EDORIUM Journals

J Case Rep Images Pathol 2024;10(2):12–16.
www.ijcripathology.com

CASE REPORT PEER REVIEWED | OPEN ACCESS

Epithelioid angiosarcoma involving the small intestine in a 3-year-old with an unusual non-aggressive behavior: Case report and review of the literature

Youssef Nasr, Elizaveta Chernetsova, Lauren Tristani, Joseph de Nanassy

ABSTRACT

Malignant vascular lesions involving the gastrointestinal tract include but are not limited to, angiosarcoma, epithelioid and/or spindle cell hemangioendothelioma, and Kaposi sarcoma. Most epithelioid angiosarcomas (EASs) are reported in adult patients, with a male predominance. Epithelioid angiosarcomas arising in the gastrointestinal tract are rare, particularly in pediatric patients. We report a 3-year-old female patient presented by a Meckel's diverticulum. Surgical excision revealed an epithelioid angiosarcoma of the small intestine. She received no additional chemotherapy or radiation after surgery as the patient's parents refused. She was followed annually by imaging and was disease-free seven years after surgery.

Keywords: Epithelioid angiosarcoma, Meckel's diverticulum, Neoplasia, Pediatric

How to cite this article

Nasr Y, Chernetsova E, Tristani L, de Nanassy J. Calcifying fibrous tumor involving the paraspinal region of a child: A rare case report. J Case Rep Images Pathol 2024;10(2):12–16.

Youssef Nasr[1], Elizaveta Chernetsova[1,2], Lauren Tristani[3], Joseph de Nanassy[1,3]

Affiliations: [1]Faculty of Medicine, University of Ottawa, Ontario, Canada; [2]Department of Pathology, The Ottawa Hospital, Ottawa, Ontario, Canada; [3]Department of Laboratory Medicine, Children's Hospital of Eastern Ontario, Ottawa, Ontario, Canada.

Corresponding Author: Joseph de Nanassy, Pediatric Pathologist, Children's Hospital of Eastern Ontario, 401 Smyth Rd, Ottawa, ON K1H 8L1, Canada; Email: jdenanassy@cheo.on.ca

Received: 13 July 2024
Accepted: 09 August 2024
Published: 26 September 2024

Article ID: 100079Z11YN2024

****

doi: 10.5348/100079Z11YN2024CR

INTRODUCTION

Epithelioid angiosarcomas (EASs) arising in the gastrointestinal tract are rare, particularly in pediatric patients. Epithelioid angiosarcoma is known for its poor outcomes, with patient's demise within months following diagnosis. An unusual case of colonic angiosarcoma has been reported in a 16-year-old female patient who was alive and well three years after surgery without adjuvant therapy [1, 2]. We present a similar case of EAS arising in a 3-year-old female who was alive and well seven years after surgery without adjuvant therapy. Our case, along with the case of the 16-year-old female, may shed light on a subtype of EAS arising in the gastrointestinal tract that may have different biological and/or molecular imprints that follow a different course with a favorable prognosis.

CASE REPORT

A female patient, 3 years and 5 months of age, presented with a 3-month history of progressively worsening emesis, intermittent abdominal pain, decreased appetite, and weight loss. A clinical workup identified a significant microcytic anemia [hemoglobin 19 g/L, mean corpuscular volume (MCV) 53 fL], initially thought to be secondary to iron deficiency due to her poor oral intake (serum iron 3 μmol/L, ferritin 19 μg/L, and platelets 828 × 109/L). Imaging studies revealed an infiltrative mass at the ileocolic area (Figure 1).

Open wedge biopsies of the mass were initially performed which yielded an inconclusive pathological diagnosis of atypical epithelioid vascular proliferation without obvious features of malignancy. Epithelioid hemangioendothelioma and a reactive vascular proliferation were also in the differential diagnosis on

microscopy. A more extensive sampling or resection of the lesion was recommended.

At 3 years and 7 months of age, the patient underwent small bowel segmental resection that included the mass. There were no other lesions in the mesentery, omentum, lymph nodes, liver, or peritoneal surfaces. The mass was resected in multiple pieces, the largest being attached to the bowel wall and measuring approximately 5.5 × 3.5 × 3.0 cm (Figure 2). Despite the mass showing extensive areas of necrosis and hemorrhage, the small intestinal mucosa overlying the mass seemed unaffected with no notable gross ulceration. The patient's family refused further therapy, including chemotherapy, and opted to follow up.

