CASE REPORT

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Malignant melanoma associated with congenital melanocytic nevus and diagnosed with intestinal metastases: Two case reports

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Congenital melanocytic nevi are hamartomatous lesions that develop from the neural crest and arise during odontogenesis. In this report, we present two malignant melanoma cases developed from congenital melanocytic nevi and revealed by gastrointestinal system metastases. The first case was a 71-year-old female who presented with pleural and peritoneal effusion and underwent biopsy due to detection of nodular lesions in the duodenum by endoscopic examination. The second case was a 36-year-old male patient who presented with abdominal pain in whom segmental ileal resection was performed due to mass lesions causing invaginations in the ileum. Histopathological examination of the lesions showed a diffuse neoplastic infiltration comprising the entire mucosal layers. In neoplastic cells having a marked atypia and pleomorphism, immunoreactions with S-100, HMB-45, and Melan A were detected. Both cases were diagnosed as malignant melanoma. Abdominal skin in the first case and the femoral region in the second case exhibited congenital melanocytic nevi, and those lesions were determined to show a transformation towards malignant melanoma in the histopathological studies. Malignant melanoma development in gastrointestinal system may have a primary or metastatic character. Definitive diagnosis always requires detailed clinical, histopathological and immunohistochemical analyses.

Key words: Malignant melanoma, congenital melanocytic nevi, gastrointestinal system

Konjenital melanositik nevüsten köken alan ve intestinal metastazları ile tanı konan malign melanoma: İki olgu sunumu

Konjenital melanositik nevüs, odontogenez sırasında ortaya çıkan ve nöral-krest'den gelişen hamartomatöz lezyonlardır. Bu çalışmada konjenital melanositik nevüsden gelişen ve gastrointestinal sistem metastazları ile bulgu veren iki malign melanoma olgusu sunulmaktadır. İlk olgu, plevral ve peritoneal efüzyon ile başvuran 71 yaşında kadın hasta olup, endoskopik incelenmede doudenumda nodüler lezyonlar saptanmış ve biyopsi yapılmıştır. Karın ağrısı yakınması ile başvuran ikinci olgu 36 yaşında erkek hasta olup, ileumda invajinasyonlara neden olan kitlesel lezyonlar nedeniyle segmenter ileal rezeksiyon uygulanmıştır. Lezyonların histopatolojik incelemesinde tüm mukoza katlarını infiltre eden diffüz neoplastik infiltrasyon görülmüştür. Belirgin atipi ve pleomorfizm içeren neoplastik hücrelerde S-100, HMB-45 ve Melan A immünreaksiyon saptanmıştır. Her iki olguya, malign melanoma tanısı verilmiştir. İlk olguda karın derisinde, ikinci olguda ise femoral bölgede konjenital melanositik nevüs saptanmış ve histopatolojik incelemelerde bu lezyonların malign melanoma yönünde transformasyon gösterdiği belirlenmiştir. Gastrointestinal sistemde malign melanoma gelişimi primer veya metastatik kökenli olabilir. Kesin tanı daima ayrıntılı klinik, histopatolojik ve immünhistokimyasal incelemeleri gerektirir.

Anahtar kelimeler: Malign melanoma, konjenital melanositik nevüs, gastrointestinal sistem

INTRODUCTION

Malignant melanoma (MM) develops from melanocytes of neuroendocrine origin. Primary tumors are most commonly observed in the skin, anal and oral mucosae, eye, esophagus, and meninges. Me-

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tastatic foci, which develop through hematogenic and lymphatic routes, are usually seen in the liver, lung, bone, and brain tissue (1). MM is one of the tumors that most frequently metastasizes to the gastrointestinal system (GIS). GIS metastases of MM are typically localized in the small intestine (50%) and colon (32%). Intestinal metastases demonstrate an asymptomatic course and generally show signs due to the development of complications. GIS hemorrhage, obstruction, abdominal pain, nausea, vomiting, and weight loss may occur. The time between primary MM diagnosis and development of GIS metastases varies between 2-180 months (2). In the presence of isolated GIS metastasis, because of acceptable mortality and morbidity rates and its positive influence over the course of the disease, surgical removal is the first-line treatment option (3-5).

