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A Case of Mucinous Signet-ring Colorectal Adenocarcinoma with Leptomeningeal Carcinomatosis: A Diagnostic Challenge

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Abstract

Mucinous adenocarcinoma is a colorectal cancer typified by excessive mucin production and often aggressive disease course. Leptomeningeal involvement is an exceedingly rare complication which is difficult to both diagnose and treat thereby conferring an adverse prognosis. This report highlights a case of mucinous signet-ring adenocarcinoma presenting with isolated leptomeningeal carcinomatosis affecting a 50 year-old male in a regional hospital setting with an emphasis on diagnostic challenges and considerations.

Keywords: Colorectal cancer; Mucinous signet-ring adenocarcinoma; Leptomeningeal carcinomatosis; Regional healthcare

Introduction

Mucinous adenocarcinoma is a subtype of colorectal malignancy characterised by increased extracellular mucin secretion. Mucin is a glycoprotein normally expressed by colorectal mucosa which plays an important physiological role in lubrication, immune defence and wound healing [1]. In the setting of cancer, mucin is upregulated, providing neoplastic cells with growth acceleration and a survival advantage; the expression of signet cells meanwhile constitutes a phenotype with heightened tendency for metastases [2]. This report describes a rare case of mucinous signet-ring adenocarcinoma presenting with progressive neurological sequalae due to leptomeningeal carcinomatosis and highlights important challenges impacting early recognition and diagnosis.

Case Presentation

A 50-year-old Caucasian male presented to a regional hospital emergency department with six days of progressive frontal and occipital headache associated with blurred vision, pre-syncope and neck pain. These symptoms occurred after a football-match tackle that resulted in a minor head injury. His medical background was significant for well-controlled asthma managed with fluticasone/salmeterol inhaler and alcohol misuse consuming six to eight standard drinks per day for several years. He reported nil known drug allergies, did not smoke and was employed as a cleaner in hospitality. There was no significant family history.

On presentation, neurological examination and non-contrast head computed tomography (CT) did not reveal any abnormalities. As such, his presentation was attributed to a minor concussive injury. He received simple analgesia and was discharged with instructions for representation in the event of worsening symptoms. Three days later he returned with nausea, vomiting and amnesia. Neurological examination did not reveal any focal abnormalities and repeat head CT was again normal (Figure 1). After 24 hours of observation in the emergency department, he was once again discharged. He presented for a third time two days later, following an unwitnessed tonic-clonic seizure and was admitted to the internal medicine unit.

On neurological examination, he was restless and anxious and exhibited an intention tremor. Laboratory investigations demonstrated lymphopenia (0.6 x 10^9/L), mild liver derangement (ALT 100U/L, ALP 183U/L, GGT 195 U/L), elevated C-reactive protein (152 mg/L) and lactate dehydrogenase (351 U/L). His venous blood gas, renal function and electrolytes were all within normal range.

A stroke-protocol contrast CT angiogram was then performed which revealed extensive mediastinal and right-sided supraclavicular lymphadenopathy, although without any intracranial lesions. Brain magnetic resonance imaging (MRI) was then undertaken and demonstrated extensive leptomeningeal enhancement overlying his bilateral cerebral hemispheres, left occipital lobe and cerebellum as shown in Figure 2. Given suspicion for malignancy, CT abdominopelvic staging was completed which demonstrated bulky intrabdominal lymphadenopathy surrounding the coeliac trunk and porta hepatis.

In consultation with neurology and neurosurgical tertiary teams, a lumbar puncture was performed which demonstrated highly atypical malignant cells and oligoclonal protein bands in the cerebrospinal fluid (CSF). Gram stain and culture were negative for microorganisms, whilst CSF glucose, protein, lactate dehydrogenase (LDH) and flow cytometry were also normal. CSF paraneoplastic and autoimmune encephalitis antibodies were not detected. Our patient was transferred to a tertiary hospital to facilitate further evaluation and management. Following transfer, positron emission tomography (PET/CT) was undertaken which demonstrated caecal and ascending colon avidity and diffuse adenopathy suggesting colorectal cancer (Figure 3). A colonoscopy was subsequently performed however, interestingly, did not identify any overt masses; gastroscopy was also unremarkable.

