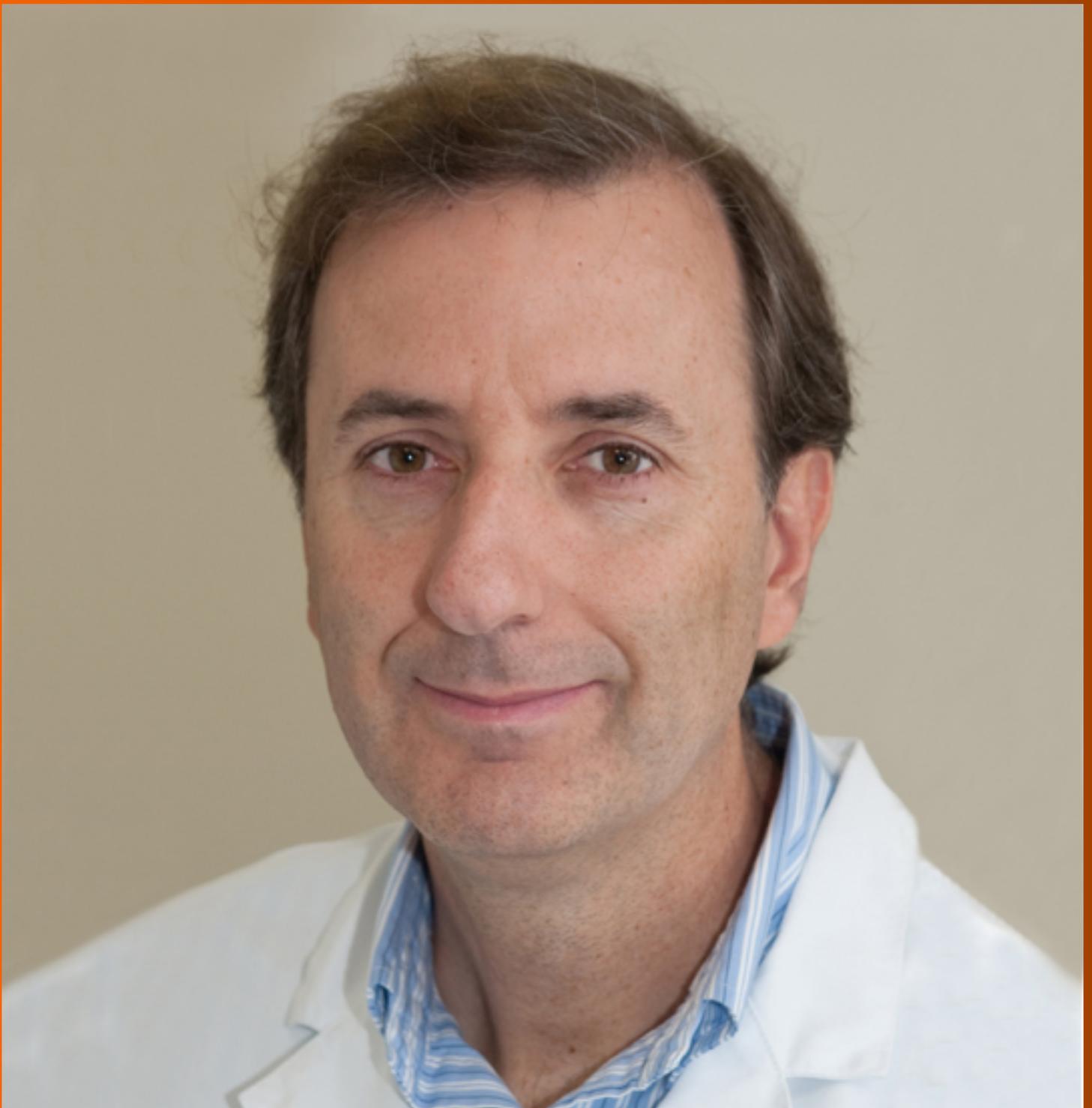


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Melanotic Xp11-associated tumor of the sigmoid colon: A case report

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Abstract

BACKGROUND

Melanotic Xp11-associated tumors are rare mesenchymal-derived tumors. So far, most primary melanotic Xp11-associated tumors have been reported in the kidney, and reports of this tumor in the gastrointestinal tract are rare.

