

Colonic malignant melanoma, primary or metastatic? Case report

Kolonda malign melanom, primer mi metastatik mi? Olgu sunumu

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Gastrointestinal malignant melanomas, either primary or metastatic, are rare and overlooked tumors. There is also controversy regarding the actual existence of primary melanoma in the gastrointestinal tract apart from the esophagus and anorectal regions, where melanocytes normally exist. A case of malignant melanoma in the cecum is presented. The patient was a 30-year-old male who presented to the hospital for abdominal pain and diarrhea. The tumor was located mainly in the submucosa and measured 14x11x4.5 cm. The cut surface was solid, gray-white and fleshy. Histologically, tumor cells were arranged in compact nests or wide cords surrounded by fibrous stroma. The tumor cells had pleomorphic nuclei and quite rich cytoplasm; multinucleated, giant tumor cells were intermingled. Although no tumor cells contained apparent brown pigment, most were found to be positive for S-100 protein, HMB-45, Melan-A, and vimentin. The possibility of a metastatic lesion was considered. While the patient had a history of a pathologically examined dorsal nevus excision two years before, there was no evidence of either cutaneous or ocular primary melanoma at the time of diagnosis. Moreover, a thorough postoperative investigation did not reveal any other lesion in any other site favoring a metastatic spread. There was also no evidence of recurrent disease or metastasis one year after the surgery. This case is presented in view of its rare occurrence in the cecum. The difficulties in the diagnostic course are discussed, together with a literature review on distinguishing a primary mucosal melanoma from a metastatic one from an unknown or regressed cutaneous primary tumor.

Key words: Malignant melanoma, cecum, gastrointestinal, Melan-A, S-100 protein, HMB-45, neoplasm

INTRODUCTION

Malignant melanomas account for 1%–3% of all malignant tumors of the gastrointestinal (GI) tract (1). They may arise throughout the length of the alimentary tract from the esophagus to the anal canal; however, the majority of these tumors

Gastrointestinal sistemin malign melanomları, ister primer ister metastatik olsun, nadir görülen ve bir anlamda da göz ardı edilmiş tümörlerdir. Dahası, özofagus ve anorektum gibi melanositlerin normal olarak bulunduğu alanlar dışında, gastrointestinal sistemin primer malign melanomunun gerçekten var olup olmadığı da tartışmalıdır. Karın ağrısı ve diyare yakınması ile başvuran ve çekumda malign melanom tespit edilen, 30 yaşında bir erkek hasta sunulmuştur. Tümör büyük oranda submukozada yerleşmiş olup, 14x11x4,5 cm boyutlardadır. Kesit yüzeyi solid, gri-beyaz renkli ve etsidir. Histolojik olarak tümör hücreleri, fibröz stroma ile ayrılmış, kompakt yuvalar ve geniş kordonlar yapma eğilimindedir. Hücreler, orta genişlikte sitoplazmaya sahip olup, pleomorfiktir ve arada dağınık halde dev hücrelerin bulunduğu dikkati çekmektedir. Belirgin bir pigment oluşumu gözlenmemiş olmakla birlikte, immunhistokimyasal incelemede malign melanoma uyumlu olacak şekilde S-100, HMB-45, melan-A ve vimentin pozitif bulunmuştur. Metastatik bir lezyon olasılığı üzerinde durulmuştur. Ancak, 2 yıl önce sırtından bir nevüs eksizyonu yapılan ve patolojik olarak incelenen olgunun öyküsünde ya da operasyon öncesi tetkiklerinde oküler ya da kutanöz melanom bulunmamaktadır. Operasyon sonrası yapılan detaylı taramalarda da metastaza rastlanmamıştır. Olgu postoperatif birinci yılında nüks ya da metastaz göstermeden poliklinik kontrol altındadır. Olgu çekumda nadir görülen bir lezyon olması ve ayırıcı tanısında yaşanan güçlükler nedeniyle; primer mukozal melanom ve bilinmeyen veya regrese bir odakta metastaz yapan malign melanom ayırıcı tanısı konusundaki literatür bilgileri eşliğinde sunulmuştur.

Anahtar kelimeler: Malign melanoma, çekum, gastrointestinal, melan-A, S-100 protein, HMB-45, neoplasm

are secondary lesions representing metastatic spread of a primary tumor (2).

