Isolated Large Vessel Vasculitis and Splenic Infarction: A Rare Presentation of Thromboangiitis Obliterans

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Abstract

Abstract: Thromboangiitis obliterans (TAO) is an inflammatory vascular disease characterized by non-atherosclerotic thrombotic occlusions, predominantly affecting small and medium-sized arteries, veins, and nerves in the extremities, particularly in smokers. Rarely, it may involve cerebral, mesenteric, coronary, and other arteries. Recent literature indicates that TAO, although rare, most commonly affects organs such as the gastrointestinal tract, heart, central nervous system, eyes, kidneys, urogenital system, mucocutaneous zones, joints, lymphohematopoietic system, and ears. Involvement of large vessels like the splenic artery is extremely uncommon and not considered typical of the disease presentation. Splenic infarction happens when the blood flow to the spleen is hindered, leading to tissue ischemia and eventual tissue death. This can occur due to blockage in either arteries or veins. The extent of infarction can vary, ranging from global involvement of the spleen to affecting only a small, localized segment, depending on the specific vessel affected. We report a rare case of a 42-year-old man with a history of smoking who presented to the emergency department with left upper quadrant pain and vomiting. Following a comprehensive evaluation and exclusion of other medical conditions, he was diagnosed with large vessel vasculitis secondary to TAO. Treatment was promptly initiated, which led to a favorable response, and at the 2-year follow-up, he remains symptom-free.

Keywords: Large Vessel Vasculitis; Splenic Infarction; Thromboangiitis Obliterans; Buerger's Disease; Vasculitides.

Introduction

Thromboangiitis obliterans (TAO), or Buerger's disease, is a nonatherosclerotic inflammatory condition that usually affects the extremities.[1] First described by Von Winiwarter in 1879, TAO is distinct from other vasculitis in several ways.[1] It features a highly cellular and inflammatory thrombus with relative sparing of the blood vessel wall.[1] Acute-phase reactants, such as the Westergren erythrocyte sedimentation rate and serum C-reactive protein levels, are usually normal.[2,3] Serologic tests for immunologic markers, including circulating immune complexes, complement levels, and cryoglobulins, as well as common autoantibodies like antinuclear antibody and rheumatoid factor, are generally normal or negative.[2,3] However, an immune reaction can be noted in the arterial intima.[1,3] Interleukin-10 (IL-10) helps maintain immune balance, but in TAO patients, its levels are lower, while IL-6 and IL-12 are higher, suggesting a shift toward a pro-inflammatory immune response.[4,5] VCAM-1, a cytokine-induced endothelial cell adhesion molecule (CAM), triggers endothelial cell activation and leukocyte adhesion, contributing to vascular lesions in TAO.[6,7] The neutrophil-to-lymphocyte ratio (NLR), a reliable marker for polymorphonuclear leukocytes (PMNL), shows strong diagnostic and prognostic value for acute-phase TAO, with an NLR cut-off >3.38 offering good specificity and sensitivity.[8,9] Mean platelet volume (MPV), which measures the average size of platelets in femtoliters, is significantly elevated in TAO, suggesting it may be an important diagnostic predictor for these patients.[10,11]

We report a rare case of a 42-year-old smoker who presented with left upper quadrant pain and vomiting. A CTA of the abdomen suggested splenic infarction due to vasculitis. After ruling out other types of vasculitides, TAO was diagnosed, and a conservative care was initiated. His symptoms have resolved, and he remains well at the two-year follow-up.

