Perivascular epithelioid cell tumor of the descending colon mimicking a gastrointestinal stromal tumor: a case report

Ryuta Iwamoto1,2, Tatsuki R. Kataoka1*, Ayako Furuhata1, Kazuo Ono2, Seiichi Hirota3, Kenji Kawada4, Yoshiharu Sakai4 and Hironori Haga1

Abstract

Background: We present a case of perivascular epithelioid cell tumor (PEComa), which clinically and histologically mimics a gastrointestinal stromal tumor (GIST).

Case presentation: A 42-year-old woman was found to have a mass in the left flank during her annual medical checkup. Computed tomography examination revealed a submucosal tumor of the descending colon. Surgeons and radiologists suspected that the lesion was a GIST, and left hemicolectomy was performed without biopsy. Microscopic examination showed that the lesion was composed of spindle and epithelioid cells, which were immunohistochemically negative for c-kit and positive for platelet-derived growth factor receptor (PDGFR) α. Initial diagnosis of PDGFRα-positive GIST was made. However, gene analysis did not reveal mutations in PDGFRα. Additional immunohistochemistry showed that tumor cells were positive for human melanin black 45 (HMB45), melanA, and the myogenic marker calponin. A final diagnosis of PEComa was made.

Conclusion: PEComa should be included in the differential diagnosis of PDGFRα-positive spindle cell tumors in the wall of the gastrointestinal tract.

Keywords: Gastrointestinal stromal tumor, KIT, Perivascular epithelioid cell tumor, Platelet-derived growth factor receptor α.
dimension, well-circumscribed but uncapsulated, and ex-
tended from the muscular propria into the subserosa
(Fig. 1a). The cut surface was hemorrhagic and necrotic
(Fig. 1b). Microscopically, the tumor cells consisted of
spindle and epithelioid cells with a granular cytoplasm
(Fig. 2a). Based on the clinical diagnosis of GIST, a panel
of immunohistochemistry including KIT, PDGFRA, dis-
covered on GIST-1 (DOG1), CD34, S100, desmin, and
Ki67 were performed. The tumor cells were positive for
PDGFRA (Fig. 2b) and negative for KIT (Fig. 2c), DOG1
(Fig. 2d), CD34, S100, and desmin. The Ki-67 index was
3% (Fig. 2e). We initially suspected the tumor to be a
PDGFRA-positive GIST. Mutational analysis did not re-
veal any mutation in PDGFRA or KIT, and suggested
the possibility of a low-grade tumor other than GIST.
Upon further examination, the tumor cells were found
to be positive for HMB45 (Fig. 2f) and calponin
(Fig. 2g), and negative for melanA, MITF, SOX10, and
actin. These results were compatible with PEComa.
This tumor was immunohistochemically negative for

---

**Fig. 1** Macroscopic findings. **a** Gross appearance. **b** Sliced specimens

**Fig. 2** Histological findings. **a** Hematoxylin and eosin (H&E) staining. Two representative fields. Immunohistochemical specimens for **b** PDGFRA, **c** KIT, **d** discovered on GIST-1 (DOG1), **e** Ki67, **f** HMB45, **g** Calponin, and **h** TFE3. Photos are ×200 magnification in **a** and ×100 magnification in **b–h**
TFE3 (Fig. 2h), but did not show rearrangement of TFE3 in fluorescence in situ hybridization (FISH) (data not shown). The patient was alive without recurrence 5 months after the resection.

Discussion
PEComa is rare in the gastrointestinal tract. To the best of our knowledge, only 36 cases of gastrointestinal PEComa have been reported sporadically [6, 7]. Doyle et al. performed a clinicopathologic study of 35 cases of gastrointestinal PEComa [5]. The current case shows similarities with previously reported cases of gastrointestinal PEComa, in terms of the clinicopathological features and immunoprofile. GIST does not show immunoreactivity for melanocytic markers [8], and expression of HMB45 is important to support the diagnosis of PEComa. Metastatic melanoma is positive for HMB45, but is also positive for S100 protein and lacks expression of myogenic markers such as calponin. Some cases of PEComa show gene rearrangement involving TFE3, and strong nuclear TFE3 expression [4, 5]. In our case, TFE3 rearrangement was not detected by FISH. This result is not incompatible with a diagnosis of PEComa because most gastrointestinal PEComas are negative for TFE3 [5]. Thus, TFE3 status may not be a diagnostic clue in gastrointestinal PEComa.

The tumor cells in our case were partly epithelioid and immunohistochemically PDGFRα-positive. These phenotypes were thought to be compatible with the initial diagnosis of GISTs with a PDGFRα mutation [3, 9]. However, GISTs with a PDGFRα mutation most commonly arise in the stomach [9, 10], and the tumor is typically DOG1-positive [11, 12]. In contrast to the case of GISTs, PDGFRα positivity and mutations in PDGFRα genes have not been reported in PEComas, to the best of our knowledge. The status of PDGFRα in PEComa should be further studied to diagnose PDGFRα-positive mesenchymal tumors in the gastrointestinal tract. Both GISTs and PEComas are treated with surgical resection and chemotherapy. GISTs are susceptible to the tyrosine kinase inhibitor imatinib [10], although PEComas are susceptible to another inhibitor, sirolimus [13]. Therefore, distinguishing between GISTs and PEComas would be important for appropriate administration of kinase inhibitors.