Primary malignant melanoma occurs most often in the skin and much less frequently in the choroid layer of the eyes, under the nail, in the leptome-

ninges, oral cavity, nasal mucosa, pharynx, esophagus, bronchus, and vaginal or anorectal mucosa (3). Malignant melanoma is the most common malignancy having the potential to metastasize to the GI tract (4).

Between 1% and 4% of all patients with malignant melanoma will have clinically apparent GI tract involvement diagnosed antemortem, and up to 60% of all patients with melanoma are found to have metastasis at autopsy (5).

Primary intestinal malignant melanoma, though extremely rare, has been reported. However, the presence of primary malignant melanoma in the GI tract other than the esophagus and rectum, where melanocytes normally exist, is still controversial (6, 15).

We report a case of solitary malignant melanoma arising in the cecum in a patient without a confirmed primary lesion.

CASE REPORT

An otherwise healthy 30-year-old man was admitted to the hospital with abdominal pain and diarrhea. Fecal occult blood test was positive. Ultrasonographic and tomographic examination revealed a mass in the cecum, which was suspicious for lymphoma. A right hemicolectomy and distal ileectomy were performed.

Macroscopically, the tumor, which had a considerable amount of mucosal involvement, was located mainly in the submucosa and measured 14x11x4.5 cm. The overlying mucosa was eroded and necrotic. The cut surface was solid, gray-white and fleshy (Figure 1). The remainder of the colon was unremarkable.

Histologically, tumor cells were arranged in compact nests or wide cords surrounded by fibrous stroma (Figure 2A). The tumor cells had pleomorphic nuclei and quite rich cytoplasm; multinucleated, giant tumor cells were intermingled (Figure 2A arrowhead). The histologic appearance varied throughout the lesion. There were areas resembling a neuroendocrine carcinoma (Figure 2B), choriocarcinoma (Figure 3), anaplastic large cell lymphoma, and even an atypical myeloma. An immunohistochemical panel including cytokeratin 20, synaptophysin and chromogranin A, which was applied to rule out a primary adenocarcinoma and neuroendocrine carcinoma, failed to prove its origin. Although no tumor cells contained apparent brown pigment, malignant melanoma was al-

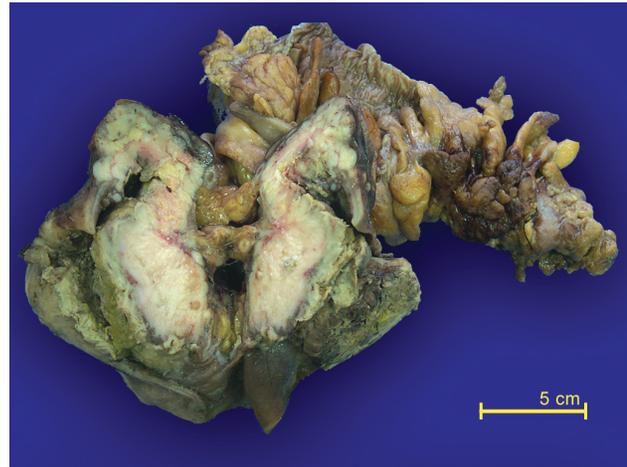


Figure 1. Gross appearance of the tumor. Note that the tumor was mainly located in the submucosa. Overlying mucosa was focally eroded. The cut surface was solid, gray-white and fleshy.

so considered in the differential diagnosis because of its unusual appearance, and most of the tumor cells were found to be positive for S-100 protein, HMB-45 (Figure 4A), Melan-A (Figure 4B), and vimentin. Thus, the tumor was diagnosed as “malignant melanoma”. Of the excised 22 lymph nodes, 13 of them were metastatic.

