



Case Report

A rare case of metastatic leptomeningeal carcinomatosis from adenocarcinoma of Caecum

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ABSTRACT

We report a patient with carcinomatous meningitis secondary to carcinoma caecum. The patient presented with multiple focal neurological signs and symptoms. Diagnosis was suggested by magnetic resonance imaging and confirmed by analysis of the cerebrospinal fluid. She received whole brain radiotherapy and other supportive measures. She succumbed to her disease while she was on treatment for carcinomatous meningitis. To our knowledge, this is only the second reported case of carcinomatous meningitis secondary to carcinoma caecum with confirmatory imaging and cytology.

KEYWORDS: Carcinomatous Meningitis, Carcinoma Caecum.

INTRODUCTION

Neoplastic meningitis (NM) is the result of seeding of the leptomeninges by malignant cells. The development of NM portends a poor prognosis, with survival ranging from 4 to 16 weeks after the diagnosis. NM is diagnosed in one to five percent of patients with solid tumors, in which case it is termed carcinomatous meningitis (CM) and the main subject of this case report [1]. CM can be a complication of caecal carcinoma, however this presentation is extremely rare. This case and the discussion that follows serve both to illustrate key clinical and laboratory features that may support the diagnosis of CM and to emphasize the setting in which this relatively rare clinical entity should be considered.

CASE REPORT

A 47-year-old lady presented to the emergency room (ER) with severe frontal headache, vomiting, generalized body pains and photophobia of one week duration. She had received symptomatic treatment for the same from a local practitioner following which her headache was temporarily relieved. Within the next two days the headache had worsened and the patient also developed altered sensorium and altered behavior. There was no history of fever. Five months ago, she was diagnosed to have an ileocaecal

growth for which she underwent laparotomy and right hemicolectomy with ileocolonic anastomosis.

Histopathological examination of the resected specimen (**Figure 1**) revealed moderately differentiated mucin secreting adenocarcinoma of the caecum with neuroendocrine differentiation. Poorly cohesive tumor cells and signet ring cells were seen adjacent to the solid areas of tumor diffusely infiltrating the submucosa. Immunohistochemical studies with chromogranin (**Figure 2**), cytokeratin and neuron specific enolase were positive. Her tumor was staged as T3N1M0 after completing the staging work up. Three weeks after surgery she was initiated on adjuvant chemotherapy. She was started on FOLFOX-4 chemotherapy regimen which consists of folinic acid, 5-fluorouracil and oxaliplatin. Each cycle of FOLFOX-4 consists of Oxaliplatin 110mg on Day 1 (2- hour infusion), Leucovorin 250 mg on Day one and two (2- hour infusion), 5-FU (bolus) 500 mg on Day one and two, 5-FU (22- hour infusion) 760 mg on Day one and two. Each cycle is repeated every 14 days. At the time of presentation to the ER with neurological complaints she completed four months of adjuvant chemotherapy and was due for the next cycle of chemotherapy. There was no other significant past history.

On physical examination she was afebrile and hemodynamically stable. Nuchal rigidity was evident and

Kernig's sign was positive. Bilateral plantar reflex was extensor and there were no other focal neurological deficits. The rest of the physical examination was unremarkable. The contrast enhanced computed tomography (CT) of the brain was normal. Magnetic resonance imaging (MRI) of brain and spinal cord showed diffuse meningeal enhancement (**Figure 4**). A lumbar puncture was performed

Figure 1: Colonic adenocarcinoma with neuroendocrine differentiation (H&E 10 X)