A right supraclavicular lymph node core biopsy was then undertaken which confirmed metastatic mucinous signet-ring adenocarcinoma as depicted in Figure 4. Immunohistochemistry stained positive for CDX2 and CK20 supporting colorectal origin (Figure 5). Conversely, CK7 and TTF1 were negative excluding a primary pulmonary tumour.

Despite planned palliative cranial radiotherapy for leptomeningeal carcinomatosis, our patient rapidly declined after a further tonic-clonic seizure, culminating in dysarthria and hemi-facial paralysis. He was therefore transitioned to best supportive care and died one month following his index presentation.

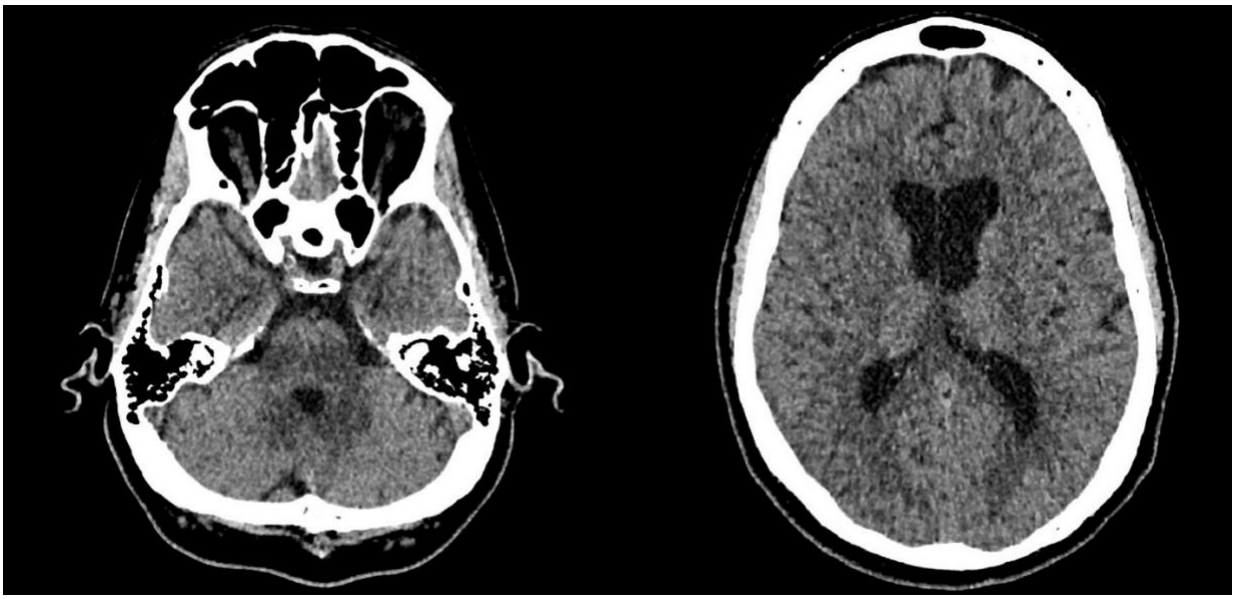

Figure 1: Non-contrast CT brain demonstrating normal anatomy.