Case Report

A 42-year-old gentleman, a smoker with no medical comorbidities, presented to the emergency department with severe left upper quadrant pain radiating to the epigastric region for one day, along with 3-4 episodes of non-projectile, non-bilious vomiting. The pain was described as constant, stabbing, and gradually increasing in intensity. There were no aggravating or relieving factors. He had no history of fever, fatigue, weight loss, genital or oral ulcers, or skin manifestations. There were no complaints of arthralgia, arthritis, ocular symptoms, vision changes, constitutional symptoms, neurological, cardiac, or respiratory symptoms. At presentation, he was hemodynamically stable. Abdominal examination revealed mild tenderness in the left upper quadrant; otherwise, it was soft, non-tender, and non-distended. Remaining systemic examinations were within normal limits. The erect chest X-ray (CXR) and supine abdominal X-ray were unremarkable. Point-of-care ultrasound (POCUS) did not reveal any features suggestive of cholecystitis, such as gallbladder wall thickening, pericholecystic fluid, sonographic Murphy's sign, gallstones or sludge, gallbladder distension, hyperemia, or an impacted stone. There was no probe tenderness in the right iliac fossa or evidence of left hydroureteronephrosis. Hematological and biochemical markers at presentation, discharge, and 2-month follow-up were normal *(Table 1).* A CT scan of the abdomen and pelvis (Figure 1) revealed multiple pyramidal wedge-shaped hypo-enhancing areas in the splenic parenchyma, predominantly towards the upper pole, suggestive of splenic infarction (yellow arrow, 1a). CT angiogram showed a distended splenic artery that was non-opacified with contrast (red arrow, 1b). The celiac trunk had significant narrowing with heterogeneous opacification, indicating a thrombus (red arrow, 1b), along with perivascular soft tissue thickening around the celiac artery (green arrow, 1b). Based on the clinical presentation, laboratory investigations, and imaging findings, a diagnosis of isolated large vessel vasculitis with splenic infarction was made; a rare manifestation of TAO. He was admitted in the ward and started on conservative treatment and anticoagulation therapy. The vasculitis workup, including panels for Molecular Myeloproliferative Neoplasms, Autoimmune disorders, Antiphospholipid Syndrome, Extractable Nuclear Antigens, and Microbiology, all showed negative results (*Table 2*). A 2D echocardiogram ruled out any left ventricular aneurysm or clot, thereby excluding a cardioembolic event. His condition showed gradual improvement with supportive measures. A follow-up CECT with angiogram on day 7 revealed that the spleen maintained an average size, with persistent subcapsular hypodense patchy areas suggestive of splenic infarcts.

Based on the aforementioned findings, a diagnosis of large vessel vasculitis, a rare presentation of TAO was made. The patient was started on Aspirin 100mg and Atorvastatin 20mg once daily, along with pulse Methylprednisolone for three days, followed by oral steroids tapered over two weeks and then stopped. The patient was discharged in a stable, pain-free condition. At the 2-month follow-up, he was asymptomatic but subsequently lost to follow-up. At 2 years, we re-evaluated him and he remained symptom-free. Follow-up imaging (Figure 1) two years later revealed near-complete resolution of the previously observed splenic infarctions (yellow arrow, 2a). There was a marked reduction in perivascular soft tissue thickening (green arrow, Figure 2b), leading to improved luminal patency of the splenic artery (red arrow, Figure 2b). However, he continues to smoke and discontinued corticosteroid therapy after completing the prescribed regimen.

Table 1: Clinical Profile: Hematological and Biochemical Laboratory Investigations at Presentation, Discharge, and 2-Month Follow-Up.

Variables	At presentation	At discharge	At 2 months follow up
Haemoglobin (11.0-14.5; 10^12/L)	14.6	14.2	13.7
Haematocrit (0.350-0.450 L/L)	0.448	0.432	0.431
Platelet count (150-450; 10 ^9/L)	278	230	217
White Cell Count (2.4-9.5; 10 ^9/L)	9.9	10.4	7.5
C- Reactive Protein (0-5 mg/L)	7	5	5

