Case Report

Supratentorial metastatic enteropathy-associated T-cell lymphoma: A case report and literature review

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Abstract

Background: We are describing a rare case of supratentorial metastatic enteropathy-associated T-cell lymphoma (EATL). While these lesions are a rare complication of EATL, the implications are grave and they must be evaluated as a diagnostic possibility when a patient with known celiac disease presents with acute neurological deterioration. In addition, multidisciplinary care teams are recommended by the authors as critical to providing the most comprehensive patient care.

Case Description: A 65-year-old female presented to the emergency room with uncontrolled abdominal pain, nausea, and vomiting. Initial abdominal computed tomography (CT) scan indicated a small bowel obstruction with a transition point at the jejunal area. Differential diagnosis included small bowel neoplasm, adhesions, or a reactive intestinal inflammatory process. Shortly after presentation, the patient’s clinical condition worsened, requiring emergency small bowel resection. Histological analysis of the resected bowel segments demonstrated medium-sized infiltrating lymphocytes with characteristic pleomorphic nuclei and prominent nucleoli. Immunohistochemical stains revealed tumor cells positive for CD-3. Immunohistochemical analysis for Ki-67 showed a markedly increased proliferative index, with 90% of lymphocytes staining positive. Polymerase chain reaction analysis for T-cell receptor-gamma gene rearrangement was positive, demonstrating the presence of a clonal population of T-cells. The combined morphological and immunophenotypic features of this lesion were consistent with jejunal EATL.

Five weeks post-diagnosis, she developed new onset neurological symptoms consisting of changes in her mental status and left facio-brachial weakness. Brain magnetic resonance imaging (MRI) demonstrated a single ill-defined, irregular, right fronto-parietal enhancing lesion surrounded by vasogenic edema. Surgical resection and histopathologic evaluation of the biopsied lesion confirmed the diagnosis of metastatic EATL involving the brain.

Conclusion: Intracranial metastasis is a rare but grave complication of EATL and must be evaluated as a diagnostic possibility when a patient with known celiac disease presents with acute neurological deterioration. Although the prognosis of these patients is dismal, aggressive oncology management is mandatory.

Key Words: Associated T-cell lymphoma, supratentorial metastatic enteropathy, brain metastasis, T-cell enteropathy
INTRODUCTION

Though intracranial spread of enteropathy-associated T-cell lymphoma (EATL) is very rare, in the presence of confirmed non-granulomatous ulcerative jejunoileitis, progressive neurological deterioration preceded by a clinical history of diarrhea, weight loss, nausea, and vomiting may raise the possibility of metastatic EATL.[2-4,6-8] However, physicians must be aware of the possibility that neurological symptoms may be masqueraded or delayed by the concomitant use of steroids, which are frequently used for the management of celiac and inflammatory bowel disease.

CASE REPORT

A 65-year-old female presented to the emergency room with uncontrolled abdominal pain, nausea, and vomiting. Medical history was significant for Type 2 diabetes mellitus, previous intestinal intussusceptions, and moderate abdominal pain. Initial abdominal CT scan indicated a small bowel obstruction with a transition point at the jejunal area [Figure 1]. Related to this finding were mildly enlarged lymph nodes in the right pelvic region. Differential diagnosis included small bowel neoplasm, adhesions, or a reactive intestinal inflammatory process.

Shortly after presentation, the patient’s clinical condition worsened, requiring emergency small bowel resection. Histological analysis of the resected bowel segments demonstrated small intestinal mucosa with intraepithelial and mucosal infiltrates of benign CD3 (+) T-cells, consistent with celiac sprue. Also found were medium-sized infiltrating lymphocytes with characteristic pleomorphic nuclei and prominent nucleoli. Immunohistochemical stains revealed tumor cells positive for CD3, weakly positive for BCL-2, and negative for CD5, CD20, CD10 and cyclin-D1. Immunohistochemical analysis for Ki-67 showed a markedly increased proliferative index, with 90% of lymphocytes staining positive [Figure 2]. Polymerase chain reaction analysis for T-cell receptor-gamma gene rearrangement was positive, demonstrating the presence of a clonal population of T-cells. The combined morphological and immunophenotypic features of this lesion were consistent with jejunal EATL. Further systemic investigations were all non-contributory. The patient was discharged and the recommended treatment for her primary condition was chemotherapy.

Three weeks post-diagnosis, the patient received a positron emission tomography CT scan from her skull to mid-thigh, which indicated no hypermetabolic lesions suggestive of active malignancy in the skull base or neck. However, five weeks post-diagnosis, she developed new onset neurological symptoms consisting of changes in her mental status and left facio-brachial weakness. Brain MRI demonstrated a single ill-defined, irregular, right fronto-parietal enhancing lesion surrounded by vasogenic edema, with associated mass effect and midline shift [Figure 3]. She underwent surgical resection of the intracranial lesion, and post-operative MRI demonstrated the resection of the right frontoparietal mass with small air fluid level and residual blood product seen at the tumor bed [Figure 4]. Histopathologic evaluation of the lesion biopsy confirmed the diagnosis of metastatic EATL involving the brain [Figure 5].

