• CASE REPORT •

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

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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 Antidiuretic 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. [*P R Health Sci J 2013;1:51-53*]

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,

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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).

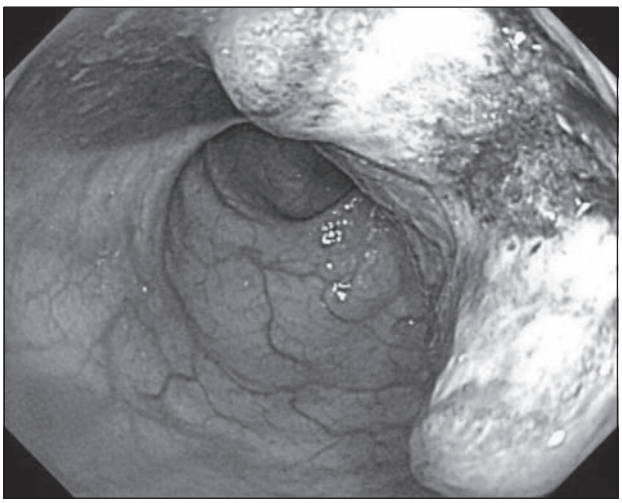

Figure 1. Endoscopic image of the anorectal lesion

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.

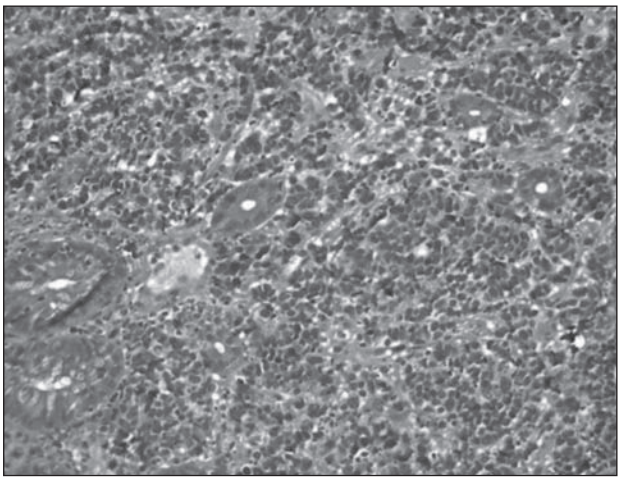

Figure 2. Hematoxylin and Eosin (H&E) showing undifferentiated neoplastic cells with nuclear molding invading between colorectal mucosa

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.

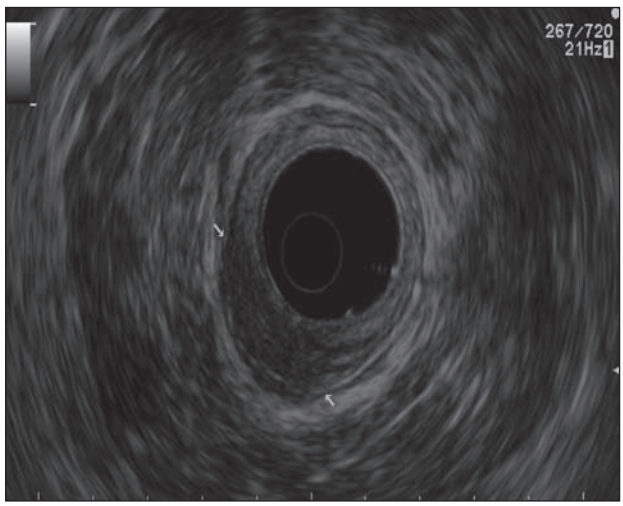

Figure 3. Endoscopic ultrasound showing hypoechoic and thickened submucosal layer in the upper anal canal

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).

The neuroendocrine nature of the tumor cells can be demonstrated immunohistochemically. Positive immunoreactivity to at least two markers is required for the diagnosis of a neuroendocrine carcinoma (8, 9). These tumors typically stain for synaptophysin, chromogranin, and NSE. Pathologic features include closely packed cells with scanty cytoplasm, nuclear pleomorphism, high mitotic rate, and necrosis (10).

Rarely, SCNC of the GI tract may secrete hormones such as vasoactive intestinal peptide, antidiuretic hormone, calcitonin, serotonin, adrenocorticotropic hormone, and parathyroid hormone-related protein (7, 9). SIADH was first described in patients with bronchogenic carcinoma, but it may occur in other malignant tumors and is caused by tumoral production of vasopressin. Our patient required treatment with a vasopressin antagonist to manage the hyponatremia. In most published cases, SIADH is related to SCNC of the lung, and only a few cases have been associated with SCNC of the esophagus and rectal adenocarcinoma (9).

Local control of SCNC of the rectum can be achieved with chemotherapy and radiation without the need for radical surgery (11). Combination chemotherapy of etoposide plus cisplatin has been reported to be effective in poorly differentiated neuroendocrine carcinomas (12), with a response rate of 41.5% and a median survival of 15 months (13). Surgical therapy is reserved for those cases in which the tumor is small and localized (14).

This case report highlights the importance of differentiating SCNC of rectum from adenocarcinoma. Our patient had a very aggressive SCNC tumor involving the rectum and anal canal, and the occurrence of SIADH made the diagnosis of SCNC of the GI tract less likely. Nevertheless, the association of a neuroendocrine tumor with a paraneoplastic syndrome may contribute to marked disease morbidity. Prompt recognition, evaluation, and treatment are needed due to the aggressiveness of this uncommon tumor.

Resumen

Los carcinomas neuroendocrinos del colon y recto constituyen menos de 1% de todos los cánceres colorrectales. 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 examinación histopatológica fue compatible con un tumor de células pequeñas neuroendocrinas. Se trató con una combinación de quimioterapia y radiación. El Síndrome Inapropiado de Hormona Antidiurética (SIHAD) fue tratado con antagonistas de vasopresina. Después de completer la terapia, hubo evidencia de enfermedad residual por ultrasonografía endoscópica, por lo cual se sometió a una resección abdominoperineal (RAP). La paciente murió 4 meses después debido a progresión de la enfermedad. A nuestro conocimiento éste es el primer caso de un tumor de células pequeñas neuroendocrinas con envolvimiento del recto y el canal anal que se presentó con un síndrome paraneoplásico, SIHAD.

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