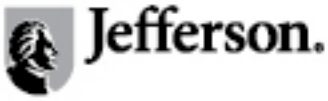

6-1-2010

Splenic infarction: an update on William Osler's observations.

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Splenic Infarction: An Update on William Osler's Observations

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ABSTRACT: **Background:** Osler taught that splenic infarction presents with left upper abdominal quadrant pain, tenderness and swelling accompanied by a peritoneal friction rub. Splenic infarction is classically associated with bacterial endocarditis and sickle cell disease.

Objectives: To describe the contemporary experience of splenic infarction.

Methods: We conducted a chart review of inpatients diagnosed with splenic infarction in a Jerusalem hospital between 1990 and 2003.

Results: We identified 26 cases with a mean age of 52 years. Common causes were hematologic malignancy (six cases) and intracardiac thrombus (five cases). Only three cases were associated with bacterial endocarditis. In 21 cases the splenic infarction brought a previously undiagnosed underlying disease to attention. Only half the subjects complained of localized left-sided abdominal pain, 36% had left-sided abdominal tenderness; 31% had no signs or symptoms localized to the splenic area, 36% had fever, 56% had leukocytosis and 71% had elevated lactate dehydrogenase levels. One splenectomy was performed and all patients survived to discharge. A post hoc analysis demonstrated that single infarcts were more likely to be associated with fever (20% vs. 63%, $p < 0.05$) and leukocytosis (75% vs. 33%, $P = 0.06$)

Conclusions: The clinical presentation of splenic infarction in the modern era differs greatly from the classical teaching, regarding etiology, signs and symptoms. In patients with unexplained splenic infarction, investigation frequently uncovers a new underlying diagnosis.

IMAJ 2010; 12: 362–365

KEY WORDS: splenic infarction, splenic infarct, bacterial endocarditis, abdominal pain, William Osler

The predominant causes of splenic infarction are thought to be bacterial endocarditis [1], sickle cell disease [2] and hematologic malignancy [3,4]. William Osler described the classical presentation in 1901: "… pain in the splenic region, tenderness on pressure, and slight swelling of the organ. On several occasions I have heard a well-marked peritoneal friction rub" [1]. Although a number of case series have been published, they do not focus on clinical presentation, nor do they reflect the typical case mix seen in modern clinical medicine. One study included asymptomatic patients diagnosed at postmortem [5]; other series were limited to patients who had undergone a splenectomy [6], whose cause was a cardiac embolus [7], and who were diagnosed by ultrasound [8]. The aim of the present study was to describe the clinical presentation of splenic infarction.

PATIENTS AND METHODS

We conducted a retrospective chart review of all cases of splenic infarction diagnosed among patients hospitalized during the period 1990–2003 at the Shaare Zedek Medical Center, a 550 bed university-affiliated hospital serving the general Jerusalem population. Demographic details, subjective complaints, findings on physical examination, results of investigations, and final diagnosis were obtained from the inpatient chart. When available, imaging studies were reviewed for the purpose of this study; if not available, original reports were analyzed. Patients whose files were missing or incomplete were excluded.

Statistical analysis was performed using the Epi 2000 version 3.2.2 program (CDC, Atlanta, USA). A P value of 0.05 was set as significant. The two-sided t-test and Fisher's exact test were used.

RESULTS

Between the years 1990 and 2003, 26 cases of splenic infarction were diagnosed at Shaare Zedek. Details of the individual cases are presented in Table 1, demographic and clinical features in Table 2, and etiology in Table 3.

More than 80% of the patients complained of abdominal pain, but in only 48% was pain localized to the left upper quadrant. Pain started a median of 4 days before presentation (range 0–60 days). Localized left upper quadrant abdominal tenderness was only found in 36% of cases. Splenomegaly was

Table 1. Clinical features of patients diagnosed with splenic infarction at Shaare Zedek Medical Center 1990–2003