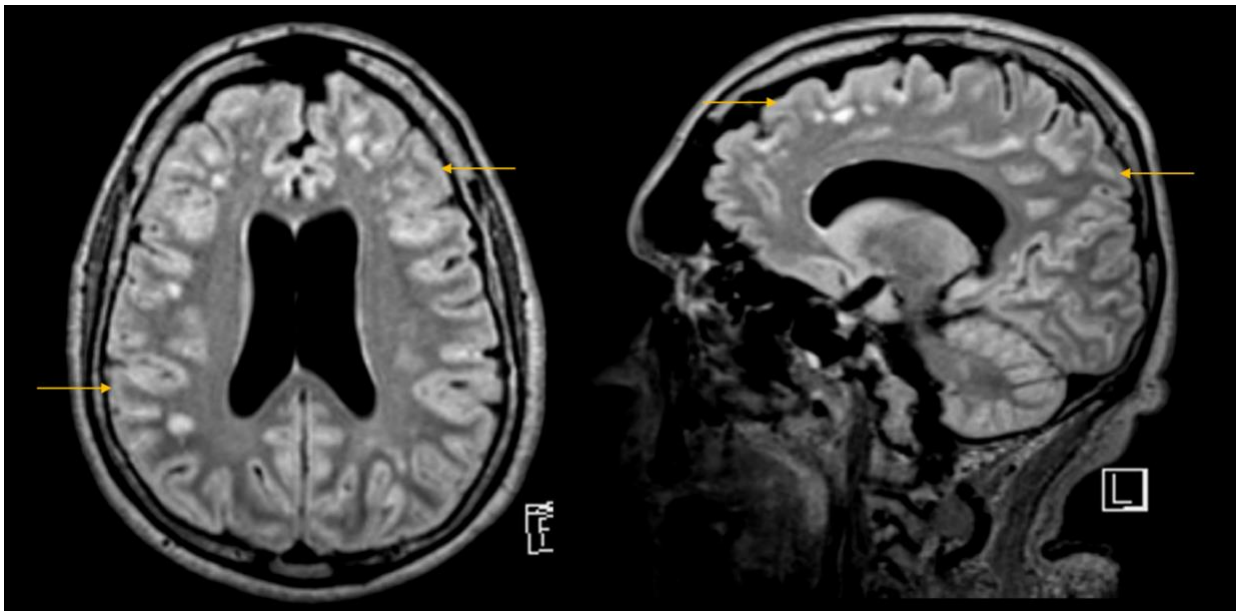

Figure 2: MRI FLAIR of brain in axial and sagittal views showing extensive gyriform/serpiginous leptomeningeal enhancement overlying bilateral cerebral hemispheres with associated FLAIR hyperintensity (arrows).