The possibility of a metastatic lesion was considered and the patient was referred for detailed dermatologic and ophthalmologic examination postoperatively, which revealed no lesions suspicious for primary melanoma. He had no evidence of ocular primary lesion or any other lesion in any other

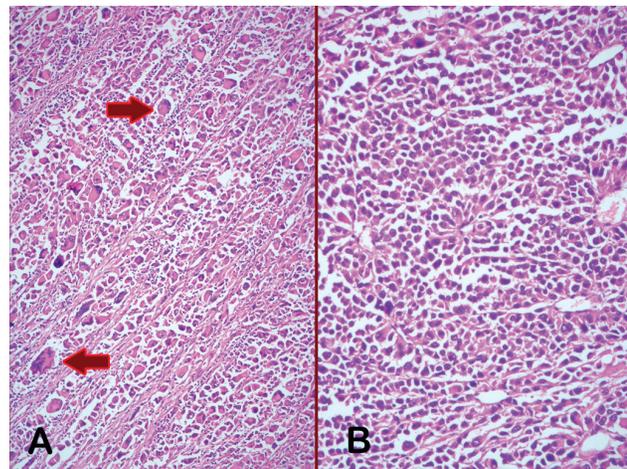


Figure 2. (A) Tumor cells were arranged in compact nests or wide cords surrounded by fibrous stroma. Tumor giant cells were intermingled (arrows) (Hematoxylin and eosin, x10). (B) Areas resembling a neuroendocrine carcinoma. Tumor cells were forming rosette-like structures (Hematoxylin and eosin, x20).

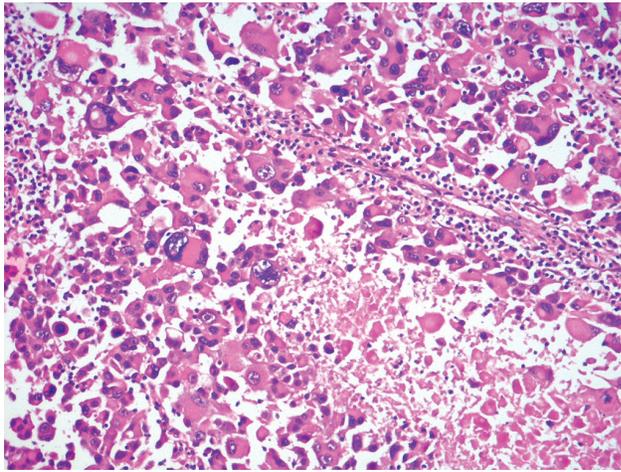


Figure 3. Areas with bizarre tumor cells. Note the necrosis and infiltrating lymphocytes. Overall appearance resembles choriocarcinoma (hematoxylin and eosin, x20).

site favoring a course of metastatic spread. Although a thorough query revealed a history of a dorsal nevus excision two years before, it was pathologically examined and reported as a “benign melanocytic lesion”. However, we were unable to review the slides of the lesion.

The patient has remained free of recurrence or metastasis one year after the surgery.

DISCUSSION

Primary GI malignant melanoma generally occurs in the esophagus and anorectal regions, where melanocytes normally exist. However, the existence of primary melanoma of the large bowel is a controversial topic. There are only a few cases reported to date as a “primary” colonic melanoma (5, 7-11).

The majority of GI malignant melanomas are secondary lesions representing metastatic spread of a primary tumor (2). Metastases to the GI tract are quite common. In autopsy cases, they are most frequently seen in the small intestines (58%), followed by the colon (22%), stomach (20%), rectum (5%), and esophagus (4%) (12). The time interval from the initial presentation of the melanoma to the development of GI involvement is approximately 40 months (13, 14). Despite their frequency in autopsy series, clinical diagnosis is unfortunately rare, probably as a result of nonspecific symptoms, such as bleeding, pain, obstruction, and weight loss, which are not attributed to a metastatic spread at first.

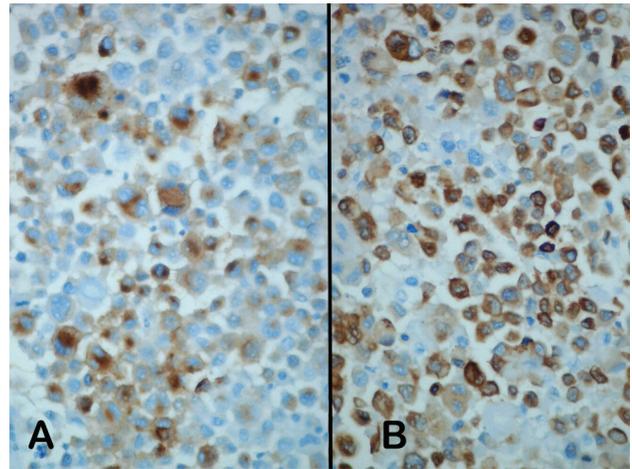


Figure 4. A, B: Immuno expression of HMB-45 (4A) and Melan-A (4B) in tumor cells (HMB-45, x40; Melan-A, x40).