Case #	Age	Gender	Presenting complaint	Chronic medical conditions	New diagnosis
1	9	F	Diffuse abdominal pain	Biliary atresia, Kasai procedure, HBV, old splenic infarction	
2	15	M	Diffuse abdominal pain	Aortic stenosis, renal artery stenosis	Cholesterol emboli from angiography, ARF
3	20	M	Center-left abdominal pain, dyspnea	Gaucher's disease	
4	20	M	Diffuse abdominal pain, sore throat	Crohn's disease	EBV, autoimmnue hemolytic anemia
5	24	F	Diarrhea, LUQ abdominal pain		Pregnancy, known wandering spleen
6	30	M	LUQ abdominal pain	None	SBE
7	31	F	Fever		CMV
8	35	M	Left abdominal pain	ASD, Eissenmenger's syndrome, 2nd polycythemia	SBE
9	40	F	LUQ abdominal pain	Psoriasis	Splenic / portal vein thrombosis, thrombophilia
10	42	M	Swollen leg, diffuse abdominal pain		Ca pancreas, cellulitis
11	47	M	LUQ pain	AML	
12	50	M	Vomiting, hemoptysis	Chronic pancreatitis, cirrhosis	Splenic vein thrombosis, MPD
13	50	M	Fever	Hemodialysis, NIDDM	Infected vascular graft
14	55	M	Epigastric pain, radiating to back	HOCM, AF, valvular heart disease	Under-coagulation
15	63	M	Dysuria	IHD, NIDDM	ARF, UTI sepsis, dehydration
16	65	M	Diffuse abdominal pain	AVR, MVR, AF	Under-coagulation
17	65	M	Swollen hand	MDS, 2nd hemochromatosis, NIDDM, IHD	Mucormycosis, infection of hand
18	67	M	LUQ abdominal pain	None	Small cell lymphoma
19	70	M	Left abdominal pain, vomiting	IHD, ET	SBE, splenic / portal vein thrombosis
20	73	F	Abdominal pain	NIDDM, PRV, HCV, nephrectomy	Splenic vein thrombosis
21	75	F	Chest pain, subsequent fever	CVA, HOCM,	MI
22	75	M	LUQ abdominal pain radiating to shoulder	AML, pneumonia	
23	77	F	Left abdominal and flank pain, hemiparesis	Rheumatic heart disease, CHF, AF	CVA
24	80	M	Chest pain, LUQ abdominal pain	IHD, diabetes	MI
25	81	M	Diffuse abdominal pain	CHF, IHD, COPD	PRV
26	87	F	LUQ abdominal pain & left flank pain	Previous CVA	

AF = atrial fibrillation, AML = acute myeloid leukemia, ARF = acute renal failure, ASD = atrial-septal defect, AVR = atrial valve replacement, CHF = congestive cardiac failure, CMV = cytomegalovirus mononucleosis, COPD = chronic obstructive pulmonary disease, CVA = cerebral vascular accident, EBV = Ebstein-Barr virus mononucleosis, ET = essential thrombocytosis, HBV = chronic hepaptits type B, HCV = chronic hepaptits type C, HOCM = hypertrophic obstructive cardiomyopathy, IHD = ischemic heart disease, LUQ = left upper quadrant, MI = myocardial infarction, MDS = myelodysplastic syndrome, MPD = myeloproliferative disease, MVR = mitral valve replacement, NIDDM = non-insulin dependent diabetes mellitus, PRV = polycythemia rubavera, SBE = subacute bacterial endocarditis, UTI = urinary tract infection

noted in one-third of subjects. Overall, 7 (27%), 10 (38%), 6 (23%), and 3 (12%) patients, respectively, presented with none, one, two or three of the features Osler associated with splenic infarction (localized left-sided abdominal pain, localized left-sided abdominal tenderness, and splenomegaly). A peritoneal friction rub was not recorded in any patient.

Liver function tests were entirely normal in 29% of cases. The most frequent abnormality was an elevated lactate dehydrogenase level, seen in 68% of subjects. Alkaline phosphatase levels were elevated in 29% of cases, and transaminase levels in only one case. Liver function test abnormalities were not influenced by the presence of underlying liver disease (data not presented).

Clinicians used a variety of modalities to diagnose the infarcts – computed tomography, ultrasound and nuclear medicine scan. In two cases (# 3 and 11) the diagnosis was based solely on clinical findings despite normal nuclear scans. Two predominant patterns of splenic infarction were seen: single (n=8) and multiple (n=16). The mean age of the patients presenting with these two patterns of infarct was similar, 43 versus 58 years (not significant). Single infarcts were more likely to be associated with fever (20% vs. 63%, $P < 0.05$) and leukocytosis (75% vs. 33%, $P = 0.06$). Palpable splenomegaly was rare in both groups but was more frequent in multiple infarcts (13% vs. 31%, not significant). Only one splenectomy was performed (case #9). All subjects survived to discharge.