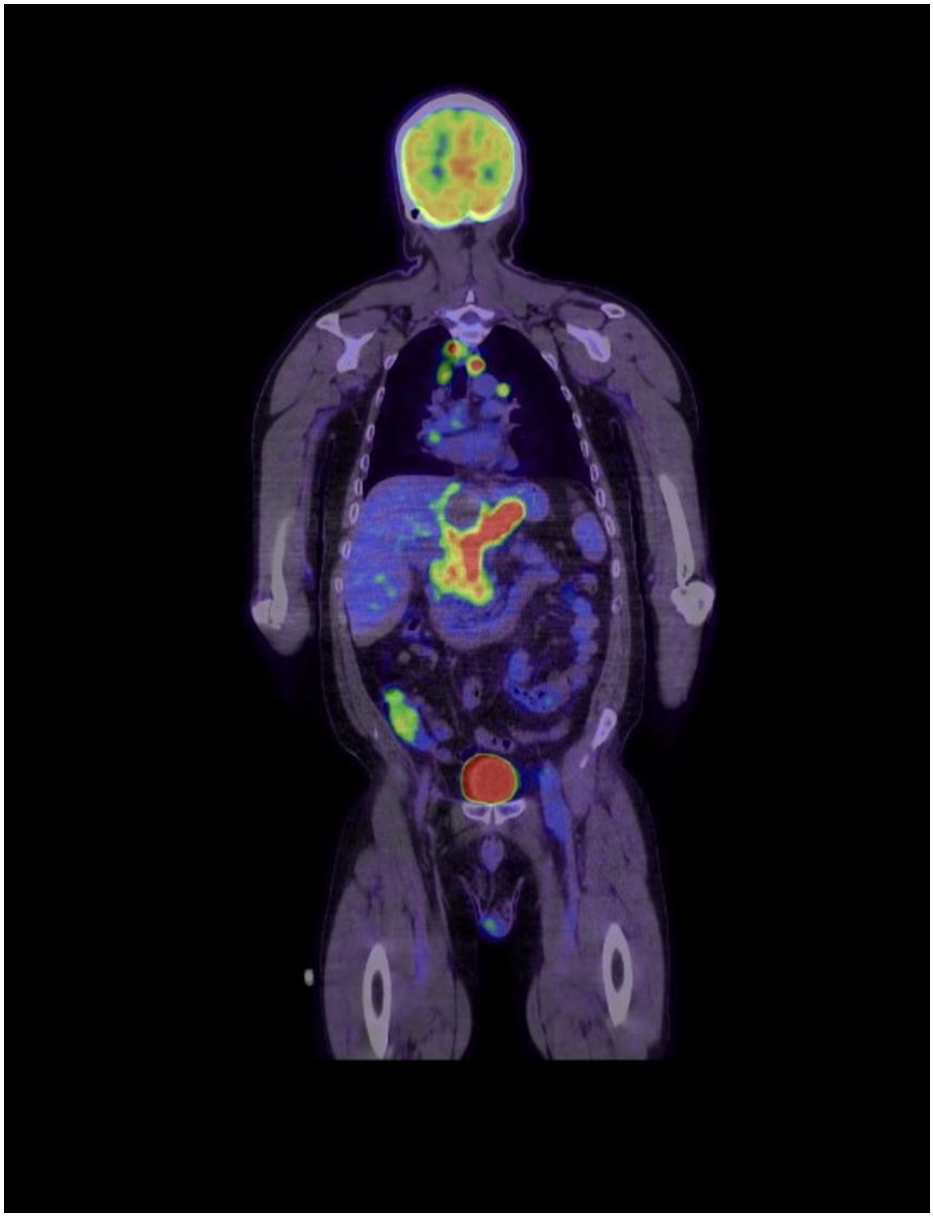

Figure 3: Fluorodeoxyglucose (FDG) PET/CT imagining showing paraoesophageal, subcarinal, portacaval and caecum/ascending colon avidity on coronal section.