Congenital melanocytic nevi (CMN) are malformations of pigment cells that develop during odontogenesis and occur during or shortly after birth. Pathogenetically, they are recognized as hamartomas developing from the neural crest. The classification based on the size of those lesions bears importance with regard to the risks for MM. While MM development risk is 540% for lesions larger than 20 cm, it varies between 0-4.9% for smaller lesions. For small-sized CMN, there is no consensus involving the best clinical approach; however, for giant lesions, total excision in the early period is recommended (1,6-9).

In the current study, two MM cases associated with CMN and diagnosed by intestinal metastases are discussed with regard to the pathobiology and clinical characteristics of those neoplasias as well as differential diagnosis criteria.

CASE REPORTS

Case 1

Clinical Characteristics: The radiological examination of a 71-year-old female patient, who presented to our clinic due to back pain, nausea, vomiting, and shortness of breath for the past one month, revealed pleural effusion alongside lesions in both lungs, which were consistent with metastasis. Cytological specimens obtained from the effusions and the histological materials from bronchial biopsies showed no pathology. Endoscopic examination of the patient demonstrated multiple nodular lesions (the largest was 4 mm) in the stomach fundus and corpus and duodenum from which biopsy materials were collected.

Histopathological and immunohistochemical findings: Sections of biopsy materials displayed malignant neoplastic infiltration composed of atypical cells with large eosinophilic cytoplasm, vesicular nucleus and marked nucleolus, which were observed to exhibit a subepithelial invasion. Positive immunoreaction was obtained from tumor cells with vimentin, S-100, anti melanoma antibody (HMB-45), and melanocyte/melanoma tumor antigen (Melan A) (Figure 1). No reaction was observed with keratin, leukocyte common antigen (LCA), smooth muscle actin (SMA), desmin, hematopoietic progenitor cell antigen (CD34), and c-kit (CD117).

Case 2

Clinical Characteristics: Segmental ileal resection was performed upon detection of mass lesions causing invaginations in the ileum in a 36-year-old patient who presented with abdominal pain.

Histopathological and immunohistochemical findings: Macroscopic examination revealed four lesions of which the largest was 3.5 cm. Neoplastic infiltration was determined to form submucosal invasions on the sections. Brown pigment and S-100, HMB-45 and Melan A immunoreactions were detected among neoplastic cells with marked atypia and pleomorphism (Figure 2). Other immune markers displayed no reactions.

Both cases were diagnosed with “malignant melanoma”. Since they had no previous MM diagnosis, systemic examination was performed in order to determine whether they were primary or metastatic tumors. CMN was detected on the surface of abdominal skin in the first case and in the femoral region in the second case; histopathological examinations showed those lesions as undergoing a transformation towards MM. Following diagnosis, the first case died in the first week, and the second case died at one year following development of pulmonary and cranial metastases in the sixth month.

DISCUSSION

Malignant melanoma (MM) development in GIS may be primary or metastatic. Primary MM in GIS is considerably rare and may develop from any area of the GIS mucosa. Amine precursor uptake and decarboxylation (APUD) cells and melanoblastic cells migrating from the neural crest to the small intestine are believed to be responsible for development of those lesions. In order to diag-