DISCUSSION

EATL typically presents as an extranodal intestinal illness linked to chronic celiac disease.[3,7,8] Recent research

Figure 1: Initial abdominal computed tomography (CT) scan sagittal (a, b, c) and axial (d) views demonstrating dilated stomach, proximal and mid small bowel segments, with a transition point at the jejunal area in the left lower quadrant, consistent with mechanical small bowel obstruction

Figure 2: (a-d) Immunohistochemical analysis of malignant lymphoma infiltrating mucosa and submucosa of small intestine. The Ki-67 showed a markedly increased proliferative index, with 90% of lymphocytes staining positive
findings based on gene analysis studies have suggested that there may be two distinct subtypes of EATL. Type I accounts for 80 to 90 percent of cases, and is strongly associated with celiac disease. Tumor cells are of variable size and morphology, and the adjacent “normal” mucosa may or may not demonstrate signs of celiac disease. The tumor cells typically express CD3 (pan T-cell marker) and CD56, and they do not express CD8. Our patient likely falls within this subtype, since medium-to-large size lymphocytes were found infiltrating the bowel segment radially with no proximal or distal involvement.

Type II, also known as “monomorphic” EATL, accounts for 10 to 20 percent of cases and is less commonly associated with celiac disease. On histology, the tumor cells are monomorphic and small-to-medium in size with infiltration of the intestinal crypt epithelium. The adjacent “normal” mucosa demonstrates villous atrophy, crypt hyperplasia, and intraepithelial lymphocytosis. There is no inflammatory background. Tumor cells generally express CD8 and CD56.

Typical histopathological evaluation of EATL demonstrates areas of necrosis, with extensive infiltration of the small intestine by medium-sized lymphocytes with nuclear pleomorphism and prominent nucleoli. The neoplastic lymphocytes stain positively for CD45 (leukocyte common antigen), CD3, CD30, and TIA-1 (cytotoxic granule marker) and Ki-67. It is important to highlight that CD30 positivity may vary, and it is more frequently expressed in large T-cell lymphomas, rather than small-to-medium-sized lesions. Serum anti-gliadin antibodies are normally positive. Similar histological findings were reported in our patient. The small bowel surgical specimen contained areas of villous blunting and epithelial infiltration by lymphocytes, suggestive of celiac disease. Routine hematoxylin and eosin (H and E) stains demonstrated medium-sized and occasionally larger lymphocytes that infiltrated mucosa, submucosa, and muscular propria with extension into the mesenteric adipose tissue. There was focal involvement of the radial marginal, but proximal and distal bowel margins were negative for malignancy.

When EATL involves the brain, it may present as lymphomatous dissemination in the form of leptomeningeal seeding, or as a parenchymal lesion. In the event of parenchymal penetration, the supratentorial compartment is more frequently affected, possibly due to greater volume of brain tissue as compared to the infratentorial counterpart. There is only a single published case description of metastatic infratentorial EATL.

Differential diagnosis of acute neurological impairment associated with chronic celiac disease may include gluten ataxia and paracoplastic cerebellar syndrome. Ang et al.

Figure 3: (a) Positron emission tomography (PET)/CT scan from her skull to mid-thigh, which indicated no hypermetabolic lesions suggestive of active malignancy in the skull base or neck. (b and c) Brain magnetic resonance imaging (MRI) demonstrated a single ill-defined, irregular, right fronto-parietal enhancing lesion surrounded by vasogenic edema, with associated mass effect and midline shift.

Figure 4: (a, b) Post-operative MRI demonstrated the resection of the right frontoparietal mass with small air fluid level and residual blood product seen at the tumor bed.
reported a case of paraconplastic cerebellar degeneration caused by disseminated T-cell lymphoma. The associated histological hallmark of this disease consisted of positive oligoclonal bands on cerebrospinal fluid (CSF), and serum antibodies to cerebellar structures.[1]

The time period from primary intestinal manifestation to central nervous system (CNS) presentation varies, with several of the reported cases describing neurological symptoms within months after primary diagnosis.[2,4,6] Tutt et al. describe a patient with isolated CNS T-cell lymphoma developing after three years of celiac sprue. In their report, the diagnosis was confirmed during postmortem examination. However, failure to diagnose the primary condition during initial bowel biopsy was suggested by the authors.[8]

Radiological diagnosis is best accomplished by performing a T1-T2-weighted MRI, which demonstrates two characteristic patents, a diffuse high intensity signal along the CSF spaces, as in the case of leptomeningeal seeding, or a localized, ill-defined, irregular, enhancing mass lesion illustrating the parenchyma penetration.[2,4,6]

Neurosurgical indications for removal of isolated symptomatic lesions are similar to other type of intracranial metastasis. Post-surgically, the best treatment options are chemotherapy, followed with cranio-spinal axis irradiation for cases where lymphomatous seeding is established.[2,4,6] Based on previous reports, the prognosis and outcome for intracranial metastatic EATL seems to be reserved, with a very hostile clinical course despite aggressive surgical and medical managements.[2,4,6,8]

Finally, the authors are in the agreement that the initial oncological treatment in our case report was suboptimal. The primary focus of our report was to describe a very rare form of intracranial metastatic lesion. Commenting on current medico-oncological guidelines, management of patients with AETL is out of scope of this description.

**CONCLUSION**

Intracranial metastasis is a rare but grave complication of EATL and must be evaluated as a diagnostic possibility when a patient with known celiac disease presents with acute neurological deterioration. When intracranial EATL metastases are present, we suggest that the most comprehensive patient care is achieved when a multidisciplinary team, including oncologists, neurologists, neurovascular surgeons and pathologists, collaboratively manage the patient’s clinical course.

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