

# Splenic Infarcts in an Adult Male with EBV Infection: A Rare Complication

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## ***Abstract***

Splenic infarction is an extremely rare complication of Epstein Barr Virus (EBV) infection. We report a case of a healthy 28-year-old male that presented with fever and pharyngitis and was diagnosed with acute EBV infection. During his hospital stay, he complained of sudden left upper quadrant abdominal pain. Abdominal Ultrasound (US) was insignificant, but Computed Tomography (CT) scan of the abdomen demonstrated hepatosplenomegaly and multiple splenic hypodense lesions suggestive of infarcts. The patient was managed conservatively and was discharged on prophylactic anticoagulation therapy with apixaban. He is currently under close clinical follow up to minimize the risk of splenic rupture. We aim to highlight the importance of suspecting splenic infarction in patients presenting with fever, splenomegaly, and new onset abdominal pain, particularly in the setting of an ongoing or recent EBV infection.

**Keywords:** EBV; Splenic Infarct; Complication; Anticoagulation.

## **Introduction**

Splenic infarction, characterized by ischemic necrosis of the splenic tissue, can lead to potentially life-threatening complications such as rupture, hemorrhage, sepsis, or abscess formation. It is a relatively rare clinical condition, typically caused by conditions that lead to embolic events, vasculitis, or direct trauma to the spleen. Infectious causes of splenic infarction are uncommon, and reported viral etiologies include cytomegalovirus (CMV), parvovirus B19, adenovirus, and, more recently, COVID-19, but Epstein Barr Virus (EBV) is rarely associated with this complication.<sup>1,2</sup> The exact pathophysiology of splenic infarcts in the setting of EBV infection is not fully understood, yet it may involve an intricate interplay of immune response, transient coagulation activation, and local vascular dynamics.<sup>3</sup> Given its potential severe consequences, a high index of clinical suspicion is essential for timely diagnosis and management. The aim of this case report is to increase awareness among clinicians about this rare but significant complication of EBV infection.

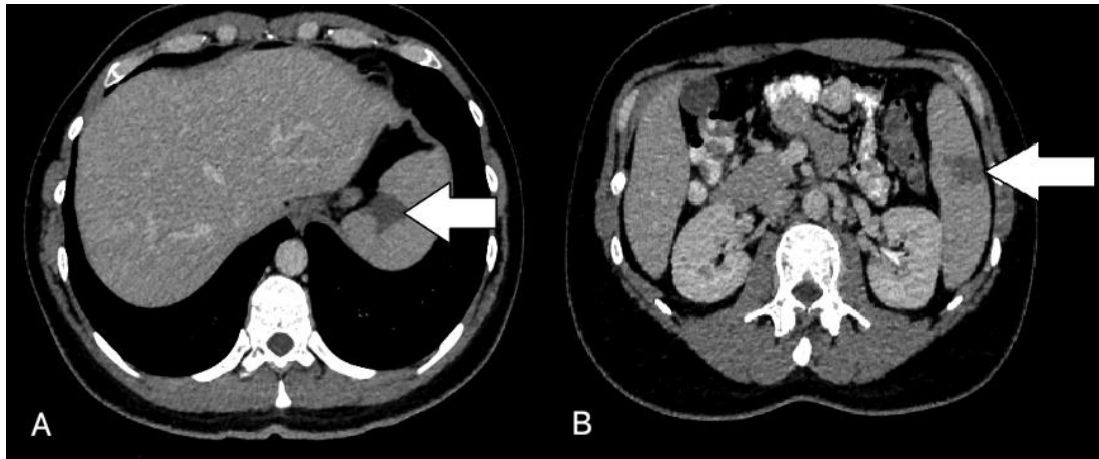
## **Case Report**

A 28-year-old male patient with no significant past medical history presented to the Emergency Department due to 5-day history of fever and sore throat. The patient did not disclose any history of smoking or illicit drug use, and his family history revealed no noteworthy thromboembolic events. Clinical examination revealed a febrile patient (t: 38.5 °C) with sinus tachycardia (112 beats per minute) and bilateral palpable superficial cervical lymph nodes with no signs of palpable spleen or liver. Laboratory examinations revealed a reversed neutrophil-to-lymphocyte ratio (WBC: 7.8K/ $\mu$ L,