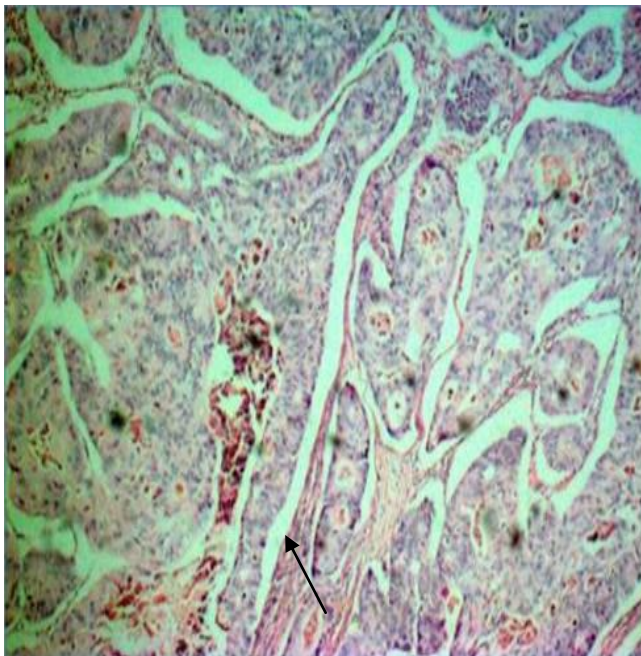
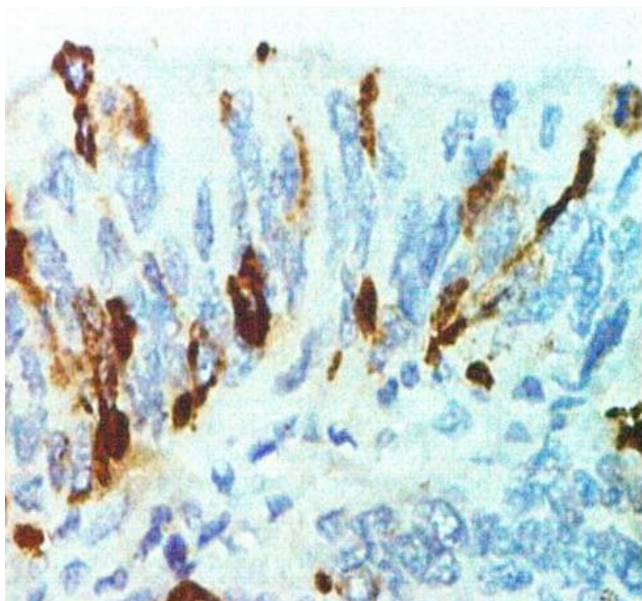


Figure 2: Immunohistochemistry showing Chromogranin positivity in tumor cells (40 X)



at this point in time, revealed raised opening pressure. Analysis of cerebrospinal fluid (CSF) revealed high opening pressure, an elevated cell count, protein of .23 g/L, glucose of 2.22 mmol/L, gram stain did not demonstrate bacteria and the specimen was sterile on culture. Cytological examination of cytocentrifuged CSF specimen revealed mucin filled neoplastic cells (signet ring cells) (**Figure 3**).

Figure 3: CSF examination showing carcinomatous cells and a mucin filled neoplastic cell (signet ring cell) (PAP 40X)

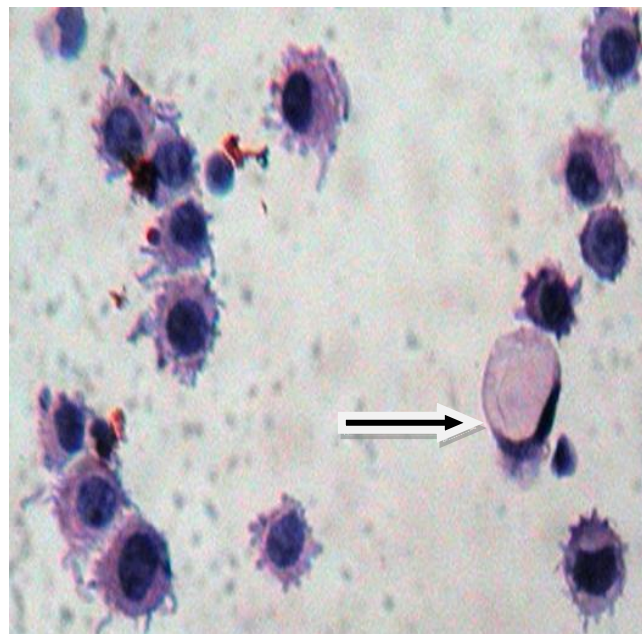
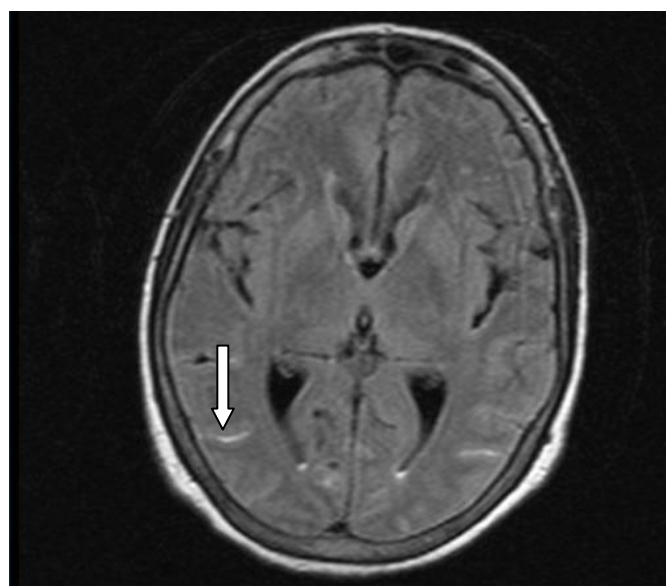