Microscopic examination of the lesion revealed a highly atypical vascular proliferation composed of large epithelioid to slightly spindled cells arranged in solid sheets with primitive vascular lumina. The neoplastic cells showed a moderate degree of nuclear pleomorphism, vesicular nuclei, prominent nucleoli, and brisk mitotic activity (up to 12 per 10 high-power fields) and extensive necrosis. Immunohistochemistry revealed that the tumor cells were diffusely and strongly positive for erythroblast transformation specific-related gene (ERG) and CD31, and patchy positive for CD34 (Figure 3).

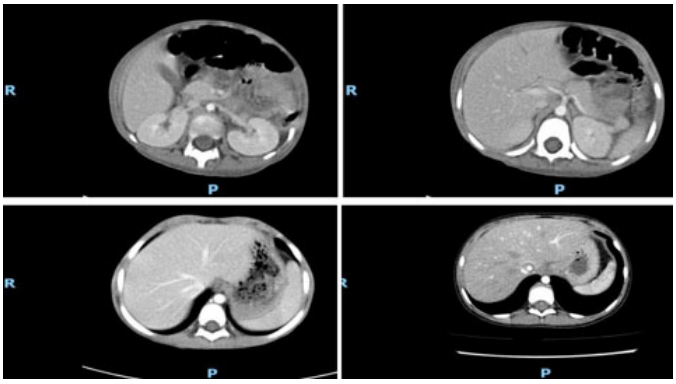

Figure 1: CT scan showing interval resolution of the mass during the follow-up period. Initial presentation on the upper left image. Follow-up after 3 years, image on lower right. In-between CT images are at 1 and 2 years follow-up.

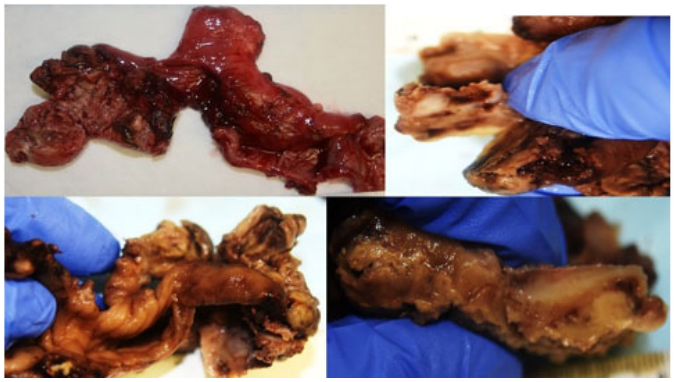

Figure 2: Gross findings of resection. Bowel resection with the mass. Note, the small intestinal mucosa overlying the mass seemed unaffected with no notable gross ulceration.

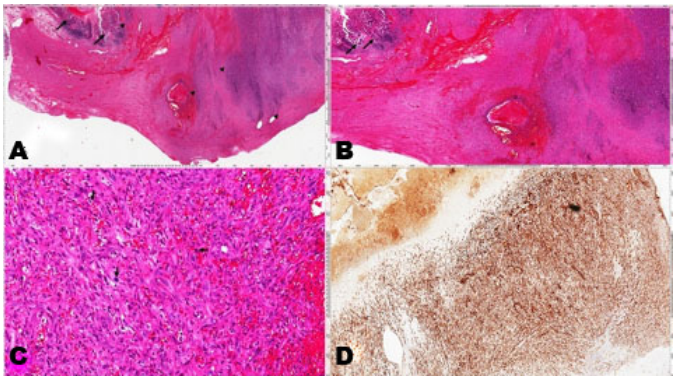

Figure 3: Microscopic examination showing low and medium power views of malignant epithelioid cohesive cells infiltrating through the intestinal wall (A and B corresponding H&E ×40 and ×200, respectively). Note black arrows highlighting the intestinal mucosa. The tumor shows sheets of spindle and epithelioid cells infiltrating through the intestinal wall. The cells are highly atypical with hyper chromatic nuclei. Note arrow heads highlighting mitotic figures (C, H&E ×400). The tumor cells are diffusely positive for CD31 (D, CD31 ×400).

CD117 focally highlighted some of the tumor cells but was considerably less intense than the more specific endothelial markers. It is worth mentioning that the native endothelial cells lining non-tumor capillaries were negative for CD117, thus acting as a negative built-in control. The tumor cells were negative for cytokeratin AE1/3, CK7, CK20, S-100, desmin, caldesmon, SMA, myogenin, CD163, D2-40, Human Herpesvirus-8 (HHV8), and Calmodulin binding transcription activator 1 (CAMTA1). Flow cytometry revealed a normal CD4/CD8 ratio at 1.57 and a normal kappa/lambda ratio of 1.78. There were no abnormal cellular clones. The resection margins were negative for tumor involvement. Cytogenetic evaluation showed a normal 46XX female karyotype. These findings were diagnosed as vascular neoplasm with atypical features consistent with EAS.

