Retrospective Study

Reappraisal of surgical decision-making in patients with splenic sclerosing angiomatoid nodular transformation: Case series and literature review

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Author contributions: Tseng H drafted the manuscript; Tseng H and Ho CM designed the study; Tseng H conducted data processing; Tseng H, Ho CM and Tien YW performed data analysis; Ho CM and Tien YW were the directors responsible for general organization and instruction; all authors have read and agreed to the published version of the manuscript.

Institutional review board statement: This study was approved by the Institutional Review Board of the National Taiwan University Hospital, Taipei, Taiwan (NTUH REC: 202102011RIND).

Informed consent statement: Because this was a retrospective study using chart review, the institutional review board waived the need for informed consent.

Conflict-of-interest statement: Tseng H, Ho CM and Tien YW all declare no conflict of interest.

Data sharing statement: The

Abstract

BACKGROUND
Many clinicians and surgeons are unfamiliar with the sclerosing angiomatoid nodular transformation (SANT), which is gaining recognition as a benign splenic tumor. We challenge that SANT is rare and whether surgical intervention could be avoided through critical imaging review.

AIM
To evaluate the incidence of SANT among splenic tumors and the decision-making process of SANT management.

METHODS
Twenty hospitalized patients who underwent splenectomy in 2018 and 2019 in a tertiary university hospital were retrospectively reviewed, and their data on imaging, diagnosis, surgical indications, and courses were recorded. All pathology results were confirmed by pathologist. Discriminative features differentiating SANT from other non-SANT splenic tumors were descriptively analyzed in this case series.

RESULTS
Fourteen out of 20 patients who underwent splenectomy had splenic tumors, including 3 SANTs (21% splenic tumors), 6 non-SANT benign lesions (43%), 2 metastatic tumors, and 3 lymphomas. Hypointensity on T2-weighted magnetic
Splenectomy is commonly performed in the setting of hematological autoimmune disease (idiopathic thrombocytopenic purpura and autoimmune hemolytic anemia) and malignancies[7], whereas for other splenic tumors (including SANT), the indications are not well recognized. In our study, we reviewed the patients who underwent splenectomy for splenic tumors and found that many SANTS were diagnosed within a short period. We hypothesize that SANT is not rare, but an
unrecognized disease entity. We aimed to evaluate the decision-making process for the management of SANT (conservative observation or surgery) by determining the typical imaging features to distinguish SANT and critically review current indications for splenectomy in the literature.

**MATERIALS AND METHODS**

We retrospectively reviewed 20 hospitalized patients who underwent splenectomy at the National Taiwan University Hospital in 2018 and 2019. Six patients were excluded from the study because the indications for splenectomy were not the presence of tumors. Fourteen eligible patients were further divided into SANT and non-SANT groups based on the histopathological diagnosis. Demographic and clinical characteristics, including age, sex, symptoms, past history, radiographic imaging findings [CT, MRI, positron emission tomography (PET)], tentative diagnosis made by radiologists, operative methods (open or laparoscopic), and postoperative complications were reviewed. Furthermore, we compared the imaging features of SANT and non-SANT tumors largely based on literature[1-3,8], with an intent to identify the decisive factor distinguishing non-SANT from SANT. This study was approved by the Institutional Review Board of the National Taiwan University Hospital, Taipei, Taiwan (NTUH REC: 20210201RIND). Because this was a retrospective study using chart review, the institutional review board waived the need for informed consent.

**Table 1 Characteristic of three patients with sclerosing angiomatoid nodular transformation**

| No. | Age (yr) | Sex | Indication | Symptoms | Size (cm) | CT | MRI | PET | Follow up | Surgery |
|-----|----------|-----|------------|----------|-----------|----|-----|-----|-----------|---------|
| 1   | 48       | M   | Diagnostic splenectomy, for atypical hemangioma MRI pattern, suspect lymphoma | 8 kg loss in 2 yr; left abdominal pain; fatigue | 5.5 | Septate enhancement | Mild progressing peripheral enhancement with centrally remained iso-hypodense | Iso-hypodense/iso-hypodense | Heterogenous gradual enhancement and diffusion restriction | Nil | 2 mo | Open |
| 2   | 61       | F   | Diagnostic splenectomy, for elevated CA19-9, malignancy cannot be ruled out | Nil | 4.1 | Mild enhancement | Mild progressing peripheral enhancement with centrally remained iso-hypodense | Iso-hypodense/hypodense | Mild peripheral enhancement | Nil | 6 mo | Laparoscopy |
| 3   | 52       | M   | Diagnostic splenectomy, for suspect lymphoma splenic involvement | Nil | 3.5 | Peripheral enhancement | Nil | Nil | Nil | 4 mo | Laparoscopy |

1Underlying with B-cell non-Hodgkin lymphoma, Ann Arbor stage IV, IPI score 2, suspected marginal zone lymphoma, status post R-CHOP (VI, 2019/1/7-2019/07/19).
2SUVmax: maximum standardized uptake value.
SUV: Standardized uptake value; CT: Computed tomography; MRI: Magnetic resonance imaging; PET: Positron emission tomography; Non contrast CT: Iso-hypodense.
Figure 1 Schema of patient selection process and splenic tumor classification. SANT: Sclerosing angiomatoid nodular transformation; HCC: Hepatocellular carcinoma; NTUH: National Taiwan University Hospital.