DISCUSSION

Recent case series of splenic infarction have concentrated on etiology, diagnosis and outcome [5-8]. Since William Osler's

Table 2. Splenic infarction: demographic and clinical features of 26 cases

Demographics		
Mean age (yrs, range)	52 (9–87)	
Male/total	18/26	69%
Presenting symptoms		
Left-sided abdominal pain	12/25	48%
Other abdominal pain	9/25	36%
Abdominal pain absent	4/25	16%
Fever › 38°C	9/25	36%
Nausea or vomiting	8/25	32%
Physical examination		
LUQ abdominal tenderness	9/25	36%
Other abdominal tenderness	8/25	32%
Abdominal tenderness absent	8/25	32%
Splenomegaly	8/25	32%
Blood tests		
Leukocytosis › 12,000/dl	14/25	56%
Elevated LDH	19/24	71%
Elevated transaminases	1/24	4%
Elevated alkaline phosphatase	7/24	29%
Abnormal thrombophilia screen	1/2	50%
Imaging		
Infarct seen on ultrasound	10/16	63%
Infarct seen on CT	15/15	100%
Infarct seen on nuclear medicine scan	8/9	89%
Echocardiogram-diagnosed source of embolus	4/7	57%
Outcome		
Splenectomy	1/26	4%
Inpatient mortality	0/26	0%

LDH = lactate dehydrogenase, CT = computed tomography,

*For clinical findings, data are (no. of patients with finding) / (no. of patients with data), %. For investigations, data are (no. of patients with positive finding) / (no. of patients for whom investigation performed), %.

Table 3. Etiology of splenic infarction

Underlying cause	Total no. of cases	New underlying diagnosis
Hematologic malignancy	6	3
Solid tissue malignancy	1	1
Infectious mononucleosis	2	1
Intracardiac thrombus*	5	4
Bacterial endocarditis	3	3
Sickle cell disease	0	0
Wandering spleen	1	0
Thrombothilia	1	1
Liver disease**	2	1
Dislodged aortic plaque	1	1
Infected vascular graft	1	0
Sepsis	1	0
Unknown	2	0
Total	26	15

The middle column represents the total number of cases attributable to that cause, the right column represents the subset of cases in which the underlying condition was diagnosed subsequent to the patient presenting with splenic infarction.

* Includes atrial fibrillation and myocardial infarction

** Includes cirrhosis and Gaucher's disease

classical description of splenic infraction in 1901 [1], little has been written on the signs and symptoms of splenic infarction.

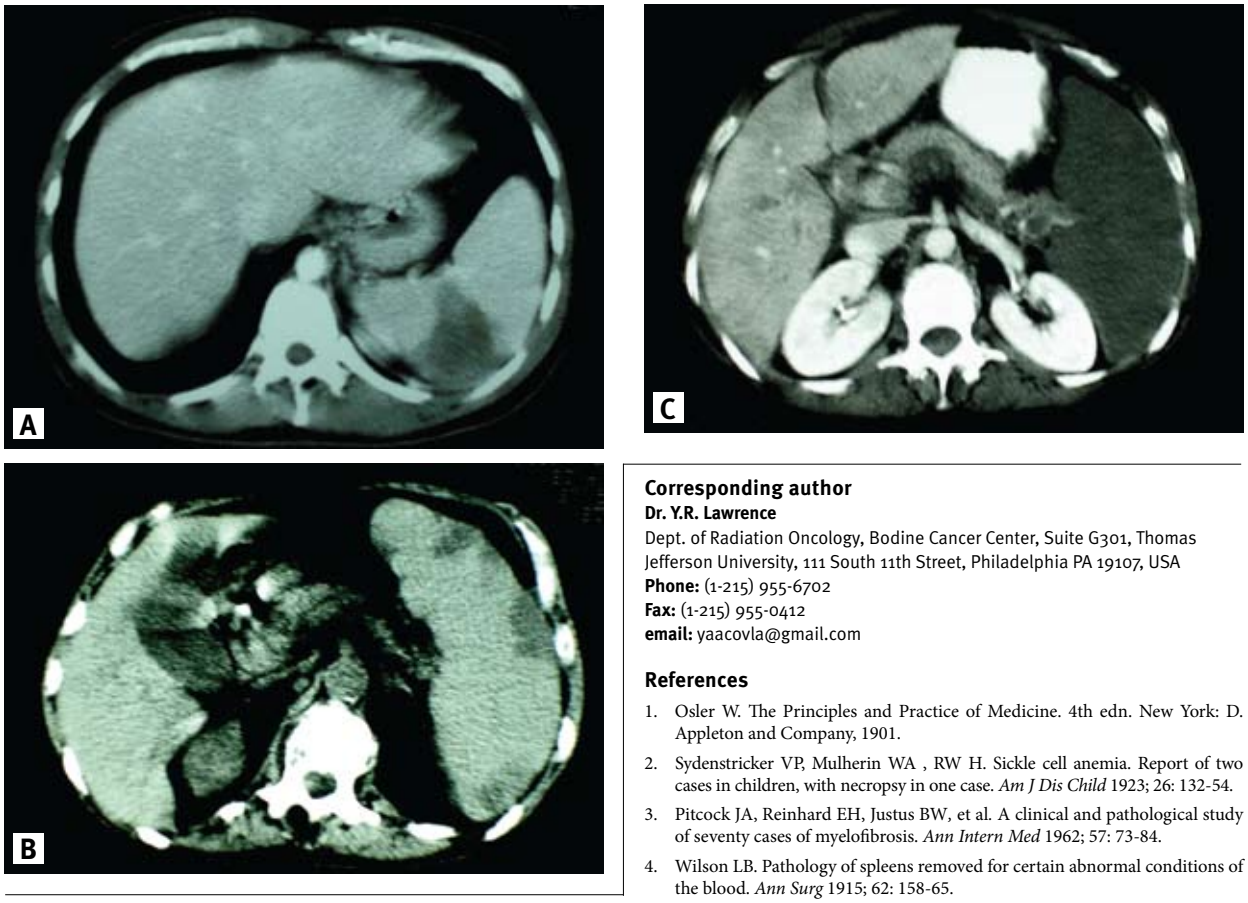
We show that splenic infarction rarely presents in the classical way described by Osler; more than 25% of patients in the present study lacked any of the features he described. This change in presentation may reflect the changes in medical practice over the course of a century. In Osler's time the only reliable means of diagnosis was surgery and autopsy; furthermore, he practiced medicine in an era that lacked antibiotics, anticoagulation and cytotoxic treatments. Contemporary practitioners, as reflected in this case series, have the double advantage of non-invasive splenic imaging and effective treatments for many of the underlying causes.

