ABSTRACT
Carcinomatous meningitis is a rare manifestation of malignancy. It is increasingly being recognized in lung carcinoma, breast carcinoma, melanomas, gastrointestinal malignancies, lymphomas, and leukemia and it is almost never seen in gallbladder malignancies. We present a case whose primary presentation was as a carcinomatous meningitis that was subsequently found to be secondary to a gallbladder primary.

Key words: Gallbladder carcinoma; leptomeningeal spread; signet ring cells

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Introduction

Carcinomatous meningitis is an uncommon manifestation of malignancy occurring in about 5% of all malignancies.\(^1\) In its pure form, meningeal carcinomatosis without brain metastasis is even less frequent. The common sites of the primary tumor are the breast, lung, ovary, melanoma, lymphoma, and leukemia.\(^2\) In this case report, we present a patient with carcinomatous meningitis secondary to a gallbladder malignancy. This is a rare presentation of gallbladder malignancy and only few cases have been reported worldwide till date.\(^3\)

Case Report

A 55-year-old manual laborer came to our emergency department with a 15-day history of new onset severe holocranial headache that was worse early morning; He did not have a past history of headaches. The headache had worsened and increased in intensity over the past few hours. It was associated with several episodes of vomiting and blurring of vision since day 1. He complained of diplopia on looking to the right. Prior to this, he had been in good health and had been able to work well. He had no known comorbidities. Other than a 6\(^{th}\) nerve palsy on the right side, there was no apparent abnormality on general physical examination.

From the history and examination, it was clear that there was raised intracranial pressure, the etiology was not certain. Differentials considered at the time were tuberculous or fungal meningitis, carcinomatous meningitis, a space-occupying lesion in the brain. Magnetic resonance imaging (MRI) of the brain was done, which was reported as normal aside from raised intracranial tension. Lumbar puncture was clearly contraindicated.

Meanwhile, the patient’s neurological symptoms worsened; he developed a VII nerve lower motor neuron palsy and started becoming drowsy. He was started on intravenous Mannitol, hypertonic saline, and dexamethasone. With best possible medical therapy for raised intracranial pressure, his headache persisted and Cushing reflex was present. A neurosurgical consultation was sought and an emergency external ventricular drainage was performed. The patient had significant relief of his headache with the procedure. Cerebrospinal fluid (CSF) from the external ventricular drainage under sterile precautions was sent for biochemical, microbiological, and pathological analysis [Table 1].

Cytospin smears of CSF were paucicellular and showed few atypical cells scattered singly and in clusters with eccentrically placed nuclei, granular chromatin, occasional with prominent nucleoli and vacuolated cytoplasm containing mucin, some resembling signet ring cells [Figure 1]. CSF tumor markers showed cancer antigen (CA)-19-9 to be very high. Carcinoembryonic antigen (CEA) in the CSF was elevated as well. Because these are quite specific for intra-abdominal malignancy, computed tomogram (CT) of the abdomen [Figure 2] done at this time revealed a primary gallbladder malignancy infiltrating the surrounding liver. An ultrasound-guided fine-needle aspiration (FNA) smears from the gallbladder [Figure 3] showed cellular smears with cohesive clusters, few acinar structures, and few irregular monolayered sheets of polygonal cells with moderate anisokaryosis, occasional prominent nucleoli, and moderate amounts of eosinophilic-to-vacuolated cytoplasm. The background contained necrotic debris and mononuclear inflammatory cells. The patient was offered chemotherapy and radiotherapy. A ventriculoperitoneal shunt (VP) was inserted for relief of raised intracranial pressure. The patient opted for palliative therapy.

Discussion

This case has many unusual features. The first being that gallbladder carcinoma rarely metastasizes to the brain or...
leptomeninges.[8] Second, that this was the first presentation of malignancy in this individual. There were no local complaints or clinical signs of the same. To date, there are only a handful of cases of gallbladder carcinoma having leptomeningeal spread and only two other cases where meningeal carcinomatosis was the primary manifestation.[9]

Gallbladder carcinoma is a silent malignancy and it is often an incidental finding during gallbladder surgery. It may present with clinical features of chronic cholecystitis, significant weight loss, and chronic pain in the right hypochondrium.[6] It may occur in the setting of gall stones, but very few patients with stones develop gallbladder carcinoma (<0.2%). Usual sites of metastasis are local lymphatics and nearby organs such as the liver. The leptomeninges are almost never involved.[7]

Carcinomatous meningitis is seen in about 5% of patients with the metastatic malignancy. Incidence is higher in autopsy studies. The tumors usually associated with carcinomatous meningitis are breast carcinoma, lung carcinoma, melanomas, lymphomas, and leukemia. The pathways of spread are controversial. Most commonly it is thought to occur due to vascular spread; arterial or venous—from Batson plexus or choroid plexus a spread can occur via lymphatics from perineural or perivascular lymphatics. Another source of spread would be a contiguous spread from bone or brain metastasis.[8]

Tumor markers such as CEA are of limited value in serum samples because they have a low sensitivity and additionally are found to be increased in a variety of benign diseases as well. There are few ways in which CEA reaches the CSF. One is from tumor cells within the leptomeninges that produce CEA. The other is from the bloodstream. For the CEA in the blood to reach the meninges, the ratio of CEA in the blood to that in the CSF has to be greater than the ratio of 60:1.[9] Ratios that are less than this imply that the production is from the CSF. A high CSF CEA has a high specificity for leptomeningeal metastasis, that is, sensitivity of 31% but specificity of 90%.[10] Our patient had elevated CSF tumor markers that helped in localizing the malignancy to the gastrointestinal tract. Hence, CSF tumors markers in the appropriate setting can help in identifying the primary in carcinomatous meningitis.

Diagnosis of carcinomatous meningitis usually requires serial cytologies from the CSF. Single cytology has a sensitivity of only 54%. Sensitivity increases to 85% with three tests.[11] The commonest malignancy isolated from the CSF cytology is usually an adenocarcinoma. Among carcinomas, signet ring cell type of carcinomas are more likely to metastasize to the leptomeninges than other cell types.[12]

Treatment options, though available, are of limited benefit. Therapeutic options available are local radiation and intrathecal chemotherapy with an Ommaya reservoir. Even with best possible treatment, survival is only for a range of 3-4 months after diagnosis. Our patient underwent a VP shunt insertion and then decided to go home. He was offered chemotherapy and radiation, which he refused.

Conclusion

Leptomeningeal spread is a rare presentation of gallbladder carcinoma. Carcinomas with signet ring type of morphology have a greater tendency to metastasize to the CSF as compared to other malignancies. CSF tumor markers, in the right setting, may offer value in locating the site of the primary.

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Conflicts of interest
There are no conflicts of interest.

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