Multiple myeloma presenting as CEA-producing rectal cancer

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Abstract

We report the case of a 57-year-old patient with multiple myeloma, characterized by extramedullary involvement of the rectum at presentation. Malignant plasma cells were found to produce carcinoembryonic antigen (CEA), a tumor antigen more commonly associated with rectal adenocarcinomas.

Introduction

Multiple myeloma (MM) is a rare tumor. It represents about 1% of all malignancies. Its common clinical manifestations are summarized by the acronym CRAB: hyperCalcemia, Renal insufficiency, Anemia, and Bone lesions.[1] The presence of extramedullary involvement in MM patients is a rare clinical manifestation, found in only 4.6% of cases. This event is usually associated with poor prognosis.[2] We previously published the largest series of MM involving the gastrointestinal (GI) tract, describing 24 cases of extramedullary involvement of the GI tract in a database of 2,584 MM patients. The rectum was the involved organ in only 2 of them.[3] Here we report a case of rectal involvement by MM in which the malignant plasma cells produced serum carcinoembryonic antigen (CEA), a tumor marker more commonly associated with rectal adenocarcinomas.

Case Report

A 57-year old Caucasian male with history of Crohn's disease was diagnosed with a rectal tumor. A surveillance colonoscopy found an ulcerated non-obstructing rectal mass, non-circumferential, 3 cm in length, with a macroscopic appearance of cancer (Figure 1).

Initially, the suspected diagnosis was rectal adenocarcinoma, not only because of the anatomical location, but also because the serum carcinoembryonic antigen (CEA) level was elevated at 10.5 ng/mL (normal, <3). Biopsy showed sheets of epithelioid cells with pleomorphic nuclei and prominent nucleoli (Figure 2).

At the immunostaining profile, cells were positive for CD138 and negative for CKAE1/3, CAM5.2, CK5/6, CK7, CK20, CD45, CD3, CD30, CD20, CD56, p63, PLAP, HMB45, S-100, synaptophysin, and chromogranin. Special stain for mucin was negative. The diagnosis of plasmacytoma was confirmed by chromogenic in situ hybridization (CISH), which showed monotypic plasma cells, positive for λ- and negative for κ-mRNA (Figure 3).

Laboratory tests provided the following results: serum immunofixation positive for monoclonal IgG-λ proteins, serum IgG 1,820 mg/dL (normal, 700-1600), M component 0.8 g/dL, serum free λlevel 3.23 mg/dL (normal, 0.57-2.63), urine proteins <100 mg over 24 hours, and β2-microglobulin 2.91 mg/L (normal, <2.5). Bone marrow biopsy showed only 2% plasma cells, polyclonal by flow cytometry. Multiple lytic bone lesions were evident at both skeletal survey and PET scan. Patient was started on corticosteroids and radiation therapy (RT), with the plan for further induction therapy and autologous stem cell transplantation. CEA normalized 2 months after the completion of RT.

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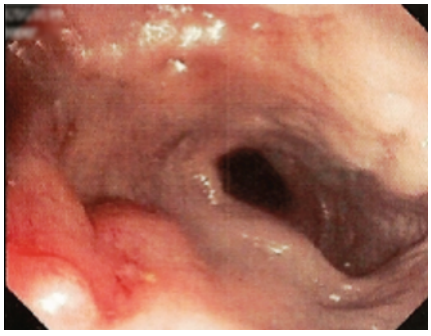

Figure 1. Gross appearance of the rectal tumor at colonoscopy.

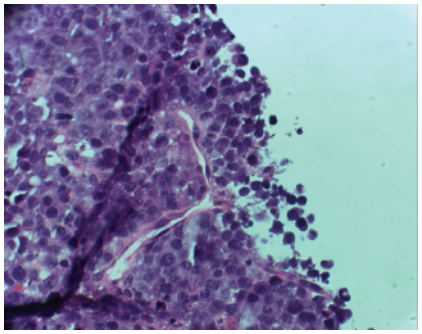

Figure 2. Histological section of the rectal tumor stained with hematoxylin and eosin.

