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An Unexpected Diagnosis of The Rectal Polyp: Perivascular Epithelioid Cell Tumor

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Colorectal polyps are one of the most common diseases of the gastrointestinal tract among children. Most polyps present as painless rectal bleeding and have no genetic predisposition to neoplasia, so polypectomy may be an adequate treatment.[1] Juvenile polyps (88.9%) are the most common pathologic type of pediatric polyps and are usually benign.[1,2] Malignant polyps are rare among children, and adenomatous polyps (6%) are the most common malignant polyps.[2]

Perivascular epithelioid cell tumors (PEComas) are extremely rare mesenchymal neoplasms composed of perivascular epithelioid cells with melanocytic and smooth muscle differentiation at various anatomic locations.[3,4] Perivascular epithelioid cell tumors exhibit different biological behaviors, ranging from benign to malignant.[4]

Although it is common in the lungs and kidneys, it is rare in the gastrointestinal tract and extremely rare in the rectum.[4-6] We report a child with rectal PEComa and discuss the clinical features and differential diagnosis.

A 10-year-old male patient weighing 30 kg was admitted to the pediatric gastroenterology department of our hospital. He complained of recurrent bloody stools for 4 months and a lesion coming out of the anus on straining. He had no abnormalities in his family history.

Anorectal digital examination revealed a polypoid solid mass on the lateral wall of the rectum. Colonoscopy revealed a large diameter and overlying hemorrhagic and inflammatory polyp at the seventh cm from the anal verge (Figure 1A). Otherwise, the colonoscopy was normal. Calprotectin and transferrin levels in the stool were positive.

In the lithotomy position, 7 cm from the anal verge and located at 3 o'clock, a thick pedunculated polyp with a diameter of 2.5 × 2 cm was removed by open surgery (Figure 1B). His vital signs were stable intraoperatively and postoperatively.

Paraganglioma, malignant melanoma, renal cell carcinoma, and gastrointestinal stromal tumor (GIST) were included in the differential diagnosis based on pathological evaluation. On immunohistochemical examination, the polypoid mass was diagnosed as PEComa (Figures 1C and 1D). The surgical margin was tumor free. The tumor cells were positive for human melanoma black-45 (HMB45), neuron-specific enolase, transcription factor-E3 (TFE-3), and progesterone and negative for melan-A, microphthalmia transcription factor family, paired box gene 8 (PAX-8), desmin, vimentin, caldesmon, chromogranin, synaptophysin, and S-100 protein. There was no cytologic atypia, necrosis, or mitosis.

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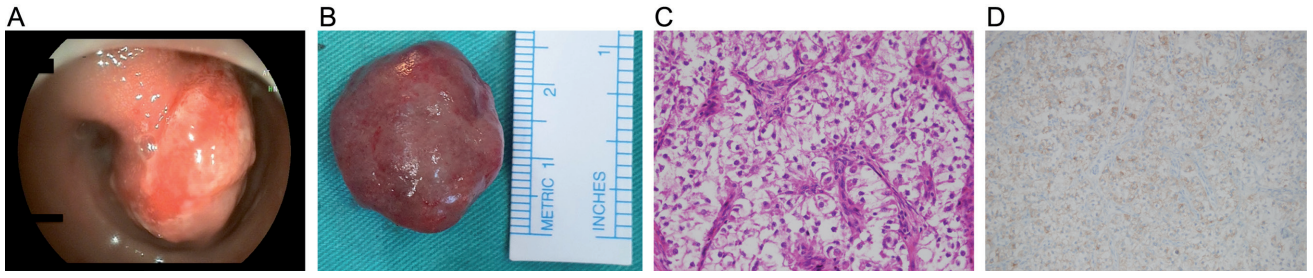

Figure 1. Colonoscopy result, the tumor, and pathological and immunohistochemical examination. (A) A thick-pedunculated, large-diameter, overlying hemorrhagic, and inflammatory polyp; (B) Surgically excised polyp; (C) 400 × magnification showing that the tumor cells were clear or with eosinophilic granular cytoplasm. (D) Immunohistochemical staining revealed positive findings for HMB-45 (200 × magnification).

Magnetic resonance imaging of the abdomen and pelvis to investigate local invasion was normal. The patient is referred to the pediatric oncology and genetics departments for possible metastasis and genetic testing.

Perivascular epithelioid cell tumors can occur in many parts of the body. It is most commonly located in the lungs and kidneys and can extend from the uterus to the vagina and from the liver to the gastrointestinal tract.[3,5] Rectal PEComas are very rare tumors, with few reports in the literature. Kou et al[6] published a review in 2022 and reported 30 colorectal PEComas, of which only 3 cases were pediatric rectal PEComas.

