotic melanomatosis and brain metastases from gastric melanoma.

DISCUSSION

Cancer in the defunctionalized distal stomach after gastric bypass for morbid obesity was first reported in 1991, 25 years after the procedure was introduced for this indication. The distal stomach has been bypassed in this operation and this segment may be subject to different influences on oncogenesis (2).

We describe a case of a patient with previous gastric bypass that presented acute ascending paraparesis as unusual clinical course of diffuse malignant leptomeningeal melanomatosis with no identified primary lesion, at first. Leptomeninges involvement produces symptoms and signs resulting from either obstruction of CSF flow or direct infiltration of nerves producing neurological deficits leading to cranial nerve palsies (III, IV, VI and VII being involved most frequently), cerebral disturbance, spinal nerve root involvement and gait disturbance (1).

Leptomeningeal carcinomatosis (LC) occurs in between 5 and 8% of patients with cancer. Common solid tumors associated with LC include, in order of frequency: breast, lung and malignant melanoma (MM). MM represents 6–18% of LC cases while 23% of MM cases will ultimately result in LC. Lumbar puncture (LP) to obtain CSF samples for cytological and biochemical assessment is the most useful test in suspected cases of LC (3). Clinicians should be aware that 50% of patients with LC have a negative cytology result on the first LP, as occurred in this case (3). The primary site was only possible to define after autopsy that diagnosed an extracutaneous melanoma, on the stomach, with the same profile of metastasis.

Primary gastric melanoma is very rare. Most of the melanomas found in the stomach are metastases from cutaneous sources (1). Since normal stomach, epithelium lacks melanocytes, the cell of origin remains obscure. Ectopic migration of melanocyte precursors or differentiation of the APUD cells (amine precursor uptake and decarboxylation cells) to melanocytes has been suggested as a possible mechanism of the development of melanoma (4). Criteria for the diagnosis of primary melanoma include the absence of other primary site melanomas and no history of the removal of a melanoma or atypical melanocytic lesion from the skin or other organs (1).

S-100 proteins and HMB-45 antibodies are very sensitive for the diagnosis of melanocytic lesions. Immunohistochemical examination of the tumor from this patient revealed a positive reaction with S-100 proteins and HMB-45 antibodies, which led us to assume a primary MM of the stomach. MMs that arise in mucosal surfaces appear to be more aggressive and associated with a worse prognosis than cutaneous MMs. This poorer prognosis may be related to late diagnosis, an inherently more aggressive behavior of mucosal MM, or earlier dissemination because of the rich lymphatic and vascular supply of GI tract mucosa (1, 4).

For the diagnosis of early stages of gastric carcinoma it is important to collect biopsies from several areas of the gastric stump, even if a carcinoma is not suspected macroscopically. Endosonography can show the degree of infiltration into the gastric wall or infiltration of the surrounding organs with an accuracy of 85%. The diagnosis of lymph node metastasis is more difficult. Screening for gastric malignancies with tumor markers has not proved to be very sensitive, because there are no specific tumor markers for gastric cancer (4).

In conclusion, this case demonstrates a leptomeningeal melanomatosis presenting as Guillain-Barré Syndrome. Although neuro-malignancy classically manifests insidiously, it can present abruptly with acute onset symptoms and signs. CSF analysis and early MR spinal imaging are crucial tools in the diagnostic work-up of paraparesis and in guiding subsequent management. Elevated CSF protein levels with evidence of leptomeningeal hemorrhage (old or new) should arouse the suspicion of malignancy, in particular melanoma, which has a recognized propensity for metastasizing to the CNS and bleeding. Primary gastric melanoma is an extremely uncommon clinical entity and amelanotic melanoma such as the one in this case can be missed in poorly differentiated tumors unless appropriate staining tests are performed. Primary malignant melanoma of the stomach may be an underdiagnosed. Early detection and surgical intervention is critical for long-term cure, though overall prognosis is very poor.

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