**Statistical analysis**

Descriptive statistics were used to summarize the characteristics (frequency distribution, central tendency, and variation) of the dataset. Data are presented as mean, median, range, or percentage when appropriate. Analysis were performed using the Statistical Package for Social Sciences (SPSS)® version 21.0 (SPSS Inc., Chicago, IL, United States).

**RESULTS**

**Patients**

Between 2018 and 2019, 20 patients underwent splenectomy (11 open and 9 Laparoscopic approaches). Their surgical indication and final pathologic diagnosis are shown in Figure 1. Among these, 14 cases were splenic tumors, and 9 (64.3%) were benign, including 3 cases of SANT. Malignant tumors included two metastatic lesions (renal cell carcinoma and lung pleomorphic carcinoma), and three newly diagnosed lymphomas, with a median hospital stay of eight days (4-105 d). One patient with diffuse large B-cell lymphoma underwent re-operation for gastric perforation 12 d after open distal pancreatectomy and splenectomy, and was transferred to the intensive care unit after re-open surgery. A total of seven patients had minor complications (two cases of intra-abdominal infection, two cases of pneumonia, and three cases of wound infection) according to the Clavien-Dindo classification.

**Clinical features of SANT**

The clinical characteristics of the three patients who were finally diagnosed with SANT are summarized in Table 1. The average tumor size was 4.7 cm (3.5-5.5 cm). On CT scan, all three tumors showed non-contrast hypodense to isodense lesions with progressive peripheral enhancement, with a hypodense center in the venous phase.
Case 1 showed a typical lobulated lesion and separte enhancement, which is referred to as centripetal enhancement or spoke wheel pattern.\(^2\) SANTs cases 1 and 2 had hypo- to iso-intense appearance on T1-weighted and T2-weighted sequences, with peripheral or lobulated enhancement (Figure 2). Case 3 underwent a PET scan for lymphoma follow-up, and presented with diffuse mild hypermetabolism within the splenic tumor (standardized uptake value max = 4.2, Figure 2F). Splenectomy was indicated for diagnostic purpose (\(n = 2\)) or symptom relief (\(n = 1\)).

**Image characteristics of non-SANT splenic tumors**

Splenectomies performed for other benign or malignant splenic tumors (\(n = 11\)) were included in this study to compare imaging features of SANT and five types of non-SANT tumors (Table 2). All 20 splenic tumors were hypodense on non-contrast CT. Some features, such as enhancement patterns (e.g., peripheral for hemangioma and poor for lymphoma) may be suggestive of SANT, but are difficult for radiologists to definitely diagnose. We reasoned that MRI outperformed CT in that hyperintensity on T2-weighted images (Figure 3) could suggest hemangioma or non-lymphoma metastasis (Figure 3B and D), and the latter is rarely found in patients without an underlying malignancy.\(^9\) In contrast, both SANT and lymphoma showed hypo-intensity on T2 and a poor enhancement pattern (Figure 3A and C). Homogeneous splenomegaly with a focal infarct (Figure 4A) or multifocal splenic tumors (Figure 4B) could indicate a systemic lymphoma; however, when isolated lymphoma presents as a solitary splenic tumor (Figure 4C), distinguishing it from SANT becomes difficult because the spoke-wheel pattern can also be seen in lymphoma (Figure 4C and D). Additional imaging, such as PET (Figure 2F), or biopsy are necessary if splenectomy is not considered.

**Splenectomy for splenic tumors**

No cases of SANT were diagnosed preoperatively. Indications of splenectomy for two cases of SANT and five malignant splenic tumors were oncological concerns. Interestingly, although one MRI reported a splenic tumor resembling lymphoma or SANT, splenectomy was still performed for the increasing tumor size, and the final diagnosis given was lymphoma. Notably, none of the three lymphomas in our series had abnormal blood parameters.

The indications for splenectomy in the two metastatic cases were a rapidly enlarging cystic lesion (8 cm in 6 mo) during follow-up and a newly suspected metastasis showing hyperintensity on T2-weighted images with central necrosis (Figure 3D).