Sodium (135-145 mmol/L)	134	138	139
Potassium (3.5-5.1 mmol/L)	4.1	4.6	4.1
Creatinine (45-84 µmol/L)	74	86	79
Estimated GFR-MDRD (ml/min/1.73 m^2)	>90	85	>90
Alanine Aminotransferase (0 - 41 U/L)	20	14	21
Albumin 35 - 52 g/L	50	47	44
Alkaline phosphatase (35-104 U/L)	104	110	113
Protein, Total (66-87 g/L)	76	76	74
Lactate Dehydrogenase (135 – 225 U/L)	371	-	-
Lipase (13 - 60 U/L)	21	22	-
Troponin (< 14ng/L)	5	-	-
Prothrombin Time (PT) (9.9 - 11.5 sec)	10.6	-	-
INR (0.90 - 1.10)	1.00	-	-
Activated Partial Thromboplastin Time (APTT) (26.8 - 36.8 sec)	33.4	-	-
Fibrinogen (1.7 - 3.6 g/L)	3.4	-	-
Thrombin Time (12.8 - 17.6sec)	15.9	-	-
Lupus Anticoagulant (LA)	not detected	-	-
LA Screen (APTT LA sensitive) (31.- 49.8 sec)	41.6	-	-
LA Screen (dRVVT) (31.0 - 46.2 sec)	39.3	-	-
Urine Creatinine (Random) (mmol/L)	13.7	17.6	-
Urine Protein (Random) (0.00 - 0.15 g/L)	0.10	0.17	-
Urine Protein/Urine Creatine (Units: mg/mmol)	7.30	9.66	-

Table 2: Clinical Profile: Molecular Myeloproliferative Neoplasm (MPN) Reflex Panel, Autoimmune Panel, Antiphospholipid Syndrome Panel, Extractable Nuclear Antigens Panel, and Microbiology Panel.

Variables- Laboratory investigations	**At presentation**
Molecular Myeloproliferative Neoplasm (MPN) reflex panel	
Suspected MPN	Not detected
BCR/ABL t(9;22) P210 (CML)	Not detected
JAK2 (V617F)	Not detected
JAK2 Exon12-14	Not detected
CALR Exon 9	Not detected
MPL Exon 10	Not detected
Autoimmune panel	
Complement C3 (0.90 - 1.80 g/L)	1.27
Complement C4 (0.10 - 0.40 g/L)	0.25

Anti-Neutrophil Cytoplasmic Antibodies	Negative
Anti-Proteinase 3(PR3) (0.00 - 20.00 U/ml)	2.00
Anti-Myeloperoxidase (MPO) (0.00 - 20.00 U/ml)	1.00
Anti-Nuclear Antibody	Negative
Rheumatoid factor	Negative
Anti-PM-SCL	Negative
Anti-Centromere Antibody	Negative
Anti-Ribosomal P antibody	Negative
Antiphospholipid Syndrome panel	
Anti-B 2 Glycoprotein 1 (IgG) (0 – 7 U/ml)	1
Anti-B 2 Glycoprotein 1 (IgM) (0 – 7 U/ml)	< 1
Anti-Cardiolipin Antibody (IgG)	1
Anti-Cardiolipin Antibody (IgM) (0 – 10U/ml)	< 1
Extractable Nuclear Antigens	
Anti-DFS70	Negative
ENA Histidyl-tRNA Synthetase (Jo-1)	Negative
Anti-Ribonuclear Proteins (RNP)	Negative
Anti-Ku	Negative
Anti-Mi-2	Negative
Anti-Scleroderma Antigen-70KD (SCL-70)	Negative
Anti-Sjogren's Syndrome-Antigen A	Negative
Anti-Sjogren's Syndrome-Antigen B	Negative
Anti-Smith Antigen (Sm)	Negative
Anti-Histones Antibodies	Negative
Anti-Nucleosome Antibodies	Negative
Anti-PCNA Antibodies	Negative
Anti-RO52 Antibodies	Negative
Microbiology panel	
HBVPCR (Qualitative) HBV	HBV DNA not Detected
Anti HCV	Negative
Hepatitis B Surface Ag	Negative
HIV 1 and 2 serology	Negative
Interferon Gamma Release Test for MTB	Negative
Syphilis Screen	Negative
SARS-CoV-2 PCR RNA*	Not detected
Urine culture	None organism detected
Blood Culture	None organism detected

* *Tested by real-time polymerase chain reaction (RT-PCR) using ModularDX kit (TIB MOLBIOL).*

