

Multifocal sclerosing angiomatoid nodular transformation of the spleen in a patient with simultaneous metachronous liver metastasis after colon cancer surgery: a first case report

A.-K. MUELLER¹, C. HAANE¹, K. LINDNER¹, P.J. BARTH², N. SENNINGER¹, R. HUMMEL¹

¹ Department of General and Visceral Surgery, ² Department of Pathology, University Hospital Muenster, Germany

Key words

Sclerosing angiomatoid nodular transformation • Splenic lesions • Splenectomy

Summary

Sclerosing angiomatoid nodular transformation of the spleen (SANT) is a benign, extremely rare vascular lesion of the spleen with unknown pathogenesis. SANT is often discovered incidentally, and can sometimes be found in patients with a history of cancer. Based on absent definitive radiological signs and varying growth patterns, distinction from malignant

processes such as metastasis can be very difficult. Therefore, surgical resection of the spleen is indicated in most cases of patients with history of cancer. We report a case of a bifocal manifestation of SANT in the spleen in a patient with history of colon cancer and newly-diagnosed metachronous liver metastases.

Introduction

Splenic lesions are very rare findings in everyday clinical practice, and are generally found incidentally in asymptomatic patients. Nonetheless, they are sometimes detected in critically-ill patients with infectious, vascular or systemic diseases, or in patients with primary or lymphoid malignancies or metastatic disease. In general, most tumours of the spleen are benign and of vascular origin, including cysts, haemangiomas, lymphangiomas, littoral cell angiomas or solid lesions such as hamartomas or inflammatory pseudotumours¹⁻⁴. The prevalence of primary neoplasms of the spleen is very low (except for lymphoma), and angiosarcoma is the most common primary malignant vascular tumour¹⁻⁵. Metastases in the spleen are also rare, but can occur in patients with primary tumours of the lung, ovary, skin (melanoma), breast or colon cancer⁶.

Sclerosing angiomatoid nodular transformation of the spleen (SANT) represents another very rare type of primary splenic lesion that was described for the first time by Martel et al. as a distinct tumour entity of the spleen

in 2004. SANT is a benign vascular lesion, well-circumscribed with multinodular angiomatoid appearance, and is characteristic for its immunostaining pattern consisting of CD31+CD34+CD8- capillaries, CD31+CD34-CD8- small veins and CD31+CD34-CD8+ sinusoids which form the angiomatoid nodules⁴. However, before the lesion was first described in 2004 and termed SANT, Krishnan et al. had very likely described the same entity as “cord capillary haemangioma” in 1993⁷. Moreover, it is likely that a number of earlier case reports on hamartomas, haemangio-endotheliomas, sclerosed haemangiomas or inflammatory pseudotumours of the spleen might refer to the same tumour entity⁴⁻⁸⁻⁹. Based on its benign nature, splenectomy without further treatment is the appropriate therapy for SANT.

To date, a fairly low number of case reports, small case series, reviews and clinicopathological studies on SANT have been published in the current literature, for a total of 108 cases reported. In this context, 15 cases of SANT have been described in cancer patients¹⁰⁻¹⁸. In this current case report, we present for the first time a case of bifocal SANT in a 63-year old patient with history of

Acknowledgements

We greatly appreciate the support of Dr. Schumacher for his collaboration in providing radiological images.

Correspondence

Ann-Kathrin Mueller, Department of General and Visceral Surgery, University Hospital Muenster, Waldeyerstr. 1, 48149, Muenster, Germany - Tel. 0049 (0) 251 83 56359 - Fax: 0049 (0) 251 83 56402 - E-mail: ann-kathrin.mueller@ukmuenster.de

colon cancer and newly-diagnosed metachronous liver metastases.

