The Spleen as an Extrapulmonary Target of COVID-19.

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The spleen has been recently reported as one of the unusual extrapulmonary organs that can be affected by COVID-19. Different splenic lesions were described in COVID-19 patients. Splenic infarction was reported frequently, and ruptured spleen and splenic abscess were also reported. Splenic involvement in COVID-19 can be caused through direct virus damage of the spleen or COVID-19 induced microvascular thrombosis and vasculitis **[1-7]**.

The hypercoagulable state induced by COVID-19 virus leads to splenic artery or vein thrombosis and splenic infarction development due to splenic hypoperfusion **[3,8]**. The management of splenic infarction is usually by heparin anticoagulation, however, with unstable cases splenectomy is life saving **[3]**.

Pyogenic splenic abscess is a rare infection often occurs in an immunocompromised patient, management is usually performed by percutaneous drainage, antibiotics or splenectomy **[9]**. The splenic abscess in patients with COVID-19 may be attributed to necrosis of the spleen caused by direct attack of the virus **[5]**. Postmortem needle autopsies from the spleen of ten dead COVID-19 patients reported by Xu et al., who showed varying degrees of T and B lymphocyte depletion, lymphoid follicles atrophy due to direct attack of the SARS-COV 2 virus as well **[10]**.

Splenic rupture (SR) is a rare life-threatening condition. Delay in diagnosis and management of SR can lead to fatal outcome. SR is mostly traumatic; however, it may complicate malignancies, hematological, inflammatory and infectious splenic diseases. The diagnosis of splenic rupture is confirmed by abdominal computed tomography scan (CT scan) or by surgical laparotomy in hemodynamically unstable patients. SR is usually managed by splenectomy; however, the spleen preserving procedures such as arterial embolization can be considered in stable patients to avoid overwhelming post-splenectomy infection. Rupture spleen in COVID- 19 may be related to direct damage to the spleen by the virus or secondary micro or macrovascular thromboembolism **[6, 7]**.

Here, we summarize a few recent reports that have described splenic lesions in association with COVID-19 (Table 1) **[1-7]**. Splenic infarction was the most frequent pathology with COVID-19 that occurred in six patients, the majority of those patients were men; one patients was young age and had no comorbidities and severe abdominal pain was present in four patients. Other abdominal visceral infarctions in addition to splenic infarction was present in two patients; one had renal infarction and the other

had intestinal ischemia. Hemoperitoneum and intraperitoneal collection were present in two patients. Treatment was by heparin anticoagulant; however, one case undergone splenectomy and resection of ischemic bowel loop **[1-4]**.

The splenic abscess in COVID-19 was described in one man 55 years old with multiple comorbidities, CT abdomen confirmed pyogenic splenic abscess with impending rupture, pneumatosis intestinalis and pneumoperitoneum. The patient had undergone emergency splenectomy, however he died due to the development of multiorgan failure, severe sepsis and pulmonary embolism **[5]**.

Notably, spontaneous splenic rupture occurred in two patients with COVID- 19, both were men, their age was above 50 years. Both patients had abdominal pain without clear evidence of bacteremia, one was shocked, that patient was managed by splenic artery embolization. Emergency surgical laparotomy and splenectomy were performed in the other patient. Both patients had hemoperitoneum, but eventually improved and discharged **[6,7]**.

To conclude, the spleen may be an extrapulmonary target of COVID-19 virus and abdominal pain is alarming in COVID-19 infection, it may indicate a serious condition. CT abdomen is helpful in diagnosis of splenic complications secondary to COVID-19. Early diagnosis and intervention are life saving in most of these patients.

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REFERENCES

1- Pessoa MSL, Lima CFC, Pimentel ACF, Costa JCG. Multisystemic infarctions in COVID-19: focus on the spleen. *European Journal of Case Reports in Internal Medicine* 2020; 7.

2- Besutti G, Bonacini R, Iotti V, Marini G, Riva N, Dolci G, et al. Abdominal visceral infarction in 3 patients with COVID-19. *Emerging Infectious Diseases* 2020; 26: 1926.

3- Qasim Agha O,Berryman R. Acute splenic artery thrombosis and infarction associated with COVID-19 disease. *Case Reports in Critical Care* 2020; 2020.

4- Karki S, Rawal SB, Malla S, Rayamajhi J, Thapa BB. A case report on spontaneous hemoperitoneum in COVID-19 patient. *International Journal of Surgery Case Reports* 2020; 75: 211-213.

