Virchows Archiv (2021) 479:847–851
https://doi.org/10.1007/s00428-021-03035-3

BRIEF REPORT

Concurrent epithelioid hemangioma and diffuse cavernous hemangioma in the rectum clinically mimicking a malignant tumor: a case report

Mariko Yasui[1] · Yoshinao Kikuchi[1] · Mutsuo Fujikura[2] · Shigeki Morita[3] · Satoe Numakura[1] · Shiori Watabe[1] · Keijiro Nozawa[4] · Keiji Matsuda[4] · Yojiro Hashiguchi[4] · Tsuyoshi Ishida[5] · Hiroshi Uozaki[1]

Received: 18 August 2020 / Revised: 11 January 2021 / Accepted: 15 January 2021 / Published online: 26 January 2021

Abstract

Epithelioid hemangioma is a rare benign vascular tumor that consists of capillary-sized vessels lined by epithelioid endothelial cells. Diffuse cavernous hemangioma is a congenital benign vascular neoplasm consisting of increased dilated vessels. We report a case of epithelioid hemangioma and diffuse cavernous hemangioma that co-occurred in the rectum. To our knowledge, this is the first report in which two rare vascular lesions coexisted. Because both epithelioid hemangioma and diffuse cavernous hemangioma are often clinically confounded by malignant tumors, differentiating these benign lesions from other possible malignant tumors is significant.

Keywords Epithelioid hemangioma · Diffuse cavernous hemangioma · Gastrointestinal tract · Vascular lesion

Introduction

Gastrointestinal hemangiomas, including diffuse cavernous hemangioma and epithelioid hemangioma, are uncommon benign vascular tumors usually found in young- to middle-aged adults [1, 2]. Patients present with a long history of painless rectal bleeding, and sometimes massive hemorrhage. Epithelioid hemangioma, also known as angiolymphoid hyperplasia with eosinophilia, is a rare vascular neoplasm that is frequently found in the skin and subcutaneous tissue of the head [1, 3, 4]. It is rarely seen in the colorectal area, and only three cases have been described in the literature [1, 3, 4]. Diffuse cavernous hemangioma in the colorectal region is a rare vascular benign tumor, which is often misdiagnosed and difficult to treat [5]. Herein, we report a case of simultaneous occurrence of epithelioid hemangioma and diffuse cavernous hemangioma in the rectum.

This article is part of the Topical Collection on *Quality in Pathology*

✉ Yoshinao Kikuchi
ykikuchi@med.teikyo-u.ac.jp

[1] Department of Pathology, Graduate School of Medicine, Teikyo University, 2-11-1 Kaga, Itabashi-ku, Tokyo 173-8605, Japan

[2] Department of Pathology, Teikyo University Hospital, Tokyo, Japan

[3] Department of Pathology, Mitsui Memorial Hospital, Tokyo, Japan

[4] Department of Surgery, Graduate School of Medicine, Teikyo University, Tokyo, Japan

[5] Department of Diagnostic Pathology, National Hospital Organization, Saitama Hospital, Saitama, Japan

Clinical summary

A 73-year-old man presented with a 4- to 5-month history of intermittent bloody feces. His medical history showed that he had several polyps in the colon, and they had been resected with endoscopic polypectomy in the past. Colonoscopy revealed a hemorrhagic submucosal tumor-like polypoid lesion of about 3 cm in diameter in the rectum, which was 15 cm from the anal verge (Fig. 1a). At the same time, the rectal mucosa around the lesion showed sporadic black spots, suggesting enlarged lymph nodes (Fig. 1b). The subsequent computed tomography (CT) scan demonstrated a polypoid lesion in the rectum (Fig. 1c). In addition, magnetic resonance imaging (MRI) showed not only a 2.4-cm lobulated mass but also multiple enlarged nodules in the mesentery of the descending colon and rectum, which suggested dilated lymph nodes. T2-weighted images revealed increased signal intensity and the