Case report

In 2013, a 63-year old male was referred to our clinic. In 2011, the patient had been diagnosed with non-occlusive cancer of the colon transversum during routine medical check-up. After exclusion of distant metastasis, the patient had undergone oncological resection of the colon transversum including lymphadenectomy at another hospital. Postoperative tumour stage was pT3, pN2a (5/16), R0, M0, G3. Based on the tumour stage with nodal involvement, surgical treatment was followed by adjuvant chemotherapy with capecitabine according to the current German S3-Guideline on Colorectal Cancer 2004/2013¹⁹. The patient had undergone regular follow-up examinations in outpatient care. One year after surgery, the patient had been doing well, and laboratory and radiological examinations (including tumour markers and a performed CT-scan as part of the routine examination) indicated no pathological findings or signs of recurrence. Twenty months after initial surgery, a second CT scan and an MRI of the liver were carried out as ultrasound showed a suspicious mass in the liver. These investigations confirmed an asymmetric lesion in the left lobe of the liver (segment IV) with a diameter of 22-24 mm, located at the branching of the intrahepatic veins, and highly suspicious for metastasis (Fig. 1). Unexpectedly, a second hypodense lesion without clear borders was detected in the caudal pole of the spleen with a maximum diameter of 45 mm (Figs. 2, 3). Based on radiological examinations, metastasis could not be ruled out. Retrospectively, this lesion was already ap-

Fig. 1. An abdominal CT scan was performed 20 months after initial surgery because of a suspicious tumour in the liver detected by ultrasound. The investigation confirmed pathological ultrasound findings by showing an asymmetric lesion located in the left lobe of the liver (segment IV) at the branching of the intrahepatic veins with a diameter of 22-24 mm, and highly suspicious for metastasis.



Fig. 2-3. As secondary finding, a highly suspicious hypodense lesion without clear borders was observed in the caudal pole of the spleen with a maximum diameter of 45 mm. Multifocal lesions could not be detected.



parent but hardly detectable in the CT scan carried out one year after surgery, and the lesion appeared slightly larger in size. Neither splenomegaly nor lymphoma was observed.

In order to evaluate possible treatment options, the patient was referred to our department. After presentation of the patient in our interdisciplinary tumour board, surgical exploration and potential resection of the liver metastasis and the spleen was recommended based on the good prognosis of singular colon cancer metastasis. Intraoperatively, there were no signs of further metastatic spread, and left hemihepatectomy and splenectomy were performed without complications. Postoperatively, the patient was referred to our intensive care unit for relevant comorbidities (including adipositas permagna (BMI 44.3 kg/m²), arterial hypertension, diabetes and COPD GOLD Stage IV with subsequent significantly increased perioperative risk. After an uneventful postoperative course, the patient was discharged in good conditions 14 days after surgery. Based on the recommendation of our interdisciplinary tumour board, postoperative adjuvant chemotherapy (capecitabine) was initiated. In

the last follow-up 4 months after surgery, the patient was free of symptoms, and there was no evidence of further metastasis or disease recurrence.

Histological examination of resected liver tissue confirmed metastasis of the resected colon cancer, with lymphangiosis and haemangiomas as well as focal necrosis. The spleen had a slightly increased weight of 311 g and a size of 13 × 10 × 5.5 cm. Macroscopically, the caudal pole of the spleen disclosed a circumscribed tan lesion measuring 3.5 cm. Moreover, an additional, well-circumscribed, firm, brown lesion with a diameter of 1 cm was found in the splenic tissue. Histology (Masson Goldner and Elastica van Gieson staining) of both lesions revealed a lobulated sclerotic lesion with multiple, intranodal fibrous septa (Fig. 4). Immunohistochemical studies showed multiple capillaries with CD34 and CD31 positive endothelia within the angiomatoid nodules (Fig. 5). Staining for CD8 and CD21 was negative. The proliferative index of cells in the angiomatoid nodules assessed by MIB1-immunohistochemistry was very low (< 2%). The remaining splenic tissue was normal. Based on the morphologic appearance and histological findings, the lesions were diagnosed as bifocal SANT of the spleen.