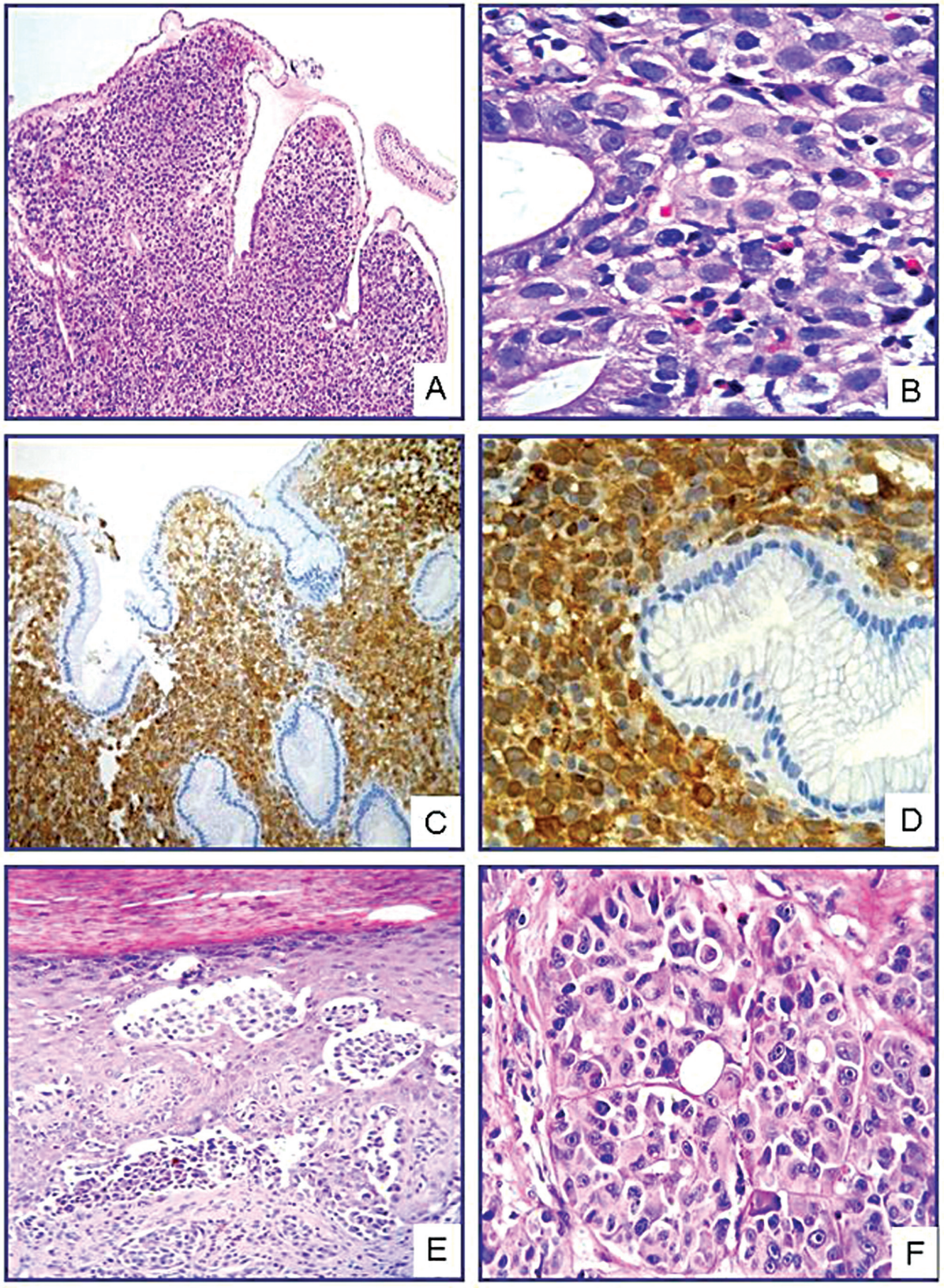

Figure 1. Endoscopic biopsies of the first case demonstrate atypical, pleomorphic tumoral infiltration with large vesicular nuclei and prominent nucleoli, which are observed to be diffuse in the subepithelial area (H&E, A: x100, B: x400). Immunohistochemical examination shows strong positive reaction with S-100 and Melan A (AEC-DAB, C: x100, D: x400). The histological views of the MM determined on the abdominal skin. Atypical melanocytic proliferation in the dermis, some of which contains melanin pigment and infiltrates into the epidermis (H&E, E: x200, F: x400).