5- Al-Ozaibi LS, Alshaikh MO, Makhdoom M, Alzoabi OM, Busharar HA, Keloth TR. Splenic Abscess: An Unusual Presentation of COVID-19? *Dubai Medical Journal* 2020;3:115-118.

6- Shaukat I, Khan R, Diwakar L, Kemp T, Bodasing N. Atraumatic splenic rupture due to covid-19 infection. Clinical infection in practice 2020:100042.

7- Mobayen M, Yousefi S, Mousavi M, Anbaran AS. The presentation of spontaneous splenic rupture in a COVID-19 patient: a case report. *BMC Surgery* 2020; 20: 1-5.

8- Del Hoyo J, López-Muñoz P, Fernández-de la Varga M, Garrido-Marín A, Valero-Pérez E, Prieto M, et al. Hepatobiliary and Pancreatic: A fatal case of extensive splanchnic vein thrombosis in a patient with Covid-19. *Journal of Gastroenterology and Hepatology* 2020.

9- Davido B, Dinh A, Rouveix E, Crenn P, Hanslik T, Salomon J. Abcès de la rate: du diagnostic au traitement. *La revue de médecine interne* 2017; 38:614-618.

10- Xu X, Chang X, Pan H, Su H, Huang B, Yang M, et al. Pathological changes of the spleen in ten patients with coronavirus disease 2019 (COVID-19) by postmortem needle autopsy. *Zhonghua bing li xue za zhi= Chinese journal of pathology* 2020; 49:576-582.

Table (1): Clinical characteristics and outcomes in COVID-19 patients with splenic lesions.

	Pessoa et al [1]		Bessutti et al [2]		Agha and Berryman [3]	Karki et al [4]	Al-Ozaibi et al [5]	Shaukat et al [6]	Mobayen et al [7]
	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
Splenic lesion	Splenic infarction	Splenic infarction	Splenic infarction	Splenic infarction	Splenic infarction& Splenic artery thrombosis	Splenic infarction	Splenic abscess	Splenic rupture	Splenic rupture
Age, sex	67, male	53, female	53, male	72, male	60, male	32, male	55, male	57, male	52, male
Comorbidites	NA	Rheumatoid arthritis	Hypertension, Mitral valve replacement	Hypertension DM, Previous MI, Stage 3 kidney failure	Hypertension DM, Morbid obesity, IgG deficiency, Asthma, OSA	NO	DM ischemic heart disease, chronic kidney disease, old cerebrovascular Stroke	OSA	NA
Clinical presentation									
Fever	Yes	Yes	Yes	NO	Yes	Yes	Yes	NO	Yes
Chest symptoms	Cough, dyspnea	Cough, dyspnea	Cough, sore throat	Cough, dyspnea	Cough, dyspnea	NO	NO	Cough	Respiratory distress
Abdominal symptoms	NA	NA	Severe left flank pain	Severe abdominal Pain	Severe left upper quadrant pain & diarrhea	Moderate to severe Periumbilical pain	Acute abdomen	Acute abdomen & anorexia & diarrhea	Abdominal Pain & nausea
Others	Weakness of left upper limb, drooping of mouth, headache	Anosmia	NO	Metabolic acidosis	NO	Rash	Aphasia, Right sided weakness, Sepsis	Shocked (Main presentation)	NO
CT chest	Ground glass opacities& pulmonary thrombo-embolism	Ground glass opacities	Bilateral Viral pneumonia	NA	NA Chest x-ray show patchy opacity in right lung	NA	NA	Ground glass opacity and consolidation	Ground glass and pleural effusion Extensive fluid collection around spleen

	Pessoa et al [1]		Bessutti et al [2]		Agha and Berryman [3]	Karki et al [4]	Al-Ozaibi et al [5]	Shaukat et al [6]	Mobayen et al [7]
	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
CT abdomen	Splenic infarction	Splenic infarction, filling defect in the subsegmental branches of splenic artery	Splenic infarction & Left kidney infarction	Massive splenic infarction & Small bowel ischemia	More than 50% splenic infarction & Acute splenic artery thrombosis	Splenic infarction, Hemo-peritoneum	Impending rupture pyogenic splenic Abscess & Pneumo-peritoneum & Colonic wall thickening with Intramural gas	Rupture spleen & Hemo-peritoneum	NA
CBC	NA	NA	Normal	Normal	Normