Small Cell Neuroendocrine Carcinoma of Rectum with Associated Paraneoplastic Syndrome: A Case Report

Jeannette A. Vergelí-Rojas, MD*; Dania L. Santiago-Caraballo, MD†; William Cáceres-Perkins, MD†; Priscilla Magno-Pagatzartundua, MD*; Doris H. Toro, MD*

Neuroendocrine carcinomas of the colon and rectum comprise fewer than 1% of all colorectal cancers. These aggressive tumors generally have a poor prognosis compared to that associated with colorectal adenocarcinoma. We describe herein the case of a 68-year-old female presenting with a bleeding rectal mass involving the anal canal, which case was associated with hyponatremia due to inappropriate serum levels of antidiuretic hormone. The histopathological examination was consistent with a small-cell neuroendocrine tumor. She was treated with combination chemotherapy and radiation therapy. The Syndrome of Inappropriate Antiuretic Hormone (SIADH) was managed with vasopressin antagonists. After the completion of therapy, endoscopic ultrasound revealed evidence of residual disease, for which she underwent an abdominoperineal resection (APR). The patient died 4 months later of disease progression. To our knowledge, this is the first report of a small-cell neuroendocrine tumor involving the rectum and anal canal that presented with the paraneoplastic syndrome, SIADH.

Key words: Small-cell carcinoma, Anorectum, SIADH

Colorectal small-cell neuroendocrine carcinoma (SCNC) is a rare tumor representing fewer than 1% of all colon malignancies (1). This tumor is thought to be derived from a proliferation of pluripotent neuroendocrine stem cells, although its etiological factors are still unknown (2). These cells commonly arise in the upper respiratory tract and lungs, although other extrapulmonary sites may include any of the following: the skin, thymus, kidneys, breasts, ovaries, uterus, bladder, hepatobiliary tree, pancreas, and salivary glands (3). The differential diagnosis of colorectal SCNC includes metastatic lung small-cell carcinoma or other more common neuroendocrine tumors such as carcinoid. Paraneoplastic syndrome has been most frequently associated with small-cell carcinoma of the lungs and only a few cases associated with small-cell carcinoma of the rectum have been reported in the literature (4). Herein we present a case of a anorectal small-cell neuroendocrine tumor complicated by paraneoplastic syndrome.

Case Report

A 68-year-old Puerto Rican female patient with a 4-week history of rectal bleeding was referred for evaluation. This was not the first time that the patient had experience this complaint; eleven years prior to our evaluation, a colonoscopy showed three subcentimeter adenomatous polyps in the rectosigmoid colon. The bleeding associated with that particular occurrence ceased, and surveillance colonoscopies during the following nine years continued to detect diminutive tubular adenomatous polyps in the rectosigmoid colon. Family history was relevant for colon adenocarcinoma, with a first degree relative diagnosed at age 80.

When first evaluated in the Medical Intensive Care Unit at the Veterans Affairs Caribbean Healthcare System, the patient presented bowel movements with red blood streaks that progressed to hematochezia. All other warning signs, such as weight loss and pencil-like stools, were claimed not to have been present. The patient’s physical examination was remarkable for diffuse abdominal tenderness, predominantly in both lower quadrants, on superficial palpation. Large and severely painful internal hemorrhoids were palpated during the rectal examination. A complete blood count reported a hemoglobin level of 12.1 mg/dL, and the serum chemistries were remarkable for hyponatremia (124 mEq/L). An abdominal CT scan showed an abnormal soft tissue mass in the rectosigmoid colon and pararectal subcentimeter lymphadenopathies. A colonoscopy revealed a large exophytic, 

*Department of Gastroenterology, Veterans Affairs Caribbean Healthcare System, San Juan, Puerto Rico; †Department of Hematology and Oncology, Veterans Affairs Caribbean Healthcare System, San Juan, Puerto Rico

The authors have no conflict of interest to disclose.

Address correspondence to: Doris H. Toro, MD, Veterans Affairs Caribbean Healthcare System, 10 Casia St., San Juan, PR 00921. Email: Doris.Toro@va.gov
friable, and ulcerated mass in the rectum and anal canal (Figure 1). Biopsies were consistent with rectal small-cell carcinoma characterized as a poorly differentiated neuroendocrine neoplasm (Figure 2). Immunohistochemical staining of the tumor was positive for neuron-specific enolase (NSE) and pancytokeratin AE1/AE3. Also, expressions of chromogranin and occasional B and T cells highlighted by CD20 and CD3 found in the tumor confirmed it to be neuroendocrine in origin. Further imaging studies showed localized tumor disease without metastasis (T3N0Mx).

The patient was treated with three cycles of combined chemotherapy with etoposide and cisplatin and a concurrent radiotherapy dose of 3960cGy. Three months after the completion of the treatment, a reevaluation of the disease with endoscopic ultrasound showed an ulcer within the anal canal extending 1 cm above the dentate line. The submucosal layer of the upper anal canal appeared thickened and hypoechoic without involvement of the muscle layers or rectal walls (Figure 3). Biopsies confirmed a residual tumor and proliferation of disease within the muscularis propria. Subsequently, the patient underwent an abdominoperineal resection (APR). The total size of the specimen was 6 cm x 1 cm; it was a brownish indurated lesion in the anal canal. Microscopic examination confirmed the existence of an infiltrative tumor disease extending into the muscle layers in the anal canal and involving the anorectal junction. Following surgery, the patient suffered from a severe intra-abdominal infection and persistent hyponatremia. A follow-up abdominal CT scan showed metastatic liver disease and diffuse abdominal adenopathies. Eventually, the clinical status deteriorated and she died four months later.

The patient continued to exhibit asymptomatic hyponatremia despite serum sodium levels being from 124-117 mEq/L. Syndrome of Inappropriate Antidiuretic Hormone (SIADH), a paraneoplastic syndrome related to small-cell carcinoma, was diagnosed, and therapy with tolvaptan was established.

**Discussion**

SCNC has a poor prognosis, even in the early stages of the disease, with frequent regional and liver metastasis identified on presentation. A 5-year survival rate for about 6% evidences the aggressive behavior of this tumor (5, 6). The incidence of SCNC is fewer than 1% of the malignancies of the GI tract, and the esophagus is the most commonly involved site, followed by the rectum and cecum (7). SCNC involving the rectum has been frequently associated, as in this case, with the occurrence of adenomatous polyps (5, 7).
Los carcinomas neuroendocrinos del colon y recto constituyen menos de 1% de todos los cánceres colohrectales. Estos tumores agresivos generalmente tienen un prognóstico peor comparado con el de adenocarcinoma colorrectal. Aquí describimos el caso de una fémina de 68 años de edad con una masa rectal sangrante que envolvía el canal anal, asociada a hiponatremia debido a niveles inapropiados de la hormona antidiurética. La evaluación, y tratamiento son necesarios debido a la agresividad de este tumor poco común.

**Referencias**