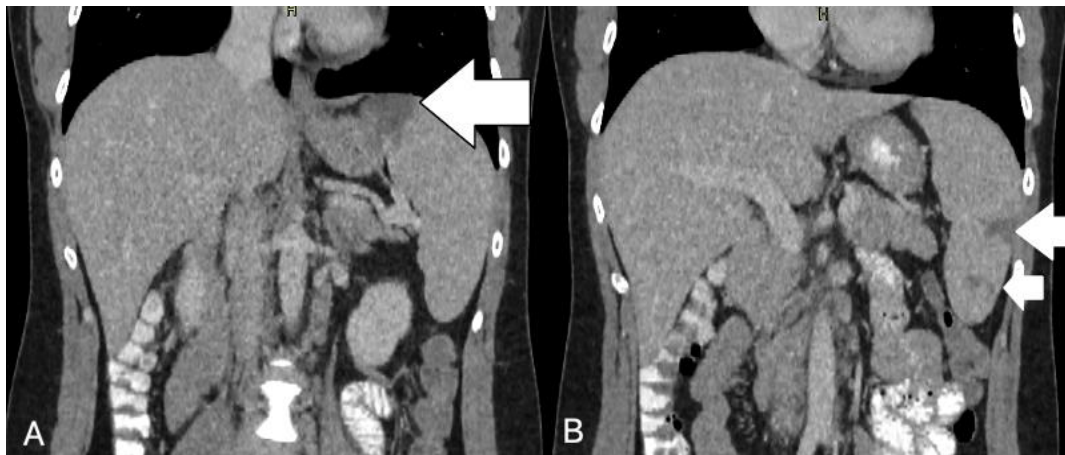
lymphocytes: 4.4K/ $\mu$ L), elevated liver function tests (AST: 99 IU/L, ALT: 280 IU/L, normal ranges: 5-40 and 5-45 IU/L respectively) and increased LDH (466 IU/L, normal range: 100-230 IU/L) (Table 1). Serological analysis yielded positive results for immunoglobulin M (IgM) antibodies specific to the Epstein-Barr virus (EBV), indicative of an acute infection. The patient was admitted for symptom monitoring and appropriate medical care. Subsequent Polymerase Chain Reaction (PCR) testing on a blood sample confirmed the diagnosis of an acute EBV infection [Table 1]. Abdominal ultrasound was negative for hepatosplenomegaly or other abnormal findings. On the fifth day of his hospital stay, the patient complained of new onset left upper quadrant abdominal pain. Clinical examination revealed mild tenderness of the left upper quadrant and a palpable spleen. A Computed Tomography (CT) of the abdomen with intravenous contrast demonstrated multiple enlarged iliac lymph nodes, hepatomegaly (178mm in the midclavicular line), moderate splenomegaly (140mm in the longitudinal axis) and the presence of multiple hypodense splenic lesions without contrast enhancement, suggestive of splenic infarcts [Figures 1 and 2]. A CT angiography of the abdomen was subsequently performed, which did not exhibit the presence of thrombi along the splenic vasculature. Hypercoagulability Workup revealed only mildly reduced protein S activity (51%, normal range 58-127.5%). Molecular testing for inherited thrombophilia (Factor V Leiden, Factor II-prothrombin, Factor XIII, MTHFR, JAK2 V617 gene mutations) yielded negative results [Table 1]. Transesophageal echocardiography showed no evidence of thrombi, vegetations, or any abnormal findings. The patient was managed conservatively with intravenous fluids, analgesics, and prophylactic anticoagulation therapy with apixaban 5 mg per os daily. A significant clinical improvement of the abdominal pain was noted after 2 days, and the patient was discharged after a total of 15 days of hospital stay. The patient was counseled to abstain from strenuous physical activities due to the risk of splenic rupture, and to avoid hepatotoxic medication for a minimum period of one month. He is under close follow-up and is scheduled for an abdominal CT scan in four weeks to evaluate the evolution of the splenic infarcts.