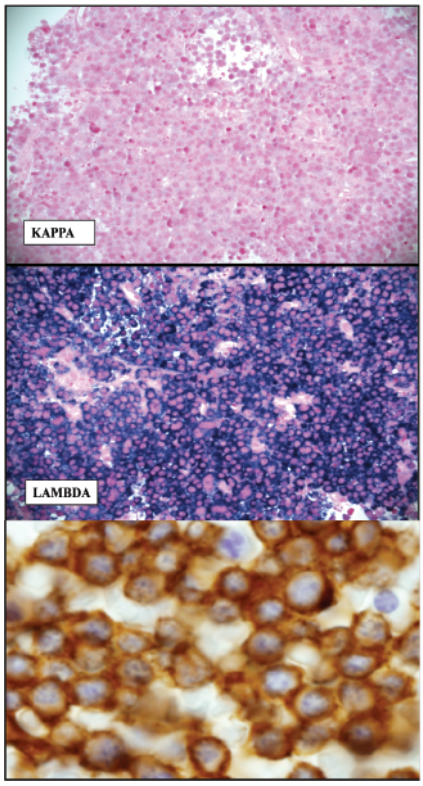

Figure 3. Chromogenic *in situ* hybridization of the tumor cells for κ- and λ-immunoglobulin light chains, and immunohistochemical staining for CEA.

Discussion

MM involving the GI tract should be distinguished from primary extramedullary plasmacytomas (PEMP), which are extraosseous tumors of monoclonal plasma cells without concomitant bone marrow infiltration. These are highly curable tumors, exquisitely sensitive to RT.[4] Our patient had extramedullary involvement of the rectum in the context of MM, an event seen in only 2 of 2,584 consecutive MM cases.[3]

The presence of Crohn's disease in our patient may be an unfortunate coincidence, but one can speculate that the chronic inflammation and immune stimulation produced by the Crohn's disease predisposed to the development of MM. Alternatively, MM could be related to the chronic immunosuppressive therapy used to control Crohn's disease in our patient, i.e., azathioprine. Whether coincidental or not, the association between inflammatory bowel disease and MM is rare: only 11 cases have been described in the medical literature since 1964.[5,6]

Another interesting aspect of our case was the elevation of the tumor marker CEA. Crohn's disease may occasionally raise CEA levels, but the immunohistochemical staining of the rectal plasmacytoma in our case suggests the direct production of CEA by the malignant plasma cells (Figure 3). CEA is one of the first known tumor antigens. It is a glycoprotein belonging to the immunoglobulin superfamily, and it is involved in cell-cell adhesion.[7] It is not a specific marker, as elevated values may be found in a wide range of neoplasms, including carcinomas of colon, rectum, stomach, pancreas, lung, and breast.[8] Although neoplastic plasma cells can frequently express other members of the CEA family, such as CEACAM1 (CD66a),[9] they usually do not produce CEA.[10,11] The first case of a MM patient with high serum levels of CEA was described by Kaito *et al.* in 2007.[12] To our knowledge, our case is the first reported instance of MM presenting with an extramedullary involvement of the rectum and associated with an elevated serum level of CEA. Our report illustrates the need for tissue biopsy and adequate pathology even in those cases that may be considered obvious by clinical oncologists. In fact, without the CISH studies, the presence of a rectal tumor associated with high CEA level could have been interpreted as adenocarcinoma, and patient could have received incorrect therapy.

We do not know the molecular mechanism that enables MM cells to produce CEA. Conventional cytogenetic analysis of plasma cells in our patient did not identify abnormalities at 19q13.2, the chromosomal region containing the *CEA* gene. It is possible that other cases of MM produce CEA, as this marker is not routinely measured in MM. We are currently screening our cases of MM and plasma cell leukemia for this tumor antigen, in order to estimate the actual frequency of CEA production among plasma cell neoplasms.

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