Figure 4: MRI brain showing contrast enhancement in bilateral parieto-occipital regions



CSF adenosine deaminase was normal. Venereal Disease Research Laboratory (VDRL) test was non-reactive, India ink staining was negative. Other laboratory investigations namely complete blood picture, renal function tests, liver function tests and serum electrolytes were normal. She was diagnosed to have carcinomatous meningitis secondary to carcinoma caecum. She was treated with whole brain radiotherapy (WBRT) (30 Gy in 10 fractions at 3 Gy per

DISCUSSION

NM is an often lethal, major neurologic complication of cancer. NM most commonly occurs in patients with leukemia, breast cancer, lymphoma, and lung cancer [2]. Adenocarcinoma is the most frequent histology that is encountered in the solid malignancies spreading to the leptomeninges [3]. However, CM is still considered infrequent, and its variable clinical manifestations make clinical diagnosis difficult. Better control of the systemic disease for prostate cancer and breast cancer with newer therapeutic agents and poor penetration of these drugs into the central nervous system (CNS) are the factors responsible for the increase in isolated relapses in the neuroaxis [4,5]. Typically there are multifocal neurological symptoms and signs at multiple levels of the neuraxis. The meningeal involvement can be classified into lesions of the cerebral hemispheres (present in 15% of patients), lesions of the spinal medulla (60%), and lesions of cranial nerves (35%) [2]. Cancer cells reach the meninges by various routes: (1) hematogenous spread (2) direct extension from contiguous tumor deposits and (3) through centripetal migration from systemic tumors along perineural or perivascular spaces [6, 7, 8].

The most useful laboratory test in the diagnosis of NM is the CSF analysis. CSF abnormalities include increased opening pressure (>200 mm of H₂O), increased leukocytes (> 4 cells per μ L), elevated protein (> 0.5 g/L), or decreased glucose (< 3.33 mmol/L), which though suggestive of NM are not diagnostic [9]. Wasserstrom et al. reported that the first CSF sampling has relatively low diagnostic sensitivity of 54%, with repeated sampling this ratio increases up to 91% [10]. Experts noted that in the presence of spinal signs or symptoms, the lumbar CSF was more likely to be positive and conversely, in the presence of cranial signs or symptoms, the ventricular CSF was more likely to be positive [11]. Median survival in untreated patients is four to six weeks, which may be extended up to six months with aggressive treatment [12, 13].

Our case is interesting as it reports a patient of mucin secreting signet ring cell adenocarcinoma caecum with neuroendocrine differentiation which progressed to carcinomatous meningitis within five months after curative resection while the patient was on adjuvant chemotherapy. The rapid progression of disease in this patient could be due to the presence of signet ring cells and associated neuroendocrine component in the primary tumor. Though the prognostic significance of focal neuroendocrine differentiation is unclear, most data indicate that extensive neuroendocrine differentiation is associated with a worse prognosis [14,15]. Signet ring carcinomas are characterized by cells demonstrating the "signet ring" morphology in which intracellular mucin accumulation displaces the nuclei

fraction), intravenous dexamethasone (0.4 mg/kg/day), 20% intravenous mannitol, intrathecal methotrexate (12 mg) and other supportive measures. Patient condition continued to deteriorate while on WBRT and she succumbed to her disease after receiving seven fractions of WBRT.

and cytoplasm toward the cellular periphery. This histology carries an adverse prognosis [16].

To our knowledge only one case has been reported by Chadda et al, with the diagnosis of CM from signet ring adenocarcinoma caecum which was not associated with neuroendocrine differentiation [17].

CONCLUSION

We report a rare case of adenocarcinoma caecum with carcinomatous meningitis. In a patient with a known primary malignancy presenting with symptoms and/or signs of meningeal irritation, it is important to consider carcinomatous meningitis in the differential diagnosis. Early diagnosis and aggressive treatment forms the corner stone in the management of this condition. Treatment options are limited and this condition carries very poor prognosis. The goal of therapy in CM is essentially palliative and not cure.

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