Splenic infarction is classically associated with bacterial endocarditis and sickle cell disease. Our 26 cases represent a far wider range of conditions, many of them associated with a hypercoagulable state. The absence of sickle cell patients in our series is a reflection of the ethnic mix in the Middle East. Our case series agrees with the recent literature [7] in noting that splenectomy is rarely required and that outcome is invariably good.

Weaknesses of our study include its retrospective nature and lack of predefined imaging protocol. The patients described were examined and treated by numerous physicians. Many of our observations were gleaned from the medical chart and we have no way of verifying the accuracy of the recorded symptoms and signs. For instance, we do not know how carefully clinicians listened for a friction rub.

We speculate that the different patterns of single or multiple splenic infarctions seen reflect the anatomy of the spleen's blood supply [9,10] [Figure 1]. Shortly before reaching the spleen, the splenic artery divides into four or five branches, each of which supplies a functionally separate splenic segment [11]. Whereas a small embolus would produce a segmental infarct, a large embolus at the entrance to the spleen would infarct the entire spleen. Low perfusion pressure in the splenic artery could produce multiple "watershed infarcts" in a process analogous to ischemic colitis; alternatively, these multiple infarcts may represent the disintegration of a larger embolus. The mechanism of infarction in hematologic malig-

Figure 1. Three patterns of splenic infarction on CT scans. **[A]** Wedge infarct in a 30 year old man with bacterial endocarditis (case #6). **[B]** Multiple infarcts in a 75 year old man with acute myeloid leukemia (case #22). **[C]** Infarct of the complete spleen (note the darkening of the entire organ) in a 40 year old woman with splenic vein thrombus and a genetic predisposition to thrombothilia (homozygous for MTHFR and heterozygous for a prothrombin mutation). She subsequently underwent splenectomy (case #9)



nancies may be either hypercoagulability or due to a rapidly hypertrophying spleen outgrowing its blood supply, similar to the necrotic areas seen in rapidly growing solid tumors.

CONCLUSION

Although the etiology and presentation of splenic infarction has changed considerably since the time of Osler, it remains an important diagnosis that must be recognized since it often brings an important underlying disease to attention.

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"If you have an apple and I have an apple and we exchange these apples then you and I will still each have one apple. But if you have an idea and I have an idea and we exchange these ideas then each of us will have two ideas"

George Bernard Shaw (1856-1950), Irish playwright, whose works deal sternly with prevailing social problems but have a vein of comedy to make their stark themes more palatable. Shaw examined education, marriage, religion, government, health care and class privilege.