Acute Splenic Infarction at an Academic General Hospital Over 10 Years

Presentation, Etiology, and Outcome

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Abstract: Few case series provide a current, comprehensive, and detailed description of splenic infarction (SI), an uncommon condition.

Retrospective chart review complemented by imaging evaluation and patient follow-up.

All adult patients with a confirmed diagnosis of acute SI discharged over 10 years from a single academic center were studied. A systematic literature review was done to compile a complete list of SI etiologies. SI was found in 32 patients, 0.016% of admissions. Ages ranged from 18 to 86 (median 64) years. Cardiogenic emboli were the predominant etiology (20/32, 62.5%) and atrial fibrillation was frequent. Other patients had autoimmune disease (12.5%), associated infection (12.5%), or hematological malignancy (6%). Nine of the patients (28%) had been previously healthy or with no recognized morbidity predisposing to SI. In 5 of 9 hitherto silent antiphospholipid syndrome or mitral valve disease had been identified. Two remained cryptogenic. Most patients presented with abdominal pain (84%), often felt in the left upper quadrant or epigastrium. Associated symptoms, leukocytosis or increased serum lactate dehydrogenase occurred inconsistently (~25% each). Chest X-ray showed suggestive L.t. supra-diaphragmatic findings in 22%. Thus, the typical predisposing factors and/or clinical presentation should suggest SI to the clinician and be followed by early imaging by computed tomography (CT), highly useful also in atypical presentations. Complications were rare and patients were discharged after 6.5 days (median) on anticoagulant treatment. The systematic literature review revealed an extensive list of conditions underlying SI.

In some, SI may be the first and presenting manifestation.

SI is a rare event but should be considered in predisposed patients or those with any combination of suggestive clinical features, especially abdominal pain CT evaluation is diagnostic and the outcome is good.

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Abbreviations: (P)AF = (paroxysmal) atrial fibrillation, APS = antiphospholipid syndrome, AVR = aortic valve replacement, CHADS2 = Risk score of arterial thromboembolism in AF, IE = infective endocarditis, LAC = lupus anticoagulant, LDH = lactate dehydrogenase, Lt = left, LUQ = left upper quadrant, RLQ = right lower quadrant, RUQ = right upper quadrant, SI = splenic infarction, SLE = systemic lupus erythematosus, TEE = trans-esophageal echocardiography, VZV = varicella zoster virus, WBC = white blood cells.

INTRODUCTION

Splenic infarction (SI) occurs when the splenic artery or 1 or more of its branches become occluded, either by an embolus or by in situ thrombosis.1 The spleen has a rich vascular supply and receives 5% of the cardiac output making it susceptible to emboli (cardiogenic, aortic, paradoxical).2 Furthermore, it is not infrequently affected by malignant hematological disorders which increase the risk of thrombosis.3,4 Only a few series of SI patients have been reported, and some of them are too old or too selective to be really useful. In addition, the current widespread availability and escalating early use of computed tomography (CT) scanning5 may have changed its etiologic distribution and presenting features. The ongoing publication of single case studies of SI in peer reviewed journals emphasizes the continued interest in the diagnostic challenge that SI often poses,6 and in its myriad etiologies which can be highly unusual.7

We have conducted a retrospective case series study of all patients diagnosed with SI at a single academic medical center over 10 years, emphasizing a detailed analysis of clinical clues to the diagnosis and including a comprehensive review of the literature listing all reported causes of SI.

PATIENTS AND METHODS

Kaplan Medical Center is an academic general hospital in central Israel caring for a mixed urban and rural population of 400,000 people. Following Institutional Review Board approval, the charts and imaging studies of all adult patients (ages 18 years and over) discharged from our 4 departments of medicine with an ICD-9 coded diagnosis of infarction of spleen were separately examined by 2 experienced clinicians and a radiologist. All patients whose SI diagnosis was confirmed were included in the study. Confirmation required unequivocal CT findings. In cases of disagreement, inclusion was dependent on a unanimous agreement following discussion. Demographic, past medical history, clinical, laboratory, and imaging details of each patient were obtained, as well as results of echocardiography, Holter monitoring and work up for an underlying disease.8 All imaging studies (chest X-ray, ultrasound, CT) were evaluated by 2 of the authors (AM, SA) to determine degree of SI (small <1/3 of the spleen; moderate; or extensive ≥2/3) and any associated supra-diaphragmatic findings (Lt. pleural effusion, Lt. lower lobe linear atelectasis, or none).
Patients who died from SI were included. Follow-up was obtained by examining hospital charts for any admissions or ambulatory visits occurring after the index admission as well as by contacting the patient’s primary care physician for an update on the patient’s condition and recommending repeated testing as needed. Statistical analysis was performed by using Chi-squared test. In addition, all related PubMed-indexed articles (spleen AND infarction or infarct; English language; since inception; adult 19+ years) were screened (n = 533). Relevant manuscripts were retrieved and read to confirm validity of the diagnoses and their references examined to compile a comprehensive list of all reported etiologic associations of SI.

