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Case report

Metastatic intestinal adenocarcinoma to a lymph node involved by follicular lymphoma: The importance of looking beyond the apparent

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ABSTRACT

Composite tumors consisting of follicular lymphoma (FL) and colorectal or small intestinal adenocarcinoma are exceedingly rare, with only four cases published in the literature, to the best of our knowledge. While in most of these cases the clinical prognosis seems to be determined by the adenocarcinoma, at least one patient has shown rapid and aggressive progression of the FL. Here we report on a 62 year-old male with colonic adenocarcinoma metastatic to a retroperitoneal lymph node involved by FL, which illustrates the importance of carefully examining the histomorphology of lymphoid elements in surgical specimens.

1. Introduction

Colorectal cancer is the third most common malignancy in men and second most common malignancy in women worldwide [1]. With regard to lymphoid neoplasms, follicular lymphoma (FL) is the second most common subtype of non-Hodgkin lymphoma, accounting for more than 31,000 newly diagnosed cases each year according to the Surveillance, Epidemiology, and End Results program of the National Cancer Institute (www.seer.cancer.gov).

While intestinal adenocarcinoma and FL are common neoplasms in and of themselves, composite lesions consisting of colon or small bowel adenocarcinoma and FL are exceedingly rare, with only a few cases documented in the literature. Since microscopic examination of lymph nodes resected as part of an oncologic surgery is often focused on the identification of metastases, there is a risk of overlooking an underlying lymphoid malignancy.

2. Case report

A 62-year-old male was evaluated at our institution for ileostomy reversal and drainage of intra-peritoneal abscesses. The patient had undergone an emergent right hemicolectomy for obstructive colon cancer in Mexico, 4 months prior to the current consultation. For this reason, we did not have access to the stage of the primary tumor. Chest and abdominal computed tomographic scans were performed, which demonstrated the presence of multiple fluid-filled intra-abdominal collections and several retroperitoneal lesions suspicious for lymphadenopathy, with no evidence of additional lymphadenopathies elsewhere. An exploratory laparotomy to drain the fluid collections, reverse the ileostomy and obtain lymph node tissue for histopathologic diagnosis was performed.

3. Pathologic findings

We received a 3.3 cm retroperitoneal lymph node with a firm consistency and a tan-yellow cut surface (Fig. 1). Microscopic examination revealed the presence of a focus of metastatic well-differentiated colonic adenocarcinoma (Fig. 2A). In addition, the background architecture of the residual lymph node tissue was completely effaced by multiple large pale nodules. Microscopically, these corresponded to transformed germinal centers that showed marked attenuation of the mantle zone, pronounced size variation, and a back-to-back arrangement with incipient fusion. Each individual nodule contained a predominant population of transformed centrocytes, while centroblast counts were consistently below 5 per high-power field (Fig. 2B). The B-cell nature

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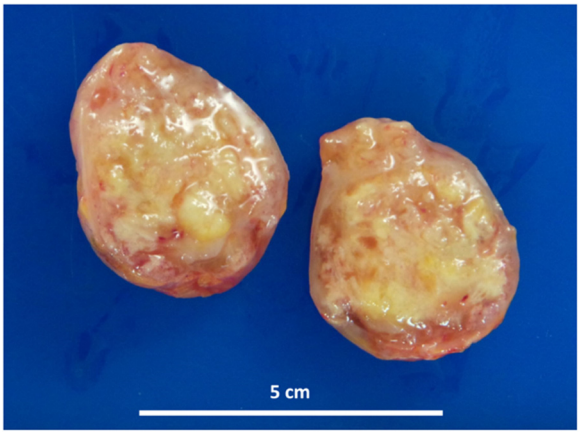

Fig. 1. Hemisection of the enlarged retroperitoneal lymph node shows a nodular, variegated tan-yellow cut surface.

of these cells was apparent by immunohistochemistry, which also revealed strong Bcl-2 expression in the transformed lymphocytes (Fig. 2C). Flow cytometry was non-diagnostic due to low cell viability, and polymerase chain reaction (PCR)-based immunoglobulin heavy chain (IGH) gene rearrangement assay on formalin-fixed paraffin-embedded tissue yielded a polyclonal result. Since the suspicion for follicular lymphoma was still high, we performed fluorescent in situ hybridization (FISH) using an IGH/BCL2 fusion probe, which revealed the presence of a (14;18) translocation in 88% of 200 analyzed cells. The final diagnosis was that of colonic adenocarcinoma metastatic to a lymph node involved by grade 1 FL. At 1 month follow up, the patient is clinically stable and without evidence of recurrence, and is being evaluated for adjuvant chemotherapy.