Following surgical resection, the patient did not receive adjuvant chemotherapy or radiation therapy. Serial multiple imaging post-resection revealed a stable thickened area of the terminal ileum, which had resolved on imaging 18 months following the surgery and did not re-appear in the follow-up imaging during the past seven years of follow-up. The patient remains clinically well at the 7-year follow-up, with no evidence of tumor recurrence or metastases.

DISCUSSION

Angiosarcomas affecting the small bowel are rare, occurring mostly in male patients, at a median age of 58 years [3]. A primary angiosarcoma of the small intestine with multiple metastases at the time of diagnosis has been reported in a male patient at age 59 years [4].

Angiosarcomas are even rarer in pediatric-age patients, especially in very young children. There is a report of a 16-year-old girl with a colonic angiosarcoma, who has remained in remission for 78 months (6.5 years) with surgical resection alone [2]. We report a 3-year-old female patient diagnosed with EAS, without evidence of metastases. She underwent surgical resection without adjuvant chemotherapy and radiation and is well, without recurrence, seven years post-resection.

Angiosarcomas as primary lesions in the gastrointestinal tract are rare and can be difficult to diagnose given a variety of histomorphological presentations [5] as well as a range of differential diagnostic considerations, both benign and malignant [6, 7]. Angiosarcomas have been most commonly described in deep soft tissues, including the retroperitoneum [8] as well as the skin [9, 10], but they may occur in any of a wide variety of locations [11–13].

Epithelioid angiosarcomas are often characterized histologically by a sheet-like undifferentiated presentation of otherwise bona fide EAS, which can be further defined using immunohistochemical stains [7]. The pan-cytokeratin marker AE1/AE3 is positive in a variable range of EAS. The differential diagnosis includes florid vascular proliferation which is a benign pseudo-neoplastic reactive proliferation of small vessels in the colon, which can mimic other benign or malignant vascular lesions. Florid vascular proliferation usually presents as a "mass" lesion and is associated with intussusception or colonic obstruction. However, the marked atypia and the unequivocal malignant histological features rule out this diagnosis. In addition, the aberrant immunostaining for CD117 in the endothelial tumor cells also tends to favor angiosarcoma over a reactive process. CD117 was positive in our case. Miettinen et al. (2000) reported positive CD117 in a subset of cases of angiosarcomas [14]. They indicated that KIT expression occurs in a subset of angiosarcomas, probably representing oncofetal regression (i.e., reversion of the tumor cell phenotype to that of fetal endothelial cells that may show KIT expression).

On similar grounds hemangiomas, including infantile hemangioma, were ruled out. Staining with GLUT1 may be positive in a minority of angiosarcomas but is specific for juvenile hemangioma [15].

The cellular proliferation index staining for Ki-67 with MIB-1 is usually high (>10%) in biologically more aggressive lesions. It usually, but not always, portends a worse clinical course including demise from disease in most of such patients. The converse is true for the prognosis if the MIB-1 is <10%. In less-differentiated cases, electron microscopy might be helpful by demonstrating features of endothelial differentiation including the possible presence of Weibel–Palade bodies.

Epithelioid angiosarcomas are essentially managed by surgical resection, while radiation and/or chemotherapy yield variable degrees of adjunctive benefits [15].

Our patient is a 3-year-old female with a surgically cured 5.5 cm angiosarcoma of the small bowel, clinically masquerading as Meckel's diverticulum. There is no evidence of tumor recurrence or metastases seven years following surgical resection, even without the use of any other adjuvant treatment modality. Her angioformative tumor occurring in relation to a loop of ileum also makes it one of the rarer presentations of this primary malignant neoplasm. The impression at surgical resection as the lesion looking like a Meckel diverticulum is explained by the fact that the tumor was likely sitting astride the small bowel wall, partially infiltrating it to the level of the submucosa, without mucosal involvement, and partially protruding away from the intestine proper toward the free abdominal cavity.

Angiosarcomas are rare in children and they often have epithelioid features. Not all pediatric patients have adverse outcomes. Deyrup et al. in 2009 documented 3 out of 15 children who could be considered long-term survivors without evidence of disease at 52-month (14-year-old male with angiosarcoma involving the arm), 108-month (2-year-old female with angiosarcoma involving the mesentery), and 132-month (3-month-old female involving right atrium) [16]. Our case is an addition to these rare cases, being the only reported case of EAS occurring in the small bowel in the pediatric population, with a recurrence-free survival of 84 months (3-year-old at time of surgery involving the small bowel).