Conclusion
PEComa should be included in the differential diagnosis of mesenchymal tumors in the wall of the gastrointestinal tract, even though tumor cells are immunohistochemically PDGFRα-positive. Mutational analysis should be performed to confirm the diagnosis of GIST, even though PDGFRα is immunohistochemically positive.

Abbreviations
DOG1: Discovered on GISt-1; GISt: Gastrointestinal stromal tumor; HMB45: Human melanin black 45; MITF: Microphthalmia-associated transcription factor; PDGFR: Platelet-derived growth factor receptor; PEComa: Perivascular epithelioid cell tumor; TFE3: Transcriptional factor E3

Acknowledgments
The authors thank Ms. Ijiri K (Department of Diagnostic Pathology, Kyoto University Hospital, Kyoto, Japan) for her secretarial assistance.

Funding
TRK was supported by a grant from the Ministry of Education, Culture, Sports, Science and Technology, Japan (15K08362).

Availability of data and materials
All data on which the conclusions of this case report are included in this manuscript.

Authors’ contributions
RI, TRK, AF, KO, SH, and HH were all involved in this report’s conception and coordination, and helped to draft the manuscript. Additionally, all authors read and approved the final version of the manuscript.

Competing interests
The authors declare that they have no competing interests.

Consent for publication
The patient signed the Kyoto University Hospital Informed Consent Form for the Non-therapeutic Use of Histopathological Materials, and the signed forms have been uploaded into her electronic health record.

Ethics approval and consent to participate
This case report does not require ethical approval.

Author details
1Department of Diagnostic Pathology, Kyoto University Hospital, 54 Syogoin-kawahara-cho, Sakyou-ku, Kyoto 606-8507, Japan. 2Department of Pathology, Japan Red Cross Society Wakeyama Medical Center, 4-20 Komatsubara-dori, Wakeyama 640-8558, Japan. 3Department of Surgical Pathology, Hyogo College of Medicine, 1-1 Mukuogawa-cho, Nishinomiya, Hyogo 663-8501, Japan. 4Department of Surgery, Kyoto University Hospital, 54 Syogoin-kawahara-cho, Sakyou-ku, Kyoto 606-8507, Japan.

Received: 27 July 2016 Accepted: 7 November 2016

Published online: 14 November 2016

References
1. Hirota S, Isozaki K. Pathology of gastrointestinal stromal tumors. Pathol Int. 2006;56:1–9.
2. Hirota S, Isozaki K, Moriyama Y, Hashimoto K, Nishida T, Ishiguro S, Kawano K, Hanada M, Kurata A, et al. Gain-of-function mutations of c-kit in human gastrointestinal stromal tumors. Science. 1998;279:577–80.
3. Hirota S, Ohashi A, Nishida T, Isozaki K, Kinoshita K, Shimosato Y, Kitamura Y. Gain-of-function mutations of platelet-derived growth factor receptor alpha gene in gastrointestinal stromal tumors. Gastroenterology. 2003;125:660–7.
4. Martignoni G, Pea M, Riechlin D, Zamboni G, Bonetti F. PEComas: the past, the present and the future. Virchows Arch. 2008;452:119–32.
5. Doyle LA, Horlick JL, Fletcher CD. PEComa of the gastrointestinal tract: clinicopathologic study of 35 cases with evaluation of prognostic parameters. Am J Surg Pathol. 2013;37:1769–82.
6. Medeiros F, Corless CL, Duensing A, Horlick J, Oliveira AM, Heinrich MC, Fletcher JA, Fletcher CD. KIT-negative gastrointestinal stromal tumors: proof of concept and therapeutic implications. Am J Surg Pathol. 2014;28:889–94.
7. Liegl-AdHZanger B, Fletcher JA, Fletcher CD. Gastrointestinal stromal tumors. Virchows Arch. 2010;456:111–27.
8. West RB, Corless CL, Chen X, Rubin BP, Subramanian S, Montgomery K, Zhu S, Ball CA, Nielsen TO, et al. The novel marker, DOG1, is expressed ubiquitously in gastrointestinal stromal tumors irrespective of KIT or PDGFRα mutation status. Am J Pathol. 2014;165:107–13.
9. Miettinen M, Wang ZF, Lasota J. DOG1 antibody in the differential diagnosis of gastrointestinal stromal tumors: a study of 1840 cases. Am J Surg Pathol. 2009;33:1401–8.

10. Chen Z, Shi H, Peng J, Yuan Y, Chen J, Song W. Perivascular epithelioid cell tumor in the duodenum: challenge in differential diagnosis. Int J Clin Exp Pathol. 2015;8:8555–62.

11. Lu B, Wang C, Zhang J, Kuiper RP, Song M, Zhang X, Song S, van Kessel AG, Iwamoto A, et al. Perivascular epithelioid cell tumor of gastrointestinal tract: case report and review of the literature. Medicine (Baltimore). 2015;94:e393.

12. Wong NA, Melegh Z. Gastrointestinal stromal tumours can express CD10 and epithelial membrane antigen but not oestrogen receptor or HMB45. Histopathology. 2011;59:781–5.

13. Bissler JJ, McCormack FX, Young LR, Elwing JM, Chuck G, Leonard JM, Schmihorst VJ, Laor T, Brody AS, et al. Sirolimus for angiomyolipoma in tuberous sclerosis complex or lymphangioleiomyomatosis. N Engl J Med. 2008;359:140–51.