Benign neoplasms in our series other than SANT were resected due to symptoms or an increase in size during follow-up, and the final pathologic reports were compatible with the preoperative diagnoses.

**DISCUSSION**

In our small cohort including patients from the 2-year study period, SANT was not uncommon, accounting for 3 out of the 14 splenic tumors. Since the first case series published in 2004\(^4\), less than 200 cases have been reported, and almost all reports defined this novel lesion as a rare benign tumor. A disease is defined as rare when the approximate case number ranges between 1/1500 and 1/2000.\(^10,11\) We argue that SANT is unidentified rather than rare in common clinical practice. Milosavljević et al [12] reported that SANT represented 3.3% of all the benign lesions that underwent splenectomy and in our series, 21.4% of all splenectomies in the 2 years. As more SANT cases are reported in the literature, the term “rare” may be inappropriate and deviates from reality.

Differential diagnosis of splenic tumors based on imaging features is generally difficult. However, T2 weighted imaging on MRI may provide additional diagnostic value for SANT (hypointensity) by excluding hemangioma and metastasis (hyperintensity). The presence of primary malignancy also suggests a diagnosis of metastatic splenic tumor\(^13\), although rare. Solitary splenic metastasis is more uncommon, with only 5% of all metastases involving the spleen.\(^9\) The chance of spleen as a metastatic focus is probably considered only in patients with an underlying known malignancy. Although rare, solitary lymphoma\(^8\) could appear very similar to SANT on CT or MRI. Clinical clues, such as lymphadenopathy, hepatomegaly, symptoms of systemic lymphoma\(^1\) tumor central necrosis, cytopenia, and size-increasing primary splenic lymphoma may help distinguish lymphoma from SANT.\(^1,14\) However, SANT may coexist with extraspelic lymphoma, as seen in case 3 in Table 1.
Table 2 Comparison of Image characteristics among common splenic tumor

| Tumor | Tumor shape, features, and characteristics | MRI T1 | MRI T2 | CT/MRI enhancing pattern | Other image characteristics probably aid diagnosis |
|-------|------------------------------------------|-------|-------|--------------------------|-----------------------------------------------|
| Benign | SANT | Well-circumscribed, commonly lobulated, solitary mass | Isointense | Hyperintense | Spoke-Wheel pattern; Poor enhancement | PET/CT: Low FDG accumulation |
| Hemangioma | Single nodule; multiple nodules; diffuse masses enlarging the spleen | Hypointense | Hyperintense | Homogenous or peripheral enhancement | Mostly small, asymptomatic, and slow growth |
| Cyst | Cystic lesion | Hypointense | Hyperintense | No enhancement | Ultrasound: Thin wall, anechoic, peripheral brightly echogenicity, and distal shadows due to wall calcification |
| Malignant | Systemic lymphoma | Homogenous splenomegaly; Infiltrative miliary lesions (1-5 mm); Multifocal lesions (2-10 cm); Uncommon solitary lesions (7-14 cm) | Isointense | Hyperintense | Poor enhancing | Splenomegaly; Splenic infarct; PET: Intense heterogenous FDG activity; Extra-splenic findings: Hepatomegaly, lymphadenopathy |
| Primary splenic lymphoma | Solitary mass > uncommonly Splenomegaly | Isointense | Hyperintense | Poor enhancing | Central necrosis |
| Metastasis | Variously | Isointense | Hyperintensity | Similar to the primary tumor | PET/CT: FDG-avid tumor; Poorly marginated; Heterogenous |

CT: Computed tomography; MRI: Magnetic resonance imaging; PET: Positron emission tomography; FDG: Fluorodeoxyglucose.

Table 3 Indication list of splenectomy proposed for splenic tumors

| Imaging features | Rationale for splenectomy |
|------------------|--------------------------|
| Benign tumor: Cyst; Hemangioma; SANT; other | Symptom-relief |
| | Probable splenic rupture |
| | Increasing tumor size or numbers |
| | Rule out malignancy with atypical image features |
| | Patient desire |
| Lymphoma | Symptom-relief |
| | Treatment for cytopenia without heavy bone marrow infiltration |
| | Diagnosis for tissue proof to determine the nature of lymphoma |
| Angiosarcoma | Treatment |
| Metastasis | Total tumor free |
| | Debunking after chemotherapy |
| | Diagnosis and total tumor free for isolated splenic metastasis |

SANT: Sclerosing angiomatoid nodular transformation.

glucose uptake in the PET scan may be a promising diagnostic feature of lymphoma, which warrants further investigation[15].