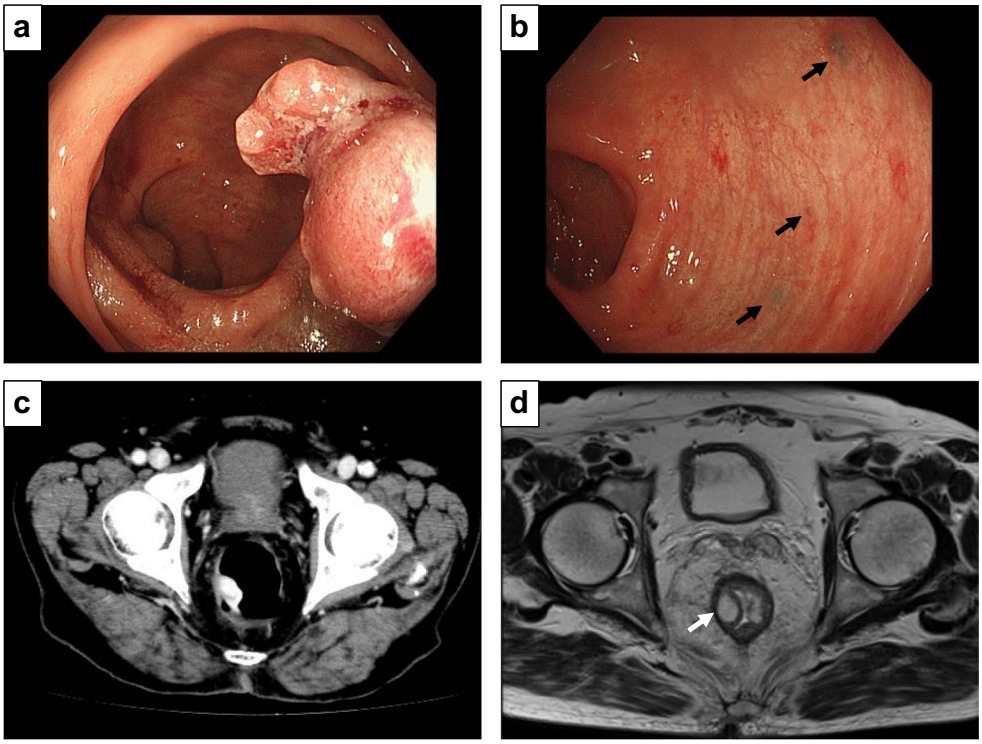

Fig. 1 Clinical images of epithelioid hemangioma and diffuse cavernous hemangioma. **a** Endoscopic image of epithelioid hemangioma. Colonoscopy shows a submucosal tumor-like polypoid lesion. **b** Endoscopic image of diffuse cavernous hemangioma. The rectal mucosa shows sporadic black spots (arrows). **c** CT finding of epithelioid hemangioma. The CT scan shows a polypoid lesion in the rectum. **d** MRI finding of epithelioid hemangioma. T2-weighted image reveals increased signal intensity and the possibility of hemorrhages and cystic changes (arrow)

possibility of hemorrhages and cystic changes (Fig. 1d). Hematological examination demonstrated hemoglobin level of 7.4 g/dl and mean corpuscular volume of 78.3 femtoliters, suggesting iron deficiency anemia. Tumor markers, such as carcinoembryonic antigen and carcinoma antigen 19-9, were not elevated. Endoscopic mucosal resection (EMR) was performed.

The patient underwent laparoscopic low anterior resection of the rectum 2 months after EMR because CT and MRI image indicated the possibility of malignancy with lymphatic metastasis. On follow-up evaluation 6 months postoperatively, the patient presented with no recurrence of rectal bleeding or blood feces.