RESULTS

During the 10 years of the study (January 2004 to December 31, 2013), there were 196,625 admissions to our division of medicine. Only 32 confirmed cases of SI have been found, 0.016% of admissions. Their essential background, presentation, pertinent laboratory data, imaging analysis, and outcome are reported in detail in Appendix, http://links.lww.com/MD/A395. Figure 1 demonstrates typical imaging findings. Patients’ ages ranged from 18 to 86 years (median 64 years) and 50% were male (n = 16). Their final etiologic classification is summarized in Table 1. Cardiogenic emboli were by far the major etiologic mechanism (20/32, 62.5%), followed by autoimmune disease and infection-associated SI (4/32, 12.5% each). Two patients had a predisposing hematological disease with marked splenomegaly and 2 remain cryptogenic despite follow up and repeated investigations. The existence of a morbidity associated with SI was known in 23 of 32 patients (72%): 20 had structural heart disease begetting atrial fibrillation (AF) and cardiogenic emboli and the remainder had hematological cancer or systemic lupus erythematosus. Notably, AF was not always documented (5/20, 3 had infective endocarditis [IE] or aortic valve replacement) and SI

TABLE 1. Etiologic Classification of All Patients Diagnosed With Splenic Infarction (SI) at an Academic Medical Center Over 10 Years (n = 32)

| I. Cardiogenic Emboli (n = 20) |
|--------------------------------|
| a. In the context of hypertensive heart disease and/or coronary artery disease 11 |
| Associated atrial fibrillation 8 (No. 4, 6, 9, 10, 11, 12, 25, 26) |
| Atrial fibrillation not demonstrated 2 (No. 20, 30) |
| Acute anterior wall myocardial infarction 1 (No. 13) |
| b. Associated with cardiac procedures (“iatrogenic”) 3 |
| After catheter ablation 1 (No. 3) |
| After electrical cardioversion 1 (No. 5) |
| After coronary angiography 1 (No. 14) |
| c. Infective endocarditis-associated 2 (No. 15, 24) |
| d. Valvular disease-associated 4 |
| Rheumatic mitral valve disease (No. 16, 29) |
| Myxomatous degeneration of the mitral valve (No. 28) |
| Aortic valve replacement (No. 17) |
| II. Autoimmune disease (n = 4) |
| Antiphospholipid syndrome 2 (No. 1, 7—both lupus anticoagulant positive and No. 18) |
| Systemic lupus erythematosus (APS not found) 1 (No. 22) |
| III. Infection-associated (n = 4) |
| Peripancreatic abscess (No. 19) |
| Varicella zoster virus (VZV) infection (No. 21) |
| Septicemia, in patients with extensive atherosclerosis (No. 23, 27) |
| IV. Hematological disease (n = 2) |
| Myeloproliferative disorder (No. 8) |
| Myelodysplastic syndrome (No. 2) |
| V. Cryptogenic (n = 2) (No. 31, 32)z |

For full individual patient data see Appendix, http://links.lww.com/MD/A395. APS = antiphospholipid syndrome.

* This patient’s presentation with PAF and SI led to the diagnosis of pericarditis with effusion.

† Trans-esophageal echocardiography before the procedure did not reveal any cardiac thrombi.

‡ Extensive investigations after the event proved negative and prolonged course (6–9 years) was uneventful without extended anticoagulant treatment. One patient (No. 18) formerly considered cryptogenic SI received a diagnosis of APS based on persistently positive anti-cardiolipin and anti-β2 glycoprotein antibodies discovered 9 years after the event.
TABLE 2. Previously Unsuspected Diagnoses Discovered in Patients Presenting With Splenic Infarction (n = 8)

| Diagnosis                          | Number of Patients |
|------------------------------------|--------------------|
| Antiphospholipid syndrome          | 3                  |
| Mitral stenosis                    | 3 (associated flutter—fibrillation) |
| Mitral regurgitation, severe       |                    |
| Infective endocarditis (multiple emboli) |                |
| Pericarditis/pericardial effusion (associated atrial fibrillation) | 1 |
| Splenic vein thrombosis            | 2                  |
| VZV infection*                     | 1                  |