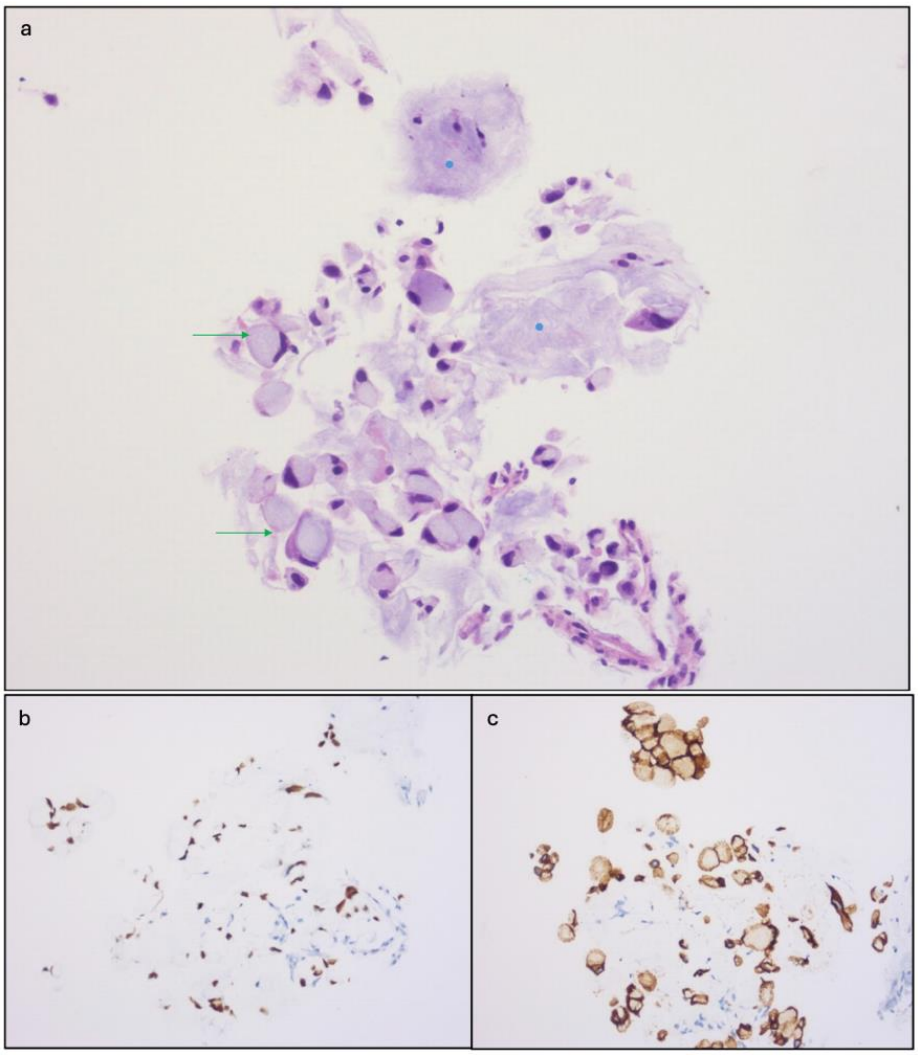

Figure 4 (a): Core biopsy of supraclavicular nodal metastasis: Hematoxylin and Eosin stain demonstrating signet-ring cells (arrows) within a mucin pool (dots);
(b): Immunohistochemistry showing positive nuclear CDX2 staining;
(c): Immunohistochemistry showing positive nuclear CK20 staining.

Discussion

Mucinous adenocarcinoma is a subtype of colorectal cancer accounting for approximately 9% of total cases [2]. According to the World Health Organization, mucinous adenocarcinoma is defined by the presence of more than 50% extracellular mucin, while signet-ring adenocarcinoma is characterized by more than 50% signet-ring cells [3]. Tumours with less than 50% of either are described as having a component of mucinous or signet-ring adenocarcinoma, respectively.

Literature to date suggests mucinous signet-ring colorectal carcinomas represent a highly metastatic phenotype [2] which is less responsive to systemic chemotherapy [4] and associated with worse prognosis relative to nonvariant adenocarcinomas [5]. To illustrate, Li et al reported a 5-year overall survival of 51% versus 59% for mucinous adenocarcinoma and non-mucinous adenocarcinomas respectively [6].

Regarding metastases, mucinous adenocarcinomas have a predilection for the peritoneum, liver and thorax in descending order of frequency which likely relates to tumorigenic factors within successive draining vascular beds. Leptomeningeal carcinomatosis is an exceedingly rare occurrence arising in <0.1% of all colorectal cancer presentations across a large retrospective study [7].

With respect to our patient, an expediated diagnosis was complicated by several key factors. Firstly, a preceding traumatic event offered a more likely diagnosis of minor concussive injury which was also consistent with his clinical presentation and neuroimaging [8,9]. The lack of substantiative medical history, examination and biochemistry at initial presentation did not necessitate further investigation. Lastly, limited on-site staffing, expertise, availability and access to equipment such as MRI may have hindered efforts for earlier or more intensive investigation: the disparities between metropolitan versus regional healthcare access in Australia is well known [10].

Conclusion

In summary, this report describes an unusual case of metastatic mucinous signet-ring adenocarcinoma presenting with isolated leptomeningeal symptoms. The importance of careful re-evaluation without premature closure of differentials is emphasised particular in regional settings which may confer additional diagnostic challenges beyond clinicopathological complexity.

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