Future studies are necessary to understand the pathological and molecular nature of this unusual tumor in the pediatric population and its clinical course [17].

CONCLUSION

To the best of our knowledge, we report the youngest published patient presenting with a 5.5 cm primary EAS masquerading as Meckel's diverticulum involving the wall of a loop of small intestine, and without evidence of tumor recurrence or metastases seven years following surgical resection in the English-language literature. Our report highlights that not all pediatric patients with gastrointestinal angiosarcoma have an adverse outcome.

REFERENCES

1. Allison KH, Yoder BJ, Bronner MP, Goldblum JR, Rubin BP. Angiosarcoma involving the gastrointestinal tract: A series of primary and metastatic cases. Am J Surg Pathol 2004;28(3):298–307.
2. Smith JA, Bhathal PS, Cuthbertson AM. Angiosarcoma of the colon. Report of a case with long-term survival. Dis Colon Rectum 1990;33(4):330–3.
3. Fletcher CD, Beham A, Bekir S, Clarke AM, Marley NJ. Epithelioid angiosarcoma of deep soft tissue: A distinctive tumor readily mistaken for an epithelial neoplasm. Am J Surg Pathol 1991;15(10):915–24.
4. Chami TN, Ratner LE, Henneberry J, Smith DP, Hill G, Katz PO. Angiosarcoma of the small intestine: A case report and literature review. Am J Gastroenterol 1994;89(5):797–800.

5. Taxy JB, Battifora H. Angiosarcoma of the gastrointestinal tract. A report of three cases. Cancer 1988;62(1):210–6.
6. Bavikatty NR, Goldblum JR, Abdul-Karim FW, Nielsen SL, Greenson JK. Florid vascular proliferation of the colon related to intussusception and mucosal prolapse: Potential diagnostic confusion with angiosarcoma. Mod Pathol 2001;14(11):1114–8.
7. Hart J, Mandavilli S. Epithelioid angiosarcoma: A brief diagnostic review and differential diagnosis. Arch Pathol Lab Med 2011;135(2):268–72.
8. Meis-Kindblom JM, Kindblom LG. Angiosarcoma of soft tissue: A study of 80 cases. Am J Surg Pathol 1998;22(6):683–97.
9. Prescott RJ, Banerjee SS, Eyden BP, Haboubi NY. Cutaneous epithelioid angiosarcoma: A clinicopathological study of four cases. Histopathology 1994;25(5):421–9.
10. Bacchi CE, Silva TR, Zambrano E, et al. Epithelioid angiosarcoma of the skin: A study of 18 cases with emphasis on its clinicopathologic spectrum and unusual morphologic features. Am J Surg Pathol 2010;34(9):1334–43.
11. Maddox JC, Evans HL. Angiosarcoma of skin and soft tissue: A study of forty-four cases. Cancer 1981;48(8):1907–21.
12. Deshpande V, Rosenberg AE, O'Connell JX, Nielsen GP. Epithelioid angiosarcoma of the bone: A series of 10 cases. Am J Surg Pathol 2003;27(6):709–16.
13. Wehrli BM, Janzen DL, Shokeir O, Masri BA, Byrne SK, O'Connell JX. Epithelioid angiosarcoma arising in a surgically constructed arteriovenous fistula: A rare complication of chronic immunosuppression in the setting of renal transplantation. Am J Surg Pathol 1998;22(9):1154–9.
14. Miettinen M, Sarlomo-Rikala M, Lasota J. KIT expression in angiosarcomas and fetal endothelial cells: Lack of mutations of exon 11 and exon 17 of C-kit. Mod Pathol 2000;13(5):536–41.
15. North PE, Waner M, Mizeracki A, Mihm MC Jr. GLUT1: A newly discovered immunohistochemical marker for juvenile hemangiomas. Hum Pathol 2000;31(1):11–22.
16. Deyrup AT, Miettinen M, North PE, et al. Angiosarcomas arising in the viscera and soft tissue of children and young adults: A clinicopathologic study of 15 cases. Am J Surg Pathol 2009;33(2):264–9.
17. Mark RJ, Poen JC, Tran LM, Fu YS, Juillard GF. Angiosarcoma. A report of 67 patients and a review of the literature. Cancer 1996;77(11):2400–6.

****

Author Contributions

Youssef Nasr – Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Elizaveta Chernetsova – Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Lauren Tristani – Acquisition of data, Analysis of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Joseph de Nanassy – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission

The corresponding author is the guarantor of submission.

Source of Support

None.

Consent Statement

Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.