The clinical presentation of PEComas depends on the tumor size and anatomical location. Colorectal PEComas in the pediatric age group may present with rectal bleeding, abdominal pain, and bowel intussusception or may be asymptomatic.[5,6] The most common clinical manifestation of pediatric colorectal PEComa is rectal bleeding, which was also a symptom of the present case.

Perivascular epithelioid cell tumors do not have distinct imaging features, and imaging studies can help identify the lesion to a certain extent. Despite the proximity of PEComas to abnormalities of the urinary tract, genitalia, and spine, computed tomography, magnetic resonance imaging, and ultrasound are not sensitive enough to allow diagnosis of colorectal mural or luminal pathologies such as polyps.[7] A polypoid lesion or fungating mass can be seen on endoscopy, and it can often present as rich vascularization with a hyaline wall or even necrosis.[5] In our case, colonoscopy showed a large diameter and an overlying hemorrhagic and inflammatory polyp.

Considering the morphological and immunophenotypic similarity of the neoplasms in the differential diagnosis of PEComa, immunohistochemical examination is important to confirm the diagnosis of this tumor. The list of diseases included in the differential diagnosis of PEComa is long (Table 1) and includes clear cell sarcoma (CCS)-like tumors of the gastrointestinal tract, alveolar soft part sarcoma (ASPS), malignant melanoma, GIST, paragangliomas, smooth muscle tumors, and metastatic renal cell carcinoma.[3,4]

The CD117 (c-Kit) positivity of PEComas and GIST indicates an important differential diagnostic problem between these tumors, and melanocytic markers such as HMB45 and melan-A aid in differentiation.[4,8] Although diffuse S-100 protein positivity in CCS-like tumors of the gastrointestinal tract excludes PEComa, transcripts of the EWSR1-CREB1 fusion gene also support the diagnosis of CCS.[3] S-100 positivity is a helpful feature in differentiating malignant melanoma from PEComa. Melanocytic differentiation is the main distinguishing feature between PEComa (diffuse) and leiomyosarcoma (focal). S-100 and endocrine marker (chromogranin-A and synaptophysin) positivity and myoid and melanocytic marker negativity are the behaviors of paraganglioma.[8,9] Smooth muscle (desmin and actin) and melanositic markers (HMB45 and melan-A) are almost always negative in ASPS.[4] Renal cell carcinoma has diffuse expression of epithelial membrane antigen and strong nuclear PAX-8 expression and is negative for melan-A, desmin,and HMB45.[9]

Because of the variable biological characteristics of the tumor, Folpe et al[3] recommended criteria for the classification of these tumors as "benign," "undetermined malignant," and "malignant." They summarized that tumor necrosis, vascular invasion,

Table 1. Immunohistochemical Differential Diagnosis of PEComa NOS. Considering the Morphological and Immunophenotype Similarity of Neoplasms, Immunohistochemical Analysis is Necessary to Confirm the Diagnosis

	hmb-45 Melan a	cd117	s100	sma	tfe3	Other
PEComa	+	+/–	+/–	+	+/–	
GIST	–	+	–	–	–	*c-Kit mutation*
Melanoma	+	–	+	–	–	*BRAF mutation*
CCS	+	–	+	–	–	*EWS/ATF-1 fusion*
Paraganglioma	–	–	+	–	–	*chromogranin-a and synaptophysin positivity*
ASPS	–	–	–	+/–	+	*translocations t(X; 17)*
RCS	–	+	–	–	–	*EMA, PAX8*

ASPS, alveolar soft part sarcoma; CCS, clear cell sarcoma; EMA, epithelial membrane antigen; GIST, gastrointestinal stromal tumor; HMB45, human melanoma black; PAX-8, paired box gene-8; PEComa, perivascular epithelioid cell tumor; RCS, renal cell carcinoma; SMA, smooth muscle actin; TFE-3, transcription factor E3.

tumor size greater than 5 cm, infiltrative tumor margin, mitotic activity ≥1/50 high-power field, high nuclear grade, and high cellularity were highly associated with recurrence and metastasis. Because our patient had none of these findings, the tumor was classified as benign according to these criteria.

Primary excision of the tumor is generally curative because most tumors are benign, but local recurrence may develop if the tumor is not removed appropriately.[6,10] Chemotherapy, radiotherapy, and immunotherapy strategies have been reported, particularly for locally advanced or metastatic disease, but clinical outcomes in the literature are variable.[3,10] The patient in our report did not receive chemotherapy, radiotherapy, or immunotherapy.

In conclusion, gastrointestinal PEComas are extremely rare in the pediatric population. Because of an unexpected occurrence in the rectum, PEComa may be misdiagnosed in this region. A complete surgical resection is the preferred treatment option. A multidisciplinary approach and long-term follow-up are crucial for patients with PEComa.

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