CASE SUMMARY

Here we describe the case of a 25-year-old woman who presented with a melanotic Xp11-associated tumor in the sigmoid colon. Colonoscopy revealed a large mucosal bulge in the sigmoid colon, approximately 32cm inside the anus. The surface was rough with local erosion. The tumor was brittle on biopsy and bled easily. Computed tomography revealed thickening of the rectal wall with edema. Postoperative pathology indicated the likelihood of a perivascular epithelioid cell tumor. Histologically, the tumor comprised plump epithelioid cells with abundant clear to lightly eosinophilic cytoplasm and round nuclei arranged in an alveolar or trabecular pattern. The tumor cells were strongly positive for HMB-45, Melan-A, Cathepsin K, and TFE3 but negative for vimentin, smooth muscle actin, S100 protein, CD10, CK20, and desmin. The tumor cells had a low Ki-67 labeling index (approximately 2%). Fluorescence *in situ* hybridization revealed TFE3 fracture. Based on these histologic and immunohistochemical features, a diagnosis of melanotic Xp11-associated tumor of the sigmoid colon was made.

CONCLUSION

In summary, we report the clinicopathological features of a primary tumor that is extremely rare in the sigmoid colon and review the clinicopathological characteristics of melanotic Xp11-associated tumors, compatible with the very rare tumor termed "melanotic Xp11 translocation renal cancer" in all aspects.

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Core tip: Melanotic Xp11-associated tumors can occur at all ages; children and young adults are particularly prone whereas it is rare in middle-aged and elderly individuals. So far, most primary melanotic Xp11-associated tumors have been reported in the kidney, and reports of this tumor in the gastrointestinal tract are rare. Therefore, data regarding the clinical features and biologic behavior of melanotic Xp11-associated tumors are limited.

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INTRODUCTION

Melanotic Xp11-associated tumors are rare mesenchymal-derived tumors. In 2009, Argani *et al*^[1] reported the clinicopathological features of a distinctive renal cell cancer (RCC) termed "melanotic Xp11 translocation renal cancer". In 2012, LeGallo *et al*^[2] reported the first case of primary melanotic Xp11-associated tumor in the ovary, for which the immunohistochemical markers were very similar to those of RCC. Melanotic Xp11-associated tumors can occur at all ages; children and young adults are particularly prone whereas it is rare in middle-aged and elderly individuals. The common pathological features are: (1) the pigments are visible; (2) the tumor cells are nested, have highly developed capillary vessels, are rich in cytoplasm, and can coexpress melanocyte markers HMB45 and Melan-A but not epithelial markers; and (3) there are *TFE3* gene rearrangement and Xp11 translocation. So far, most primary melanotic Xp11-associated tumors have been reported in the kidney, and reports of this tumor in the gastrointestinal tract are rare. Therefore, data regarding the clinical features and biologic behavior of melanotic Xp11-associated tumors are limited. Here we report the clinicopathologic features of a sigmoid colon tumor in a 25-year-old woman showing morphologic, immunohistochemical, and molecular genetic features identical to those of melanotic Xp11 translocation renal cancer, and performed a review of the published literature.

CASE PRESENTATION

Chief complaints

A 25-year-old woman presented with a 4-d history of abdominal pain, melena, and nausea that were aggravated 1 d prior to admission. She had diarrhea approximately four times a day.

History of present illness

The patient presented to a local Chinese Medicine Hospital and was diagnosed with hemorrhoids. Her condition did not improve after the medical treatment, so she presented to our hospital for further evaluation.

History of past illness

There was no obvious abnormality in the past illness.

Personal and family history

She denied any family history of related diseases.

Physical examination upon admission

No obvious positive signs were found in the abdomen.