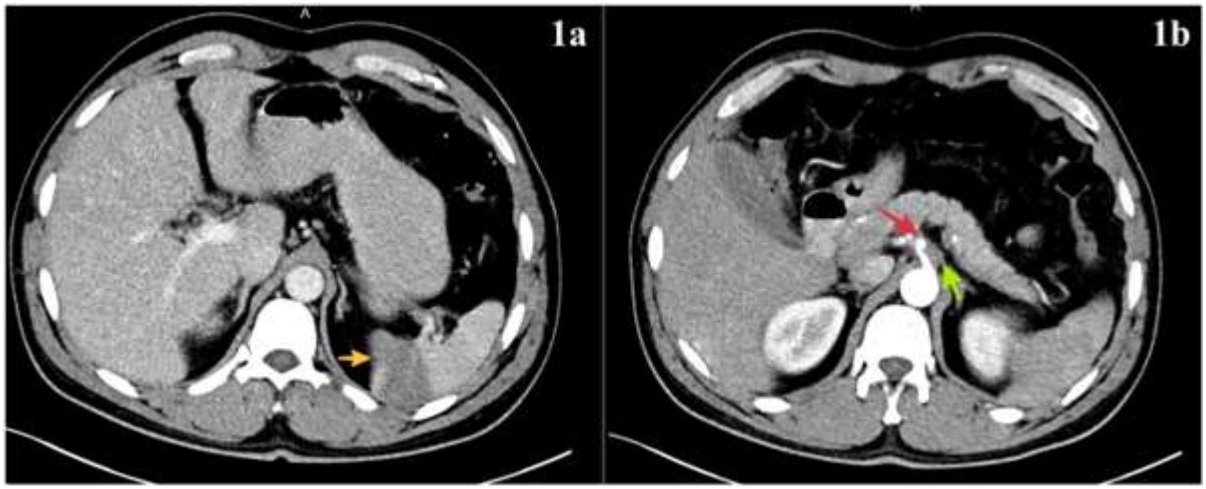

Figure 1: Contrast-Enhanced CT and Angiographic Findings. (a) *At presentation, a CT scan of the abdomen and pelvis revealed multiple pyramidal wedge-shaped hypo-enhancing areas in the splenic parenchyma, predominantly towards the upper pole, suggestive of splenic infarction (yellow arrow). (b) The CT angiogram showed a distended splenic artery that was non-opacified with contrast (red arrow). The celiac trunk had significant narrowing with heterogeneous opacification, indicating a thrombus (red arrow), along with perivascular soft tissue thickening around the celiac artery (green arrow).*