Management of splenic tumors involves conservative follow-up or surgical resection. Surgical resection (total or partial splenectomy) is universally recommended for the diagnosis and treatment of SANT in the literature[16]; however, since a diagnosis can be made without pathology, the indication for surgery is questionable. Recently, Jin et al[16] reported a large series of 37 patients who were diagnosed with SANT over a 10-year-period, estimating an average of 4 cases per year. This finding was consistent with our statement that SANT should not be considered a rare tumor. A further review of 37 patients revealed that progressive enhancement was present in 9 cases on dynamic contrast-enhanced MRI studies that also looked more like
Figure 2 Typical image features of sclerosing angiomatoid nodular transformation. A-C: Computed tomography (CT), non-contrast (A), arterial phase (B), venous phase (C) (Case 2); D and E: Magnetic resonance imaging (MRI), MRI T1 (D), MRI T2 (E) (Case 1); F: Positron emission tomography-CT (Case 3).

malignant disease. Splenectomy could have been avoided in at least 28 cases, if SANT was identified by the clinicians[16]. We propose a list of indications for splenectomy for splenic tumors (Table 3). For those with typical imaging features of benign tumors, such as cysts, hemangiomas, and SANTs, symptoms were the most reasonable indication for splenectomy, although malignant splenic tumors tend to be more symptomatic than benign tumors[17]. For suspected benign splenic tumors, surgical intervention is appropriate for increasing size, splenic rupture, patient decision, and diagnostic purpose. In addition to surgical complications, splenectomy may be associated with an increased risk of infection, thromboembolism, and possibly cancer development[18]. When diagnosed, malignant splenic tumors do not always require splenectomy. Accumulating evidence has shown that splenic lymphoma can be effectively treated with immunotherapy, resulting in a decreasing need for therapeutic splenectomy[19,20]. Splenectomy for splenic lymphoma is reserved for patients who experience abdominal fullness due to large spleens and cytopenia due to spleen sequestration[19,20]. Diagnosis of tissue proof to determine the nature of lymphoma could be another important indication of splenectomy for highly suspected systemic lymphoma with absence of a definite diagnosis from another site. Splenectomy for splenic metastasis can be beneficial in metastatic carcinoma, either to achieve tumor-free status or to reduce tumor load in debulking surgery (such as ovarian cancer)[9]. Splenectomy could be avoided in disseminated metastatic disease because the benefit of survival or diagnosis remains low.
If surgery is not performed based on the radiological findings, the best strategy for the follow up of these patients and how the patients are counselled require additional consideration. In patients with underlying malignancies, the follow-up interval could be in line with the current schedule. As for incidental cases, 6-mo or 12-mo follow-up imaging is recommended[13]. The changing nature of tumor in images or clinical presentation should initiate a surgical re-evaluation. However, if patients do not feel reassured after counselling, an individualized decision of a short-interval follow-up recommendation or a direct referral to a surgeon is also justified.

Our study is limited by the small number of patients and its retrospective nature, precluding an extensive analysis of the specificity and sensitivity of imaging features. Patients who underwent conservative management of splenic tumors were not included. However, we aim to raise the awareness of this emerging diagnosis of SANT, which is currently categorized as a rare disease, but hopefully will be more commonly recognized with time, among clinicians and surgeons. We hope that this would assist the decision-making in the future management of splenic tumors, particularly SANT.

CONCLUSION

SANT should be considered uncommon. The surgical indications for SANT should be reconsidered. Further studies are needed to confirm the diagnostic features of SANT in imaging, such as hypo-intensity on T2-weighted images of MRI and spoke wheel enhancing pattern.
ARTICLE HIGHLIGHTS

Research background
Clinicians are not familiar with the sclerosing angiomatoid nodular transformation (SANT), which is gaining recognition as a benign splenic tumor.

Research motivation
We challenge that SANT is rare and whether critical imaging review could help avoid unnecessary splenectomy.

Research objectives
This study aimed to evaluate the incidence of SANT among splenic tumors and the decision-making process of SANT management.

Research methods
Twenty hospitalized patients who underwent splenectomy in 2018 and 2019 in a tertiary university hospital were retrospectively reviewed. Discriminative features differentiating SANT from other non-SANT splenic tumors were descriptively analyzed.

Research results
Fourteen splenectomies were indicated for splenic tumors, including 3 SANTs (21%). Hypointensity on T2-weighted magnetic resonance imaging, spoke wheel enhancing pattern, and cold spot in positron emission tomography scan helped establish the diagnosis of SANT. Splenectomy need not be performed in patients with typical imaging features of SANT.

Research conclusions
SANT is not rare. Splenectomy should not be routinely indicated as the only management option for SANT with typical imaging features.
**Research perspectives**

Further studies are needed to confirm the diagnostic imaging features of SANT in the future.

**ACKNOWLEDGEMENTS**

We thank Dr. Chen CY (Division of Hematology, Department of Internal Medicine, National Taiwan University Hospital) for providing critical comments.

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