Laboratory examinations

The laboratory findings revealed normal routine blood parameters, coagulation

function, tumor markers, and biochemistry results. Blood pressure was 90/70mmHg, heart rate was 90 beats/min, and the heart rhythm was normal. Immunohistochemically, the tumor cells were strongly positive for HMB45, CD34 (vascular+), CD117, CD163, CD68, and Melan-A and negative for CK, Vimentin, S100, CK7, CK20, CD10, Dog-1, Des, CgA, SYN, LCA, EMA, smooth muscle actin (SMA), and SOX-10. Mitotic figures were approximately $\geq 2/5$ per high power field, Ki-67 labeling index was approximately 2%, and there was a partially invasive boundary. The initial diagnosis was a gastrointestinal tract malignancy with perivascular epithelioid cell tumor (PEComa). However, we excluded primary melanoma and primary clear-cell sarcoma of the gastrointestinal tract. The patient was advised to have a genetic test or pathological consultation. Pathological consultation and a fluorescence *in situ* hybridization (FISH) test were subsequently performed at Xijing Hospital, Fourth Military Medical University; immunohisto-chemistry showed that the tumor cells expressed a melanin marker and TFE3, accompanied by *TFE3* gene translocation (Figure 1). FISH for *TFE3* rearrangement showed that the *TFE3* gene was fractured (Figure 1). The tumor showed an abnormal signal pattern consistent with rearrangement of the *TFE3* locus in 52% of the cells. Taking into account all these immunohistochemistry and FISH tests, the final diagnosis was a melanotic Xp11-associated tumor. There was no intraoperative evidence of metastasis or involvement of other abdominal organs. Moreover, subsequent staging studies showed no evidence of metastatic disease.

Imaging examinations

Colonoscopy revealed a large mucosal bulge in the sigmoid colon, approximately 32cm inside the anus. The surface was rough with local erosion. The tumor was brittle on biopsy and bled easily. Computed tomography revealed thickening of the rectal wall with edema. Gastroenterography revealed a filling defect at the junction of the sigmoid and the descending colon. Sputum passed through, the local wall was stiff, and the mucosal destruction was interrupted. Barium sulfate passed through, the local wall was stiff, and the mucosal destruction was interrupted. A malignant tumor was suspected after we completed the relevant examinations. Laparoscopic-assisted resection of the large sigmoid colon mass (about 10 cm × 2.1 cm) was performed. Postoperative pathology indicated the likelihood of a PEComa.

FINAL DIAGNOSIS

Melanotic Xp11-associated tumor of the sigmoid colon.

TREATMENT

Laparoscopic-assisted resection of the large sigmoid colon.

OUTCOME AND FOLLOW-UP

She was followed by imaging studies of the chest, abdomen, and pelvis as well as colonoscopy every 3 mo. At 6 mo after the initial diagnosis, she was disease-free.

DISCUSSION

Since Argan *et al*^[1] first reported Xp11 translocation RCC in 2009, increasing numbers of melanotic tumors have been reported. In 2012, LeGallo *et al*^[2] first reported melanotic Xp11-associated tumor originating in the ovary. The common pathological feature are that the tumor cells are nested, have highly developed capillary vessels, and are rich in cytoplasm, and the pigments are visible, which makes it very similar to PEComa, and tumor cells can coexpress melanocyte markers HMB45 and Melan-A^[3,4]. Melanotic Xp11-associated tumors originating in the digestive system are rare. Therefore, most previous reports on this disease misdiagnosed it as a PEComa. So far, no relevant clinical data can predict the prognosis of these rare postoperative melanotic Xp11-associated tumors^[2]. Due to the fact that melanotic Xp11-associated tumors are extremely rare and their histologic features vary, a differential diagnosis to exclude other tumors is important. The differential diagnosis of melanotic Xp11-associated tumors includes various types of epithelial and mesenchymal tumors, including PEComa, malignant melanoma, clear-cell sarcoma, gastrointestinal stromal