Pathological findings

EMR specimen

Macroscopically, the resected lesion was a tan-white exophytic mass that measured 30 mm in size (Fig. 2a). Microscopically, proliferation of various sizes of vessels was observed in accordance with the macroscopic tan-white lesion. The surface showed erosion and ulceration. The proliferated vessels involved the stroma of the lamina propria and muscularis mucosae, but existing crypts remained. In addition to lymphocytes and plasma cells, abundant eosinophils had infiltrated into the stroma (Fig. 2b). Some vessels had well-formed walls, whereas others were merely canalized, consisting of epithelioid-like endothelial cells. The endothelial cells had ovoid nuclei with slight anisokaryosis, showing an epithelioid sheet-like growth pattern (Fig. 2c). Unlike pyogenic granuloma, no explicit lobular structure was evident. Prominent pleomorphism was not evident. A few nucleic mitoses were seen, but atypical mitosis was not detected. The surgical margin was negative for the lesion. Immunohistochemical analysis was performed. CD31, CD34, and factor VIII were positive in the endothelial cells, whereas epithelial membrane antigen was negative in almost all endothelial cells (Fig. 2d). FOS-B was focal and weak positive in the endothelial cells (Online Resource 1). All components were positive for p53, and 10% of the endothelial cells were positive for Ki-67.

Surgical specimen

Macroscopically, no protruded lesion remained, and the EMR scar was barely detected as a fibrous scar (Fig. 3a,b). Black spots were diffusely observed mainly in the subserosal layer (Fig. 3c). Microscopically, enlarged vessels of various sizes were spread throughout the whole specimen, and most of the proliferated vessels were observed from the submucosal layer to the subserosal layer (Fig. 3d). Although endothelial proliferation was identified, cellular atypia was not remarkable. Some vessels were accompanied by fibrosis or hyalinization. Most of the lesions showed characteristics of cavernous hemangioma, but proliferation of lymphatic-like vessels was also observed. Some vessels contained organized blood clots (Fig.

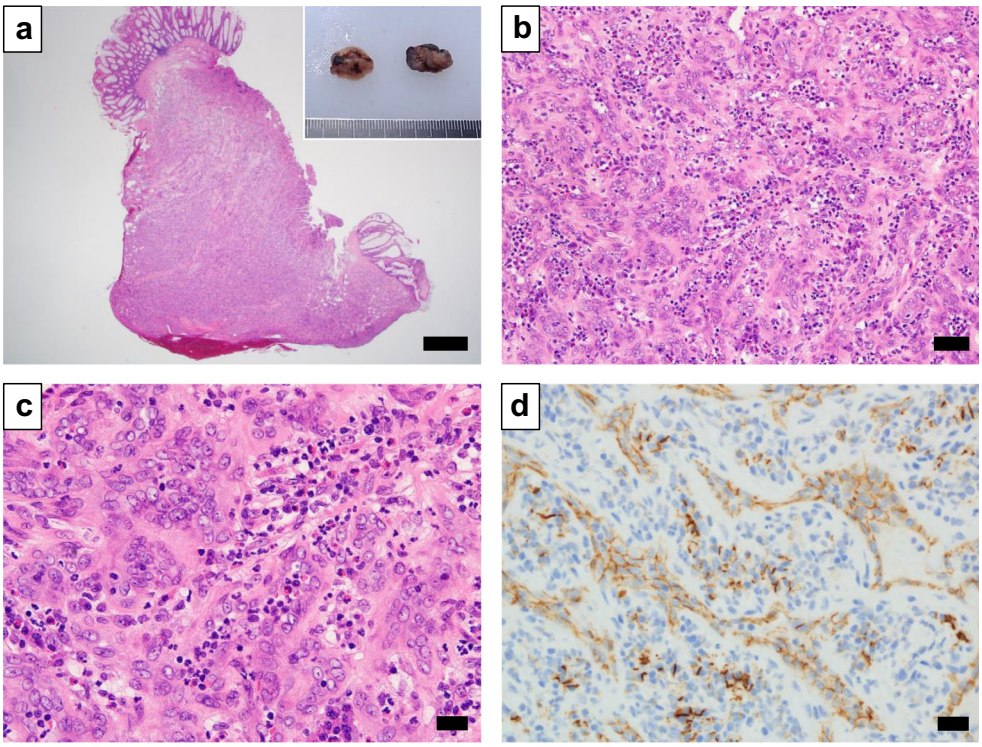

Fig. 2 Pathological findings of epithelioid hemangioma. **a** Histological and macroscopic (inset) appearance of epithelioid hemangioma. The lesion is a tan-white polypoid mass, involving the stroma of the lamina propria and muscularis mucosae. Hematoxylin and eosin (H&E) staining. Bar, 1000 μm. **b** Vessels of various sizes have proliferated with abundant infiltration of eosinophils, lymphocytes, and plasma cells. H&E staining. Bar, 50 μm. **c** Proliferated endothelial cells have ovoid nuclei but no prominent nucleic pleomorphism. H&E staining. Bar, 20 μm. **d** Immunostaining for CD31. Bar, 20 μm

3e). In the subserosal layer, some lymph nodes into which the enlarged vessels proliferated were evident (Fig. 3f). Despite the thorough examination, no remaining lesion of the epithelioid hemangioma was found in the additional surgical resection specimen.

Discussion

In this case, we identified two distinctive benign vascular tumors, an epithelioid hemangioma and a diffuse cavernous hemangioma, arising simultaneously in the rectum. To our knowledge, this is the first report in which two rare vascular lesions coexisted.

Epithelioid hemangioma is a benign vascular tumor that consists of capillary-sized vessels lined by epithelioid endothelial cells [1, 3, 4]. The lesion consists of solid sheets of epithelioid to spindle-formed cells with prominent infiltration of inflammatory cells such as eosinophils and lymphocytes. Epithelioid hemangioma in the colorectal area is a rare mesenchymal tumor, and only a few cases have been reported [1, 3, 4]. Epithelioid hemangioma may be sometimes misdiagnosed as pyogenic granuloma due to its morphological similarity with the latter. One of the characteristics of both lesions is proliferation of capillary vessels with abundant inflammatory cell infiltration [1, 3, 4, 6]. Although pyogenic granuloma shows an explicit lobular structure, epithelioid hemangioma is rarely lobulated [7]. Also, epithelioid hemangioma has long been confused with Kimura's disease; however, these two lesions are now categorized as different entities [7]. One of the most prominent differences is the vascular proliferation. Unlike epithelioid hemangioma, the vascular proliferation in Kimura's disease is relatively minor and is sometimes difficult to detect microscopically [7]. Moreover, solid forms of epithelioid hemangioma occasionally lead to misdiagnosis of malignant tumors such as epithelioid sarcoma or epithelioid angiosarcoma. However, epithelioid angiosarcoma shows prominent nuclear atypia that clearly contrasts with epithelioid hemangioma [7].

Diffuse cavernous hemangioma is a congenital benign vascular neoplasm consisting of increased dilated vessels [2, 5]. Diffuse cavernous hemangioma occurs in various regions such as the skull, spleen, and rectum [2, 5, 8, 9]. The rectum in particular is a common site of occurrence [2, 5]. About 350 cases of diffuse cavernous hemangioma of the rectum have been reported [5]. Diffuse cavernous hemangioma is often confounded by malignant tumors [10]. As its name suggests, this lesion tends to spread throughout vast areas [2, 5, 10]. In this case as well, a CT scan indicated that the lesion had diffusely spread throughout the rectum and lymph nodes, suggesting that the lesion had malignant potential with lymphatic metastasis. At first, the lesion was considered to be a rectal carcinoma with lymphatic metastasis. Endoscopic examination also suggested the malignant potential of the lesion (the polypoid lesion and black spots), such as rectal carcinoma or sarcoma. However, the pathological findings clearly showed that the lesion had typical histological features of epithelioid hemangioma and diffuse cavernous hemangioma.

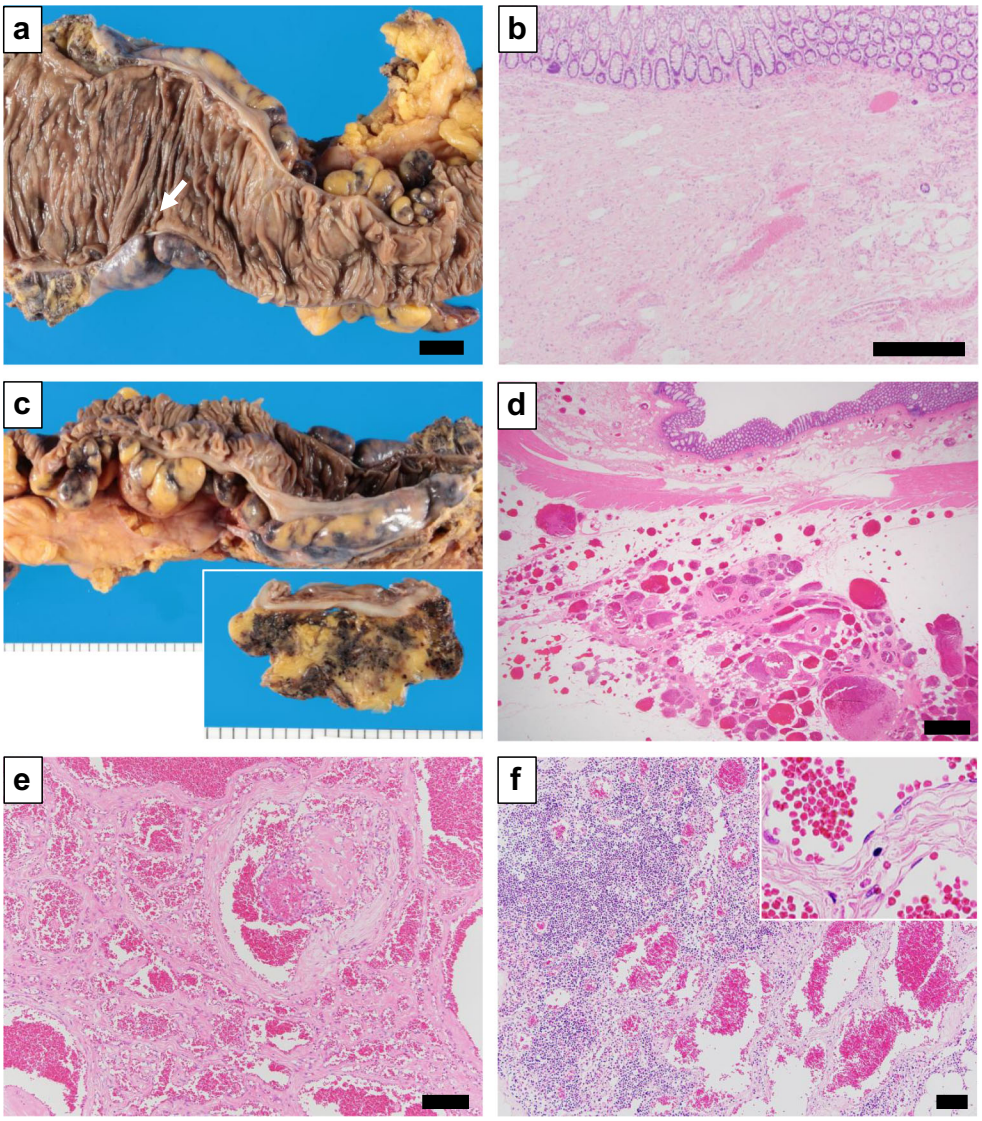

Fig. 3 Pathological findings of diffuse cavernous hemangioma. **a** The EMR scar (arrow) was barely detected. **b** Histological appearance of the EMR scar. Bar, 500 μm. **c** Macroscopic appearance of diffuse cavernous hemangioma. Diffuse black spots were observed in the subserosal layer (inset). **d** Histological appearance of diffuse cavernous hemangioma. Enlarged vessels of various sizes were spread throughout the whole specimen, and most of the proliferated vessels are present from the submucosal layer to the subserosal layer. Hematoxylin and eosin (H&E) staining. Bar, 1000 μm. **e** Some of the vessels contain organized blood clots. H&E staining. Bar, 100 μm. **f** The enlarged vessels have proliferated into the lymph nodes. Cellular atypia was not remarkable (inset). H&E staining. Bar, 100 μm

Differentiating these benign lesions from other possible malignant tumors is significant.

No reports of epithelioid hemangioma and diffuse cavernous hemangioma co-occurring in the gastrointestinal tract have been published, and the mechanism of how the two lesions co-occur is unclear. Because the epithelioid hemangioma was completely resected by EMR and no remaining lesion was found in the additional surgically resected specimen, the relationship between epithelioid hemangioma and diffuse cavernous hemangioma remains unclear. There are several possibilities of how the two lesions co-occurred. One of the possibilities is that the diffuse cavernous hemangioma is merely a malformation that occurred after the removal of the epithelioid hemangioma. This possibility is quite unlikely because MRI taken before performing EMR showed multiple nodules in the colon and rectum, corresponding to the diffuse cavernous hemangioma. Another possibility is that both lesions stemmed from one single hemangioma and differentiated into two distinct morphological patterns. It is less likely that they have the same origin because these two lesions did not show histological mixture or similarities. The most conceivable possibility is that the two independent lesions co-exist in the same area. Evans et al. mentioned that epithelioid hemangioma often accompanies vascular malformation as a background, suggesting its reactive pathogenesis [11]. In this case as well, the epithelioid hemangioma may have arisen in the context of the diffuse cavernous hemangioma.

Although the pathogenesis of epithelioid hemangioma and diffuse cavernous hemangioma was not detected in the current case, genetic and molecular mechanisms may underlie the morphogenesis of both lesions. Some peculiar genetic and molecular features have been reported. For instance, FOS and FOS-B rearrangements are found in about 20 to 30% of epithelioid hemangioma [12]. Positive immunohistochemical reaction for FOS-B is said to reflect its genetic activation in

pseudomyogenic hemangioendothelioma and epithelioid hemangioma [13]. In this case, we performed immunohistochemical analysis for FOS-B but could not determine its activation (Online Resource 1). Also, cavernous hemangioma exhibits some genetic changes such as variations in cerebral cavernous malformation (CCM)–related genes and vascular endothelial growth factor (VEGF) A, B, and C [14]. However, reports of those molecular and genetic changes are limited, and the precise mechanisms of how these lesions are generated remains unknown. In the current case, both epithelioid hemangioma and diffuse cavernous hemangioma are vascular lesions, and other unknown genes and molecular mechanisms may be involved.

In conclusion, we reported a case of epithelioid hemangioma and diffuse cavernous hemangioma co-occurring in the rectum. A correct diagnosis of both lesions is critical for optimal patient management.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00428-021-03035-3.

Code availability It is not applicable to this work.

Author contribution All authors contributed to the study conception and design. Material preparation and data collection and analysis were performed by Mariko Yasui, Yoshinao Kikuchi, Mutsuo Fujikura, Shigeki Morita, Shiori Watabe, and Tsuyoshi Ishida. Keijiro Nozawa, Keiji Matsuda, and Yojiro Hashiguchi gave the patient's clinical information. The first draft of the manuscript was written by Mariko Yasui. Satoe Numakura and Hiroshi Uozaki commented on previous versions of the manuscript and provided a critical review. All authors read and approved the final manuscript.

Data availability Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Declarations

Ethics approval and consent to participate It is not applicable to this work.

Written informed consent was obtained from the patient for publication of the case report.

Consent for publication Written informed consent was obtained from the patient for publication of the case report.

Informed consent Written informed consent was obtained from the patient for publication of the case report.