**Table 1:** Patient's laboratory examinations.

	Patient's Laboratory Examinations			Reference Range
	On presentation	Day 5	Discharge	
WBC	7.8	4.7	4.1	4-10 K/ $\mu$ L
Lymphocytes	4.4	2.1	2.2	1.2-3.8 K/ $\mu$ L
Monocytes	0.3	0.4	0.4	0.2-1 K/ $\mu$ L
Platelets	220	265	273	140-440 K/ $\mu$ L
INR	1.11	1.09	1.03	0.85-1.15
Fibrinogen	265	257	278	180-400mg/dL
aPTT	27.9	29.2	32.4	26-36 Sec
EBV IgM	5.03 (Positive)			<1
EBV IgG	0.01 (Negative)			<1
PCR EBV (serum)	9.2x10 <sup>3</sup>			2.77x10 <sup>3</sup> copies/mL
AST	99	78	47	5-40 IU/L
ALT	280	314	104	5-45 IU/L
LDH	466	303	223	100-230 IU/L
$\beta$ 2 glucoprotein IgM, IgG		0.87/3.53		< 20 U/mL
Lupus anticoagulant		30.5 / --		30.5-40.6 Sec
Anticardiolipin IgG, IgM		1.83/4.08		<7 U/mL
Protein C activity		82.1		70-140%
Protein S activity		51		58-127.5%
Factor V Leiden mutation		Negative		
Prothrombin gene mutation		Negative		
Antithrombin III activity		81.3		75-125%
MTHFR gene mutation		Negative		
JAK2 V617 mutation		Negative		



**Figure 1.** Axial contrast- enhanced CT scan demonstrating wedge-shaped hypodense splenic lesions without contrast enhancement indicative of splenic infarcts (white arrows), located at the T10 level (panel A) and at the L2 level (panel B).



**Figure 2.** Coronal abdominal CT scan with intravenous contrast demonstrating multiple splenic infarcts (white arrows), located at the superior (panel A), as well as the middle and lower parts of the spleen (panel B).

## Discussion

Epstein Barr Virus (EBV) is the most common cause of infectious mononucleosis (IM), affecting up to 95% of the healthy population.<sup>4</sup> Main symptoms include fever, fatigue, sore throat, cervical lymphadenopathy, and hepatosplenomegaly.<sup>5</sup> Splenic infarction is an extremely rare complication of acute EBV infection, with 33 cases reported in the literature since 1990.<sup>6</sup> To our knowledge, the majority of cases involve young adults with no inherited predisposition for a prothrombotic state.<sup>3,6</sup>

The exact mechanism of splenic infarcts due to EBV remains unknown. Various hypotheses have been implicated, including an insufficient arterial blood supply for the enlarged spleen during the acute phase,<sup>3,4,7</sup> an increased B-cell mediated immune response,<sup>1,4,6</sup> and a transient activation of the coagulation cascade.<sup>1,4</sup>

Clinical presentation of splenic infarction due to EBV typically involves vague and non-specific symptoms, including left upper quadrant pain, splenomegaly, fever, vomiting or chest pain, occasionally radiating on the left shoulder.<sup>5,6,8</sup> Rarely, it can present as a potentially life-threatening hemorrhage, while others may remain asymptomatic and the diagnosis is made incidentally.<sup>9</sup> Typically, the manifestation of splenic infarction occurs one to three weeks following the initial onset of infection mononucleosis

symptoms.<sup>5</sup> In our case, the patient exhibited signs indicative of splenic infarcts ten days after symptom onset.