Distinguishing between a primary mucosal melanoma and a metastatic melanoma to the GI tract from an unknown or regressed cutaneous primary melanoma can be difficult, if not impossible. According to the criteria of Sachs et al. (16), primary intestinal melanoma: 1) is a solitary lesion, 2) has no metastatic lesion at other organs, 3) has precursor lesions or melanosis histologically, and 4) has a disease-free survival period of at least 12 months after diagnosis (15, 16). The authors who deny that it exists postulate its origin from a previously removed and regressed cutaneous melanoma. As the most accepted theory, the concept of tumor regression is well established and has been shown to be particularly applicable to melanoma (17). According to others, on the basis of animal studies using chick embryos, neural crest cells with the potential to differentiate and migrate to reach the gut could explain the origin for a primary GI melanoma (18). According to another hypothesis, ectodermic cells are capable of differentiation into multiple cell lines, and they may approach the distal ileum and right colon via the omphalomesenteric duct, thus being the precursor of primary intestinal melanoma (5). Development of a heterotopic melanocyte population derived from primitive stem cells present within the gut should also be considered among the “primary-favoring” theories (19).

Despite the presence of controversies, one can argue that previously reported “metastatic” cases are generally presented with multiple organ involvement at the time of diagnosis or just after diag-

nosis (20), whereas in the “apparent primary” cases reported in the literature, no other organ was found to be simultaneously involved by the tumor, as in our case (21).

From a clinical point of view, both primary mucosal malignant melanoma and metastatic malignant melanoma are more aggressive than their cutaneous counterparts and have worse prognosis. Median survival for those patients is 4-6 months. The relatively high five-year survival rate is 10% (15, 22). Primary treatment for cutaneous, head and neck malignant melanoma is an extensive and curative surgery, followed by postoperative radiation therapy, chemotherapy and immunotherapy for microscopic or macroscopic residual disease or nodal involvement (23). Aggressive surgical resection is essential even in the presence of metastasis to the GI tract, since surgery is not only palliative but also affects prognosis (from 23 to 48 months) (15, 22). However, as primary mucosal melanomas are exceedingly rare, there are no randomized clinical trials comparing the efficacy of the various treatment modalities. It is likely that regardless of the therapy used, the prognosis is grave (23).

In the presented case, the possibility of a metastasis from a regressed primary melanoma could not be excluded since the slides of the previous “nevus” excision could not be reviewed by our center. The partly submucosal localization of the tumor and absence of precursor lesions were also suspicious features for a metastatic lesion. However, the tumor was a solitary lesion and the patient neither had a metastatic lesion in other organs at the time of diagnosis nor developed any in a period of 12 months after the diagnosis, favoring a

possibility of a primary colonic malignant melanoma. Although rare, possibility of a primary “clear cell sarcoma (CCS) of the GI tractus” was also considered. It is difficult to distinguish CCS from primary or metastatic melanoma based on morphology, immunohistochemical profile, and even with ultrastructural features. Covinsky et al. (24) emphasized the use of molecular genetic testing for accurate diagnosis of CCS, which harbors EWS-ATF1 fusion transcript and the associated t(12;22)(q13;q12) translocation, in contrast to cutaneous melanoma. This possibility could not be excluded because of the lack of fresh tissue and available molecular testing. However, it is possible that some GI tumors diagnosed as metastatic melanoma actually represent primary GI CCS.

In conclusion, the histologic diagnosis of malignant melanoma as either primary or metastatic is challenging. Thus, not only pathologists but also clinicians should remember the possibility of malignant melanoma when a case is admitted with colonic mass. Suspicion should arise especially when the histologic picture fails to properly fit an ordinary intestinal adenocarcinoma. On that occasion, the case should be evaluated using a panel of antibodies including malignant melanoma markers or even with molecular genetic testing to rule out a CCS, along with the detailed clinical history. When the diagnosis is established, the case must be searched thoroughly to determine the presence or not of a primary lesion, reserving the possibility of metastasis from a regressed primary malignant melanoma. This case is presented in view of its rare occurrence in the colon and the difficulties in its diagnostic course.

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