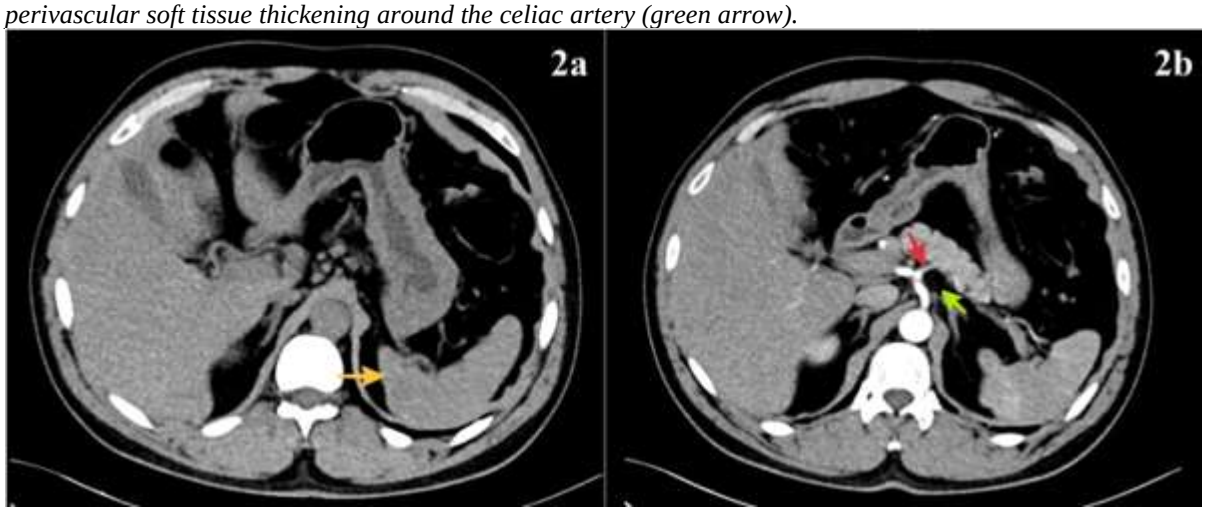

Figure 2: Contrast-Enhanced CT and Angiographic. *Follow-up imaging two years later (a) revealed near-complete resolution of the previously observed splenic infarctions (yellow arrow). (b) There was a marked reduction in perivascular soft tissue thickening (green arrow), leading to improved luminal patency of the splenic artery (red arrow).*

Discussion

Patients with TAO typically present with ischemic symptoms in the extremities, reflecting the disease's classic manifestation.[1,2] However, TAO can also manifest systemically, affecting arteries beyond the limbs, such as the splenic artery, leading to stenosis and subsequent ischemic events like splenic infarction.[3,12] In our case, a young man with a history of smoking presented with sudden onset left upper quadrant abdominal pain radiating to the epigastrium, without other specific systemic complaints. Initial laboratory tests ruled out cardiac or gastrointestinal manifestations like pancreatitis. While POCUS with Doppler can detect changes in blood flow, it may not always provide a definitive diagnosis of splenic infarction. Persistent pain prompted a CT abdomen scan following a normal POCUS in the ED. CT imaging confirmed focal areas of non-enhancing splenic parenchyma consistent with infarction, and subsequent angiography identified stenotic lesions in the splenic artery secondary to a vasculitic process.

Various types of systemic vasculitides have been linked to splenic infarction, such as polyarteritis nodosa (PAN), systemic lupus erythematosus (SLE), granulomatosis with polyangiitis (GPA), and microscopic polyangiitis (MPA).[13,14] These diseases can affect the splenic artery, leading to stenosis or occlusion and

subsequent infarction. PAN, a systemic necrotizing vasculitis primarily affecting medium-sized arteries, may involve the splenic artery.[15] SLE, a multisystem autoimmune disorder affecting multiple organs including blood vessels, can also contribute to splenic infarction through vasculitic involvement of the splenic artery.[16] Additionally, ANCA-associated vasculitis, including GPA and MPA, although less frequently reported to involve visceral arteries, presents a potential risk for splenic infarction, demonstrating the systemic impact of vasculitis on visceral organs beyond peripheral vasculature.[12,16] Despite extensive vasculitis workup with negative results, the clinical presentation and imaging findings led to the diagnosis of TAO, a condition considered rare among the spectrum of vasculitides.

Management of splenic infarction in the context of vasculitis requires a comprehensive approach aimed at both addressing the underlying inflammatory process and managing potential complications. Central to this strategy is the use of immunosuppressive therapy, with corticosteroids serving as the cornerstone to diminish inflammation and prevent further vascular damage.[17,18] In cases of severe or refractory vasculitis, additional immunosuppressive agents such as methotrexate or cyclophosphamide may be required.[17,18] Alongside pharmacological interventions, supportive care plays a crucial role, focusing on effective pain management while carefully monitoring for complications like splenic abscess formation. Long-term management emphasizes regular clinical assessments and laboratory tests to monitor disease activity and adjust treatment accordingly, with periodic imaging studies to assess the resolution or progression of splenic infarction over time. Fortunately, our patient did not develop a splenic abscess on routine imaging and was discharged after a week with tapering dose of oral steroid therapy, antiplatelets and HMG-CoA reductase inhibitors showing good progress at the two-year follow-up.

Conclusion

Splenic artery involvement and subsequent infarction due to TAO are uncommon, clinicians should be aware of the potential for systemic vascular complications in TAO patients and consider comprehensive evaluation and management strategies to optimize patient care.

Disclosure

No conflict of interest. The authors confirm that they have acquired all necessary patient consent forms, including consent from the patient, to share his clinical information in this journal report. The patient acknowledges that the patient's names and initials will not be disclosed, and every effort will be made to protect her identity, although complete anonymity cannot be assured.

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