Conflict of interest The authors declare no conflict of interest.

References

1. Bui M, Draper N, Dessureault S, Nasir N, Cooper H, Nasir A, Coppola D (2010) Colonic angiolymphoid hyperplasia with eosinophilia masquerading as malignancy: a case report and review of the literature. Clin Colorectal Cancer [Internet] 9(3):179–182. Available from. https://doi.org/10.3816/CCC.2010.n.025
2. Zeng Z, Wu X, Chen J, Luo S, Hou Y, Kang L (2019) Safety and feasibility of transanal endoscopic surgery for diffuse cavernous hemangioma of the rectum. Gastroenterol Res Pract [Internet] 2019. https://doi.org/10.1155/2019/1732340
3. Nonose R, Priolli DG, Cardinalli IA, Máximo FR, Galvão PSP, Martinez CAR (2008) Epithelioid hemangioma of the colon: a case report. Sao Paulo Med J [Internet] 126(5):294–296. https://doi.org/10.1590/S1516-31802008000500011
4. Berney DM, Griffiths MP, Brown CL (1997) Angiolymphoid hyperplasia with eosinophilia in the colon: a novel cause of rectal bleeding. J Clin Pathol [Internet] 50(7):611–613. https://doi.org/10.1136/jcp.50.7.611
5. Wang HT, Gao XH, Fu CG, Wang L, Meng RG, Liu LJ (2010) Diagnosis and treatment of diffuse cavernous hemangioma of the rectum: report of 17 cases. World J Surg [Internet] 34(10):2477–2486. https://doi.org/10.1007/s00268-010-0691-1
6. Val-Bernal JF, Mayorga M, García-Somacarrera E (2012) Pyogenic granuloma of the large intestine: case report and review of reported cases in the adult. Pathol Res Pract [Internet] 208(11):687–690. https://doi.org/10.1016/j.prp.2012.08.010
7. J.R.Goldblum ALF& SWW (2019) Enzinger & Weiss's soft tissue tumors, 7th ed, 7th edn. Elsevier, Amsterdam, Nederland
8. Tang JY, Chen J, Pan C, Yin MZ, Zhu M (2008) Diffuse cavernous hemangioma of the spleen with Kasabach-Merritt syndrome misdiagnosed as idiopathic thrombocytopenia in a child. World J Pediatr [Internet] 4(3):227–230. https://doi.org/10.1007/s12519-008-0042-6
9. Liu H, Chang X, Shang H, Li F, Zhou H, Xue X (2019) Diffuse cavernous hemangioma of the skull misdiagnosed as skull metastasis in breast cancer patient: one case report and literature review. BMC Cancer [Internet] 19(1):1–6. https://doi.org/10.1186/s12885-019-5341-x
10. Chatu S, Kumar D, Du Parcq J, Vlahos I, Pollok R (2013) A rare cause of rectal bleeding masquerading as proctitis. J Crohn's Colitis [Internet] 7(3):e99–e102. https://doi.org/10.1016/j.crohns.2012.05.022
11. Evans HL, Raymond AK, Ayala AG (2003) Vascular tumors of bone: a study of 17 cases other than ordinary hemangioma, with an evaluation of the relationship of hemangioendothelioma of bone to epithelioid hemangioma, epithelioid hemangioendothelioma, and high-grade angiosarcoma. Hum Pathol 34(7):680–689
12. Shon W, Billings SD (2019) Epithelioid vascular tumors: a review. Adv Anat Pathol [internet] 26(3):186–197. https://doi.org/10.1097/PAP.0000000000000228
13. Hung YP, Fletcher CDM, Hornick JL (2017) FOSB is a useful diagnostic marker for pseudomyogenic hemangioendothelioma. Am J Surg Pathol 41(5):596–606
14. Huang C, Huang J, Yu G (2018) Co-suppression of VEGF-A and VEGF-C inhibits development of experimental hemangioma. Am J Transl Res 10(9):2911–2919