Laboratory examinations typically reveal mild leukocytosis, an elevated LDH (lactate dehydrogenase), and a transient hypercoagulable state.<sup>1,6</sup> Additionally, EBV infection may affect platelet parameters, leading to elevated platelet count or alterations in the mean platelet volume-to-platelet count ratio. Notably, a high mean platelet volume-to-platelet count ratio is recognized as a diagnostic marker for an increased risk of liver function damage in EBV-infected patients,<sup>10</sup> while Mean Platelet Volume (MPV) is implicated in the development of vascular complications.<sup>11</sup> Therefore, EBV should be considered among the primary differential diagnoses when these parameters are affected.<sup>12</sup> In our case, these parameters were meticulously monitored and remained within normal limits during the patient's entire hospital stay.

This hypercoagulable state is additionally indicated by the presence of lupus anticoagulant, anticardiolipin antibodies (ACA), antiphospholipid antibodies, or a reduced activity of protein C and protein S.<sup>1,6,8</sup> The specific correlation between the elevation of anticardiolipin antibodies (ACA) and the occurrence of splenic infarcts in individuals with EBV infection has been documented in existing literature.<sup>13</sup> In our case, the patient exhibited an elevated LDH, while the hypercoagulability workup was normal, except for a slightly reduced activity of protein S.

On abdominal ultrasound, splenic infarcts demonstrate hypoechoic lesions with absent Doppler signal.<sup>9</sup> Thus, abdominal ultrasound is not recommended as the sole imaging modality due to a low sensitivity (reported around 18%), especially in the acute setting.<sup>6,9,14</sup> Imaging modality of choice is the Computed Tomography (CT) scan with intravenous contrast, in which splenic infarcts commonly present as wedge-shaped hypodense lesions with no enhancement after contrast administration.<sup>6,7</sup> On magnetic resonance imaging (MRI), splenic infarcts are visualized as lesions exhibiting low signal intensity on both T1-weighted and T2-weighted images.<sup>9</sup> In our case, ultrasound did not demonstrate any abnormal lesions suggestive of infarcts, that became evident on CT scan with intravenous contrast as wedge-shaped lesions with no contrast enhancement.

Symptomatic management with intravenous fluids, analgesics and prophylactic anticoagulation on a case-to-case basis is the treatment of choice in almost all cases.<sup>6,15</sup> Close follow up for at least four weeks, or until resolution of splenomegaly or infarcts has been proposed for all patients with EBV related splenic infarcts, due to the risk of potential complications, namely hemorrhage, splenic rupture, abscess, or pseudocyst formation.<sup>9,15,16</sup>

To our knowledge, this represents the 32<sup>nd</sup> documented case of a splenic infarct associated with an EBV infection reported in the literature since 1990.<sup>6,17</sup> Most patients were otherwise healthy adults diagnosed due to evaluation of new-onset abdominal pain in patients with acute EBV infection.<sup>6</sup> A transient hypercoagulable state was observed in most cases, as indicated by various affected parameters, namely elevated D-dimers, antiphospholipid antibodies, lupus anticoagulant, ACA,  $\beta_2$  glucoprotein I, and reduced protein C or S activity or antithrombin III, among others.<sup>6,15</sup> CT scan was the predominant diagnostic method in the majority of cases and management focused primarily on symptomatic interventions.<sup>5,15</sup>

Given the widespread prevalence of EBV infection in the general population, along with the fact that only a limited subset of patients undergoes an abdominal imaging procedure during the course of their infection, there is a substantial possibility that cases of splenic infarction secondary to EBV are undiagnosed, and thus underreported.<sup>7</sup> Additionally, the rarity of this complication could contribute to a lower level of clinical suspicion, which in turn may lead to missed or delayed diagnosis. Therefore, continuous clinical vigilance and reporting of such cases is vital to gain a better understanding of the predisposing factors and clinical presentation, as well as to optimize treatment practices for splenic infarctions associated with Epstein-Barr Virus (EBV) infection.

## Conclusion

Splenic infarction is an extremely rare complication of EBV infection, with potentially severe complications such as rupture, abscess, or pseudocyst formation. Raised clinical suspicion of this

complication is important, particularly in patients presenting with abdominal pain and a recent history of EBV infection.

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