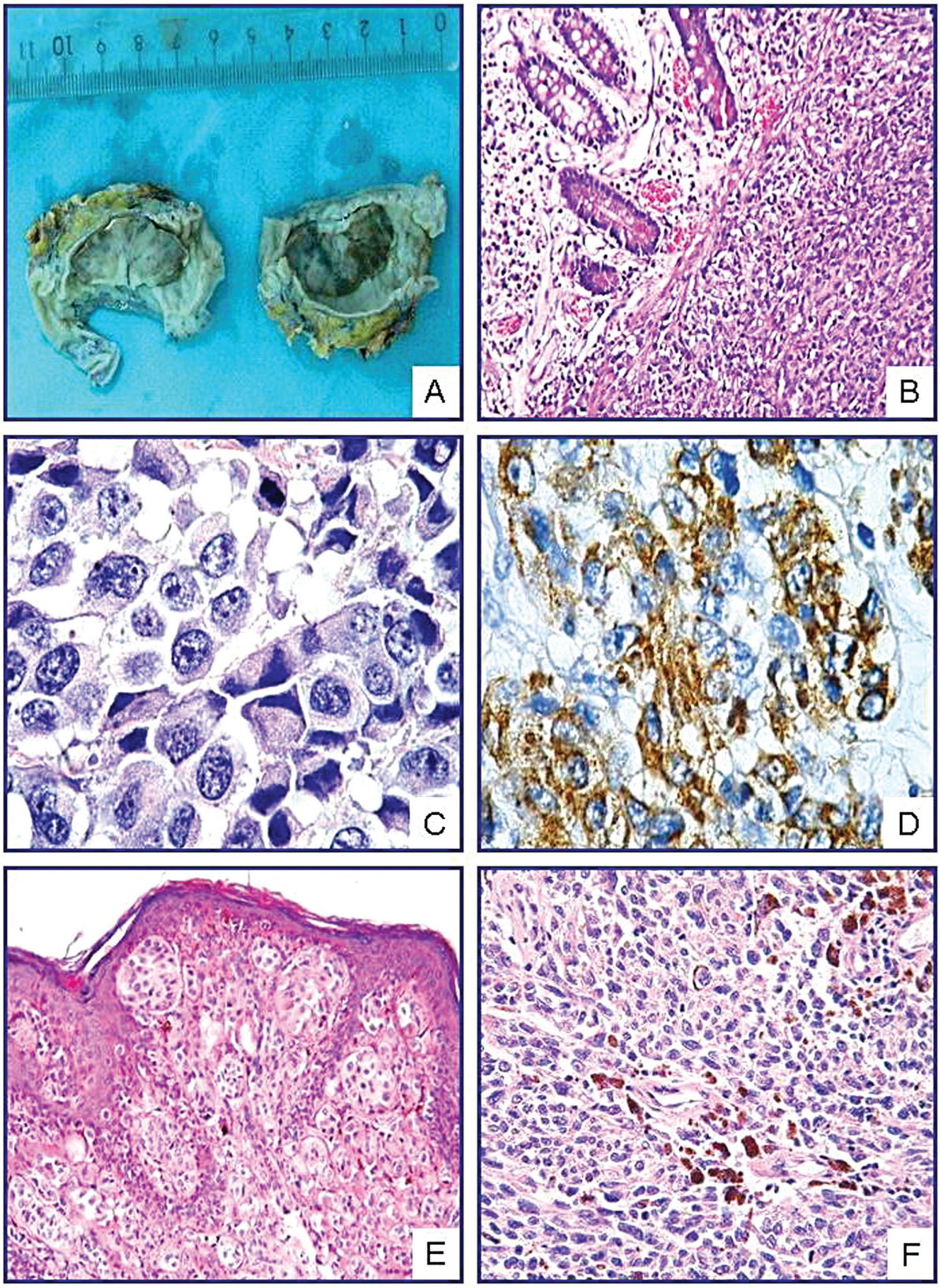

Figure 2. (A) Macroscopic view of the second case. The section of the ulcerated and polypoid mass extending to the small intestine lumen demonstrates a solid character and includes hemorrhagic areas. Sections of the ileal mucosa exhibit a diffuse tumoral infiltration over the subepithelial area. Tumor cells show positive immunoreaction with HMB-45 (H&E, B: x100, C: x1000, AEC-DAB, D: x200). Microscopic views of the MM determined in the thigh region of the second case. Atypical melanocytic infiltration with abundant cytoplasm, large vesicular nuclei, and prominent nucleoli, which were forming invasions in the dermis and epidermis (H&E, E: x200, F: x400).