Discussion and conclusions

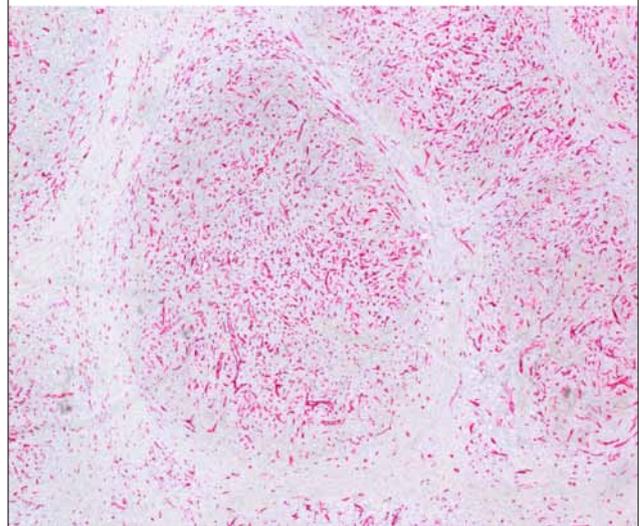
Herein, we present a case of bifocal SANT found in a 63-year old patient with history of previously resected colon cancer and in whom metachronous metastases in the liver and spleen were suspected. To our best knowledge, this is the first report of a multifocal manifestation of SANT, and there have been no previous reports on SANT in patients with simultaneous metachronous liver metastasis following surgery for colorectal cancer in the current literature. Due to the patient's history of colon cancer, the lesion in the spleen was initially suspected to be metastatic, but histological examination revealed a benign morphology of SANT.

Tumours of the spleen, either benign or malignant, are rare. Among these, SANT is an extremely rare, benign, recently recognised vascular lesion of the spleen with unclear pathogenesis, which usually affects middle-aged adults. Women are considered to be affected more frequently, however the gender predilection may be reconsidered in the near future as a consequence of an increasing number of published cases⁵. We found a total of 108 cases of SANT published in the current literature; 15 of these cases were reported in patients with history of various cancers including melanoma, basal cell carcinoma, squamous cell carcinoma^{11-13 18}, retroperitoneal spindle cell sarcoma¹⁴, renal cell carcinoma⁴, urothelial carcinoma, carcinoma of fallopian tube¹³, prostate carcinoma¹⁵, lung cancer¹⁶, gastric carcinoma^{4 20}, adenocarcinoma of the pancreatic head¹⁷ and colorectal cancer^{10 20 21}. As these lesions are usually asymptomatic without epigastric or abdominal pain, discomfort, fever, anaemia or splenomegaly, SANT are often incidental findings in

Fig. 4. Histologically, the splenic tissue displayed focal lobular sclerosis (EvG-stain).



Fig. 5. CD34 immunohistochemistry labeled densely packed slender capillaries located with the lobular sclerosis.



routine imaging in patients with a history of malignancy. This was the case in all 15 patients described above. If splenic lesions such as SANT are detected in cancer patients, a diagnostic dilemma arises. There are many differential diagnoses of SANT that on the one hand include a broad variety of benign neoplasms such as cysts, haemangioma, lymphangioma, littoral cell angioma, hamartoma, inflammatory pseudotumour and congestive splenomegaly, and on the other malignant processes such as metastases. It is very difficult to differentiate splenic lesions using only radiologic studies^{1-3 5}. By ultrasound, vascular masses in the spleen are detectable, but there are no conclusive patterns that can demonstrate a diagnosis of SANT²². Lewis et al. tried to distinguish SANT from other splenic masses using CT-scan and MRI methods. In their studies, SANT showed

a characteristic pattern in both CT and MRI: the lesion presented as solitary, round, lobulated mass with early peripheral enhancing radiating lines and progressive enhancement of the angiomatous nodules. Furthermore, delayed enhancement of the fibrous tissue and hypointense T2 signal intensity could be observed²³. However, these “SANT-specific” radiologic findings could not be detected in our case, and various radiological characteristics of SANT have been described in the literature¹⁷.

In addition, SANT seems to present a different growth pattern. Langer et al. described a patient with rectal cancer who developed a rapidly growing splenic mass two years after surgical treatment. Due to the rapid increase in size, from 8 to 20 mm within 11 months, a metastatic or infectious process was favoured, but diagnosis of SANT was made based on histological examination¹⁰. Another case report by Raman et al. described a progressive splenic lesion in a patient with ductal adenocarcinoma of the pancreatic head/tail that was finally demonstrated as SANT¹⁷. In our case, the splenic lesion showed a slight progression in size as well. Unfortunately, there have been no reports in literature on exact growth rates and growth patterns of SANT. However, as SANT is known to be a benign lesion, one would expect no increase in size and a stable appearance in radiological controls. If this is not the case, malignancy should at least be considered.

To sum up, diagnostic workup of suspected SANT remains unsatisfactory as these lesions show a different growth pattern and do not exhibit specific radiologic characteristics that demonstrate diagnosis of SANT in all cases. Hence, it is virtually impossible to exclude a malignant process by preoperative radiologic studies, and malignancy has to be considered as the main differential diagnosis.

Since in our case the patient had a history of surgical resected colon cancer, and as there was an additional simultaneous lesion in the liver that was highly suspicious of metachronous liver metastasis, the splenic tumour had to be considered malignant unless otherwise proven. Even in case of radiological signs that favour a benign process in the spleen, this would not have changed further treatment which included splenectomy to rule out metastasis in the spleen. We conclude that in case of cancer patients, splenic lesions should be treated as potential metastatic lesions. Therefore, regardless of radiological findings, histological examination should be recommended in most cases for diagnosis and treatment. On occasion, fine needle aspiration biopsy might be used to ascertain a pathologic diagnosis. However, this intervention bears the risk of bleeding and tumour dissemination in case of malignancy²⁴. Therefore, splenectomy – usually being carried out by laparoscopic surgery – is performed in most cases^{25,26}. Although there are few indications for spleen preserving procedures, SANT could be considered an indication for performing partial splenectomy with potential benefit especially in younger patients²⁷.

In conclusion, SANT is an extremely rare vascular benign lesion of the spleen that is usually detected incidentally.

Our case report presents for the first time a multifocal manifestation of SANT that was found in a patient with simultaneous metachronous liver metastasis after surgery for colon cancer. Despite the fact that SANT should be considered as a differential diagnosis in any patient presenting with a splenic lesion, patients with a history of cancer present a very unique subgroup of patients with splenic lesions. Although malignant lesions of the spleen are very rare, no definitive radiological signs of SANT have been identified, and SANT seems to show differing growth patterns. Therefore, in our opinion splenectomy is indicated in most cases regardless of radiological findings that might suggest SANT, as a final diagnosis of SANT is made on the basis of histopathology only. Due to the fact that most tumours of the spleen are benign, suspicious splenic lesions – even in patients with a history of malignancy – never preclude potentially curative treatment strategies.

References

- Kaza RK, Azar S, Al-Hawary MM, et al. *Primary and secondary neoplasms of the spleen*. *Cancer Imaging* 2010;10:173-82.
- Warshauer DM, Hall HL. *Solitary splenic lesions*. *Semin Ultrasound CT MR* 2006;27:370-88.
- Arber DA, Strickler JG, Chen YY, et al. *Splenic vascular tumors: a histologic, immunophenotypic, and virologic study*. *Am J Surg Pathol* 1997;21:827-35.
- Martel M, Cheuk W, Lombardi L, et al. *Sclerosing angiomatoid nodular transformation (SANT): report of 25 cases of a distinctive benign splenic lesion*. *Am J Surg Pathol* 2004;28:1268-79.
- Falk GA, Nooli NP, Morris-Stiff G, et al. *Sclerosing Angiomatoid Nodular Transformation (SANT) of the spleen: Case report and review of the literature*. *Int J Surg Case Rep* 2012;3:492-500.
- Kamaya A, Weinstein S, Desser TS. *Multiple lesions of the spleen: differential diagnosis of cystic and solid lesions*. *Semin Ultrasound CT MR* 2006;27:389-403.
- Krishnan J, Frizzera G. *Two splenic lesions in need of clarification: hamartoma and inflammatory pseudotumor*. *Semin Diagn Pathol* 2003;20:94-104.
- Silverman ML, LiVolsi VA. *Splenic hamartoma*. *Am J Clin Pathol* 1978;70:224-9.
- Kaw YT, Duwaji MS, Knisley RE, et al. *Hemangioendothelioma of the spleen*. *Arch Pathol Lab Med* 1992;116:1079-82.
- Langer R, Dinges J, Dobritz M, et al. *Sclerosing angiomatoid nodular transformation of the spleen presenting as a rapidly growing tumour in a patient with rectal cancer*. *BMJ Case Rep* 2009. 2009. Epub 2009 Sep 15.
- Lee D, Wood B, Formby M, et al. *F-18 FDG-avid sclerosing angiomatoid nodular transformation (SANT) of the spleen: case study and literature review*. *Pathology* 2007;39:181-3.
- Thacker C, Korn R, Millstine J, et al. *Sclerosing angiomatoid nodular transformation of the spleen: CT, MR, PET, and 99(m)Tc-sulfur colloid SPECT CT findings with gross and histopathological correlation*. *Abdom Imaging* 2010;35:683-9.
- Koreishi AF, Saenz AJ, Fleming SE, et al. *Sclerosing angiomatoid nodular transformation (SANT) of the spleen: a report of 3 cases*. *Int J Surg Pathol* 2009;17:384-9.
- Sitaraman LM, Linn JG, Matkowskyj KA, et al. *Sclerosing angiomatoid nodular transformation of the spleen masquerading as a sarcoma metastasis*. *Rare Tumors* 2010;2:e46.