4. Discussion

The IGH/BCL2 gene rearrangement resulting from t(14;18) is the hallmark of FL, and is found in 80–89% of cases, depending on the detection method [2]. In recent years it has become apparent that the IGH/BCL gene rearrangement can be present in a myriad of benign clinical conditions, ranging from otherwise normal individuals to patients with reactive hematologic processes [3]. In fact, Tellier et al. demonstrated the presence of an IGH/BCL2 fusion gene by quantitative polymerase chain reaction (PCR) in 14% of 85 reactive lymph nodes [4]. While the positive cells were most frequently distributed in the germinal centers, they only accounted for 1/25,000 to 1/1500 cells [4]. The rarity of BCL-2-positive germinal center B-lymphocytes in reactive lymph nodes was confirmed by immunohistofluorescence, which showed a maximum of 53 BCL-2 positive cells per 100,000 cells [4]. This is in sharp contrast with our case, which showed a rate of BCL-2 positivity well over 50% by immunohistochemistry, and t(14;18) in 88% of the cells by FISH. Also, the complete effacement of the normal lymph node architecture, together with a lack of morphologically normal germinal centers argues strongly in favor of follicular lymphoma in our patient. Although the PCR-based clonality assay failed to show a monoclonal population of lymphocytes, this does not preclude the diagnosis of FL. In fact, Halldórsdóttir et al. reported a high failure rate for PCR-based IGH rearrangement clonality assays in FL [5].

Composite tumors consisting of colonic or small bowel adenocarcinomas and FL are exceedingly rare, with only four previous reports, to the best of our knowledge (Table 1) [6–9]. All cases presented in males older than 50 years of age with microscopic evidence of a composite adenocarcinoma-FL in the primary bowel tumor (2 patients), in regional lymph nodes (this patient) or in both sites (2 patients). This suggests that some of these compound lesions might represent true collision tumors - that is two origi-

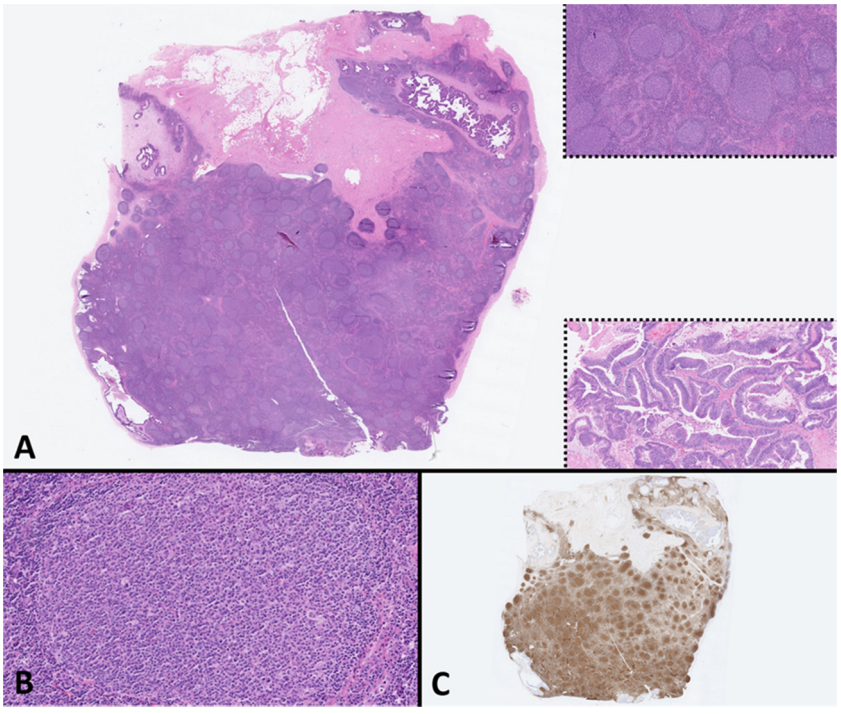

Fig. 2. Microscopic appearance of the retroperitoneal lymph node. (A) Panoramic view of the lymph node showing complete effacement of the normal architecture by a nodular proliferation, and a focus of metastatic carcinoma (original magnification 6×, hematoxylin & eosin stain). At a higher magnification, the nodules correspond to enlarged lymphoid follicles with expanded germinal centers displaying a "back-to-back" arrangement (right superior corner inset, original magnification 50×, hematoxylin & eosin stain). The metastatic tumor is consistent with colonic adenocarcinoma (right inferior corner inset, original magnification 100×, hematoxylin & eosin stain). (B) The expanded germinal centers show a predominant population of transformed centrocytes, with a paucity of centroblasts (<5 per high power field) (original magnification 200×, hematoxylin & eosin stain). (C) The nodules show a diffuse intense positivity for bcl-2 (original magnification 6×, bcl-2 immunohistochemical stain).