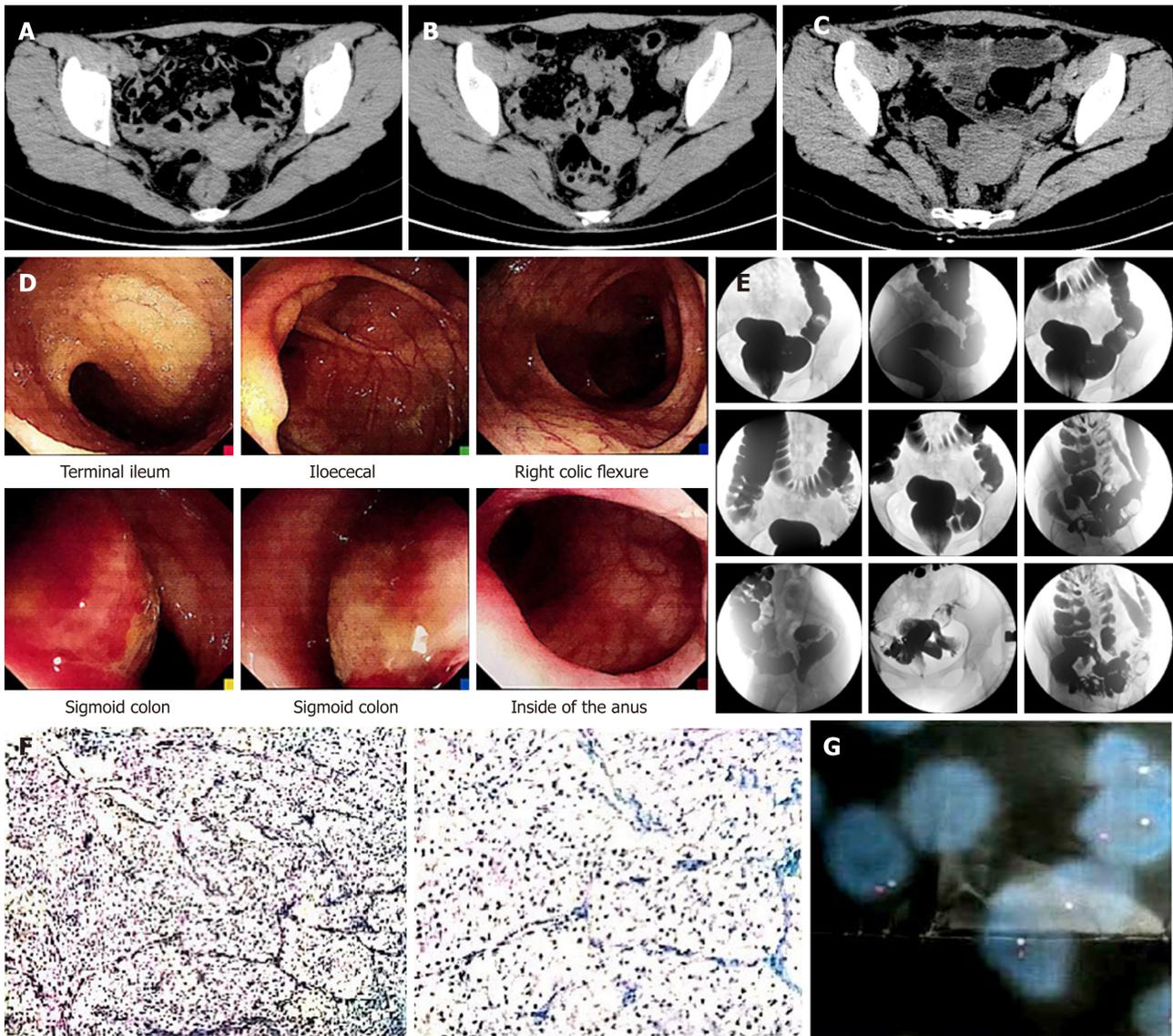


Figure 1 The examination results of the patient. A and B: Preoperative computed tomography (CT) showing thickening of the rectal wall with edema; C: Postoperative CT showing a high-density suture shadow in the operation area; D: Approximately 32cm inside the anus, a large mucosal bulge can be seen in the sigmoid colon. The surface was rough with local erosion. The tumor was brittle on biopsy and bled easily; E: Preoperative gastrointestinal angiography showing a filling defect at the junction of the sigmoid and the descending colon. The barium sulfate passed through, the local wall was stiff, and the mucosal destruction was interrupted; F: Pathological consultation at Xijing Hospital. The tumor cells in the muscle layer of the sigmoid colon were scattered in the nest, and capillaries were separated. The cytoplasm of tumor cells was rich and lightly stained. The nucleus was medium-sized and round or oval (note the nucleolus). The nuclear division was rare, and a small amount of pigment was visible. Immunohistochemistry showed that the tumor cells expressed a melanin marker and TFE3, accompanied by *TFE3* gene translocation, consistent with pigmented Xp11-related tumors. Tumor cells were positive for TFE3 and Cathepsin, and fluorescence *in situ* hybridization (FISH) results showed *TFE3* gene fragmentation (see the FISH report). Original immunohistochemistry results showed HMB45 (+), Melan-A (+), Ki-67 (+, approximately 5%), smooth muscle actin (-), CK (-), and EMA (-); G: Results of FISH test at Xijing Hospital shown that the *TFE3* is fractured.

tumor (GIST), metastatic RCC, and epithelioid leiomyosarcoma. It is well known that the morphology and immunohistochemical features of these unique melanotic Xp11-associated tumors overlap with the morphologic and immunohistochemical features of PEComa. Although the distinction of melanotic Xp11-associated tumors from PEComas is difficult, we believe that the overall morphologic features of the current tumor, particularly the presence of large amounts of melanin, the absence of SMA expression, the lack of the tuberous sclerosis complex gene mutation, and the presence of *SFPQ/TFE3* fusion^[3,5-8], encouraged us to interpret this lesion as a melanotic Xp11-associated tumor (Table 1), thereby making it less difficult to differentiate. The detailed differences are shown in Table 1. FISH is the most commonly used method for gene detection^[9]. Malignant melanoma and clear-cell sarcoma have a high positive rate of S100 protein and *TFE3* recombination but a lack of expression of myogenic markers^[10,11]. Therefore, the melanin and myogenic immune markers can be used for identification. GIST is the most common tumor of the gastrointestinal mesenchymal tissue, which has a morphology very similar to that of