nose primary GIS MM, the possibility of metastatic spread should be eliminated. MM is known to be among the tumors that most frequently show metastasis to the GIS. Autopsy series show GIS involvement in 60% of patients with systemic involvement; however, antemortem diagnosis rate does not surpass 2%. Because MMs developing in the GIS follow an asymptomatic course, detection in the early period is very rare. Many cases present with systemic involvement and therefore exhibit a very poor prognosis. In some cases, the primary focus regresses and goes undetected. In such cases, it may not be possible to differentiate primary and metastatic MM. In the presence of precursor melanocytic lesion or melanosis in the mucosa, the possibility of GIS MM being of primary nature increases (3,6,10).

While GIS involvement can be seen in all the histological subtypes of MMs, that with a superficial spread more commonly leads to GIS metastases. Metastatic lesions may occur as intraluminal mass, ulcerated polypoid lesion, diffuse infiltrative lesion, or mesenteric implant. Moreover, they may appear as pigmented or amelanotic (1).

While radiological examinations contribute considerably to the diagnostic process, it is not adequate in 30-40% of the cases. In those cases, endoscopic examination and histopathological evaluation bear importance. Endoscopic examination is usually not applied in serosal and mesenteric lesions. Diagnostic laparotomy may be required in those cases. Pathological differential diagnosis should comprise particularly less-differentiated carcinoma, malignant lymphoma, and gastrointestinal stromal tumor (GIST), as well as primary and metastatic tumoral lesions other than MM. The majority of the cases require immunohistochemical analysis, which should include low and high molecular-weight keratin, vimentin, LCA, S-100, and melanocytic markers (HMB-45, Melan A, S-100) (2,5,11).

In our study, the first case was a woman at an advanced age in whom we investigated the primary focus of the metastatic lesions in the lung. After determining the lesions in the GIS, MM diagnosis was established. In this case, metastatic focus of the GIS was localized in the duodenum, which had multiple nodular lesions of millimetric size. Microscopic examination of those lesions revealed malignant neoplastic proliferation with subepithelial localization and diffuse infiltration pattern. Histomorphological properties of tumor cells showing no pigmentation did not provide adequate diagnostic findings. The definitive diagnosis was reached by demonstration of positive immunoreaction with melanocytic markers in the neoplastic cells. In this case, MM was found to be originated from a CMN in the abdominal skin. Despite applying chemotherapy due to diffuse metastases, the patient died in the first week. The other case was a middle-aged male patient. Medical histories of the patient and his family showed no remarkable event. He was diagnosed with MM due to ileum metastases causing intestinal obstruction. In this case, the metastatic focus was the typical appearance of GIS MMs, which is polypoid lesion growth towards the lumen. Histopathological examination showed a diffuse atypical melanocytic proliferation that forms submucosal invasion and contains melanin pigment. Immunohistochemical analyses supported the histomorphological diagnosis. CMN determined in the thigh region was found to undergo a transformation towards MM. The patient began chemotherapy after the operation; however, he developed lung and brain metastases at six months and died in the first year.

In conclusion, GIS MMs can demonstrate significantly different clinical and histomorphological characteristics. Before establishing a primary GIS MM diagnosis, skin and mucosae should be examined carefully with regard to melanocytic lesions. Since those lesions are rarely seen and usually show an asymptomatic course, preoperative diagnosis is considerably difficult. Definitive diagnosis always requires detailed clinical, pathological and immunohistochemical examinations.

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