*Patients who were previously healthy or had no known disease predisposing to splenic infarction.

sometimes followed planned cardiac procedures (3/20) (Table 1). Nine of the patients (28%) had been previously healthy or with no disease predisposing to SI. A new diagnosis underlying the SI was discovered in 6 (66.6%) including 3 antiphospholipid syndrome (APS), 2 unsuspected mitral valve disease, and 1 splenic vein thrombosis associated with a peri-pancreatic abscess (Table 2). One APS patient was considered cryptogenic on discharge and diagnosed when retested during our study. In 2 patients, the SI was considered cryptogenic on discharge and diagnosed when retested during our study. In 2 patients, the SI was diagnosed when retested during our study. In 2 patients, the SI was diagnosed when retested during our study. In 2 patients, the SI was diagnosed when retested during our study. In 2 patients, the SI was diagnosed when retested during our study. In 2 patients, the SI was diagnosed when retested during our study.

### DISCUSSION

The survey of the literature clearly demonstrates the great diversity of mechanisms and etiological association reported for SI, which cannot be fully captured by any patient series (Table 3). Varied mechanisms of arterial embolization and hypercoagulability may mediate SI and SI can even be their first presenting manifestation (Table 3).8,9 The spleen may also become susceptible to infarction by anatomic abnormalities facilitating torsion, or by intragenic damage following diverse abdominal procedures.10,11 Nevertheless, SI is a rare event. In our retrospective series, only 32 patients with an ICD-9 coded diagnosis of SI (confirmed by a review of the actual imaging) were found over 10 years in a single academic hospital—0.016% of admissions. Although the proportion of admissions was not previously reported, this observation is in agreement with previous studies. For example, a surgery-based group from Cleveland identified 75 patients over 10 years (1974–1984)12 and an emergency department-based study reported 48 patients over a similar period (1996–2007).13 We believe that the low incidence, the varied nonspecific clinical presentation, and the possible occurrence of SI as the first manifestation of an unsuspected disease add considerably to the diagnostic challenge and may contribute to underdiagnosis of SI.

Our study adds to the existing literature since not many series of SI have been published, and of those, quite a few are too old (80s),13,14 too selective (surgical-based; autopsy-based; exclusively embolic)14,16 or too laconic (providing only basic patient information).13,17 One study reports on 75 patients but only 15 of 75 had a CT scan; understanding of hypercoagulability was at its infancy; and 39 of 75 patients were asymptomatic and diagnosed at autopsy.12 Later series were limited to SI diagnosed at autopsy,13 on splenectomy,15 or included only patients who had SI after splenic emboli.16 Thus, they are informative but obviously highly selective and different from “real world” patients. Only 2 studies were more generalizable, but provide little individual patient detail; use nonspecific cutoff-points of WBC counts and LDH levels; and suffer from partial workup.13,17

Our study captures all patients with SI diagnosed over a decade in a single academic center and reports them in detail. Data derived are likely generalizable to other countries as well. Additional strengths of our study are the actual review of all imaging and extended follow-up by contacting the patients’ primary physicians and initiating repeated studies (eg, for APS) for patients whose SI had no clear etiology.

We found that roughly 2 of 3 of the patients had an obvious condition predisposing to SI. The majority had a known cardiovascular disease associated with cardiogenic splenic emboli (17/32, 53%; 3 other embolic SI patients had no known predisposing disease). Documented atrial fibrillation (AF) was often etc. and high likelihood of paroxysmal atrial fibrillation (PAF) that was etc. Three patients had SI in the setting of cardiac procedures despite a preceding normal trans-esophageal echocardiography. In previous series emboli also constitute the predominant pathogenetic mechanism of SI, ranging from 17% to 66.6% (median 38%), as compared to 62.5% in our series (Table 1, I). These data highlight a high potential of preventability of SI that is only partially exploited. More intensive monitoring techniques of patients at risk can detect hitherto unsuspected silent episodic AF and timely treatment can be initiated.18 Emboli originating from extensive aortic atherosclerotic plaques constitute an important subset according to the literature (Table 3) and a potential cause of SI.19 Between 19%
to 26.6% of embolic SI may originate in the aorta. 12,14 Many of these patients with extensive atherosclerosis are also at an increased risk of AF and once detected, embolic risk can be likely reduced by anticoagulant treatment. Even in the presence of an obvious cause of SI, an open mind for a new diagnosis should be kept. Two such patients (6.25%) had a new diagnosis underlying SI (IE and pericarditis) (Table 2). Among patients with a known susceptibility the minority had a hematological malignancy associated with splenomegaly (Table 1, IV). In former reports, a median of 26% hematological malignancy patients had been reported (range 8% to 51%), differences that can be related to ethnic factors.