- ¹⁵ Gutzeit A, Stuckmann G, Dommann-Scherrer C. *Sclerosing angiomatoid nodular transformation (SANT) of the spleen: sonographic finding*. J Clin Ultrasound 2009;37:308-11.
- ¹⁶ El Demellawy D, Nasr A, Alowami S. *Sclerosing angiomatoid nodular transformation of the spleen: case report*. Pathol Res Pract 2009;205:289-93.
- ¹⁷ Raman SP, Singhi A, Horton KM, et al. *Sclerosing angiomatoid nodular transformation of the spleen (SANT): multimodality imaging appearance of five cases with radiology-pathology correlation*. Abdom Imaging 2013;38:827-34.
- ¹⁸ Chouchane Mlik O, Lardenois S, Salmon R, et al. *[Sclerosing angiomatoid nodular transformation of the spleen]*. Ann Pathol 2008;28:317-20.
- ¹⁹ Pox C, Aretz S, Bischoff SC, et al. *[S3-guideline colorectal cancer version 1.0]* Z Gastroenterol 2013;51:753-854.
- ²⁰ Kashiwagi S, Kumasaka T, Bunsei N, et al. *Detection of Epstein-Barr virus-encoded small RNA-expressed myofibroblasts and IgG4-producing plasma cells in sclerosing angiomatoid nodular transformation of the spleen*. Virchows Arch 2008;453:275-82.
- ²¹ Diebold J, Le Tourneau A, Marmey B, et al. *Is sclerosing angiomatoid nodular transformation (SANT) of the splenic red pulp identical to inflammatory pseudotumour? Report of 16 cases*. Histopathology 2008;53:299-310.
- ²² Cao JY, Zhang H, Wang WP. *Ultrasonography of sclerosing angiomatoid nodular transformation in the spleen*. World J Gastroenterol 2010;16:3727-30.
- ²³ Lewis RB, Lattin GE Jr, Nandedkar M, et al. *Sclerosing angiomatoid nodular transformation of the spleen: CT and MRI features with pathologic correlation*. AJR Am J Roentgenol 2013;200:W353-60.
- ²⁴ Caraway NP, Fanning CV. *Use of fine-needle aspiration biopsy in the evaluation of splenic lesions in a cancer center*. Diagn Cytopathol 1997;16:312-6.
- ²⁵ Mohr Z, Klippel S, Spiethoff A, et al. *[Laparoscopic splenectomy for sclerosing angiomatoid nodular transformation]*. Chirurg 2011;82:714-8.
- ²⁶ Kim KH, Lee S, Youn SH, et al. *Laparoscopic splenectomy for sclerosing angiomatoid nodular transformation of the spleen*. J Korean Surg Soc 2011;80(Suppl 1):S59-62.
- ²⁷ Budzyński A, Demczuk S, Kumiega B, et al. *Sclerosing angiomatoid nodular transformation of the spleen treated by laparoscopic partial splenectomy*. Wideochir Inne Tech Malo Inwazyjne 2011;6:249-55.