gastrointestinal PEComa, and can also coexpress the CD117 tumor marker, which increases the difficulty in differentiation of this disease. However, GIST does not have the characteristic of expressing the melanin marker; hence, we can use the melanin marker to distinguish it^[12-15].

CONCLUSION

In summary, we report the clinicopathological features of a primary tumor that is extremely rare in the sigmoid colon and review the clinicopathological characteristics of melanotic Xp11-associated tumors, compatible with the very rare tumor termed “melanotic Xp11 translocation renal cancer” in all aspects. Xp11 melanoma should be considered in the differential diagnosis of abnormal melanomas, particularly in cases involving PEComas or unusual primary melanoma tumors. Melanotic Xp11-associated tumors are a special type of tumor with a low incidence, especially for tumors originating in the gastrointestinal tract. The etiology, pathogenesis, and related biological behaviors of this disease remain unclear. Postoperative management, including adjuvant chemotherapy, has not been established yet. A further study of these particularly rare tumors is necessary to understand their biological behavior and pathogenesis. Therefore, patients with postoperative melanotic Xp11-associated tumors should be carefully followed.

Table 1 Comparative features of melanotic Xp11 tumors and perivascular epithelioid cell tumors

	Melanotic Xp11 tumors	PEComas
Sex predilection	Females > males	Females > males
Age	Children and young adults, but may affect older adults	Middle age, but may affect children and older adults
Family history		Tuberous sclerosis
Site	Kidneys, uterus, ovaries, cervix, colon, pancreas, bladder, and pelvis	Genitourinary tract, viscera, skin, soft tissue, and bone
Histology	Epithelioid with clear cytoplasm	Spindled, epithelioid, or sclerosing
Melanin pigment	Usually present	Usually absent
Muscle marker expression	Usually absent	Usually present
Melanocytic marker expression	Present	Present
Epithelial marker expression	Absent	Absent
Molecular genetic alteration	Xp11 translocation; <i>PSF-TFE3</i> fusion	Loss of <i>TSC1</i> (9q34) or <i>TSC2</i> (16p13.3) gene

PEComa: Perivascular epithelioid cell tumor.

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