When SI occurred in the absence of any known risk factors (9/32 patients, 28%) a new diagnosis was very likely (Table 2). Since unsuspected mitral valve disease and APS were prominent newly discovered etiologies, echocardiography and lupus anticoagulant testing are key investigations in this group. Four of 32 (12.5%) had infection-associated SI (other than IE). While associated sepsis/septic emboli had been previously reported, the occurrence of splenic vein thrombosis and SI in the wake of...
peri-pancreatic abscess is unusual and possibly related to septic thrombophlebitis, not unlike Lemierre syndrome.20 Another patient developed SI during an acute varicella zoster virus (VZV) infection as reported in other herpesvirus infections (Epstein–Barr virus and cytomegalovirus).13,21 not VZV.22 In 2 patients, SI remained cryptogenic (6%).

Our review of the literature in search of the full spectrum of diagnoses that were reported to be associated with SI was extensive, systematic, and reproducible. Table 3 summarizes all etiologic entities found to be associated with SI. We are not aware of any similar effort in the existing literature to date. The classification of etiologies into 3 categories (disease-associated; iatrogenic or traumatic; and cryptogenic SI) is useful in exposing the large variety of pathologic entities that may be associated with SI as well as its rarity—many have been described in isolated case reports. Intriguingly, SI may be the presenting symptom of several important conditions (Table 3), as our study also demonstrates.

While recognizing a known predisposing condition in a patient with unexplained abdominal pain may help clinicians in risk stratification and in considering SI, we found that at least 1 in 4 SI patients may have no known risk factors. Clinical features remain therefore crucial in raising the index of suspicion and suggesting the diagnosis. However, in our series, abdominal pain was the only reliable symptom or sign, and even that most consistent symptom may sometimes be absent (16% in our patients and 16% to 20% painless presentation in other recent series).3,11 Nevertheless, most patients presented with significant abdominal pain, often felt at the left upper abdomen (17/32, 53%) or epigastrum (6/32, 19%). Only few had associated vomiting or fever and the latter was usually related to IE or sepsis, not the infarction. Physical examination was noncontributory showing no more than mild diffuse abdominal tenderness. Previous studies discuss leukocytosis and LDH as helpful in diagnosis. However, mild elevations of the WBC are common and nonspecific and many blood samples show small factitious LDH elevation due to in vitro hemolysis. Using more stringent cut-off points, we found that significant leukocytosis or LDH increases occur in 25%, each, without inter-correlation, limiting their diagnostic utility. Furthermore, in patients who presented with without abdominal pain, neither were increased. The chest X-ray may demonstrate changes in the left hemithorax which are secondary to the subdiaphragmatic SI. Their detection on admission may offer an important clue; however, their sensitivity was low (22%). Thus, early imaging by CT remains crucial for SI diagnosis. A recent study examined imaging strategies for detection of urgent conditions in patients with acute abdominal pain.23 Although no patients with SI were captured (supporting the rarity of this diagnosis), prospective data collection among >1000 patients demonstrated that the initial strategy of choice for patients without right upper quadrant or right lower quadrant tenderness was early CT. Among patients with SI, despite data indicating frequent complications requiring surgery in 20.5% to 34%,12,15 our group fared generally well with a median hospital stay of 6.5 days and full recovery on supportive and anticoagulant treatment (in all but 1 case). This observation held true even for patients with extensive SI or associated infarctions.

Our study had several limitations including generalizability; the relatively small number of patients identified; the possibility that additional SI patients were admitted directly to surgical wards against hospital policy; the reliance on CT diagnosis; and the distinct possibility that additional patients with SI may have been missed. However, we believe that our results accurately describe all patients admitted with a confirmed diagnosis of SI and that they are generalizable to other populations. A review of admissions to surgery failed to discover additional SI patients. Nevertheless, the possibility that some patients with SI have not been admitted due to atypical presentation, low index of suspicion and failure to obtain imaging are realistic and supported by our data.

In conclusion, we presented a detailed analysis of a consecutive series of patients with SI, a rare diagnosis, diagnosed and treated over a decade at a single academic center. Myriad conditions can lead to SI (Table 3) and the patient population can be very heterogenic in its clinical presentation. A “full” or “typical” picture is often not found and diagnostic suspicion must depend on either the recognition of established predisposing factors or attention to suggestive presenting features (or both) leading to an early use of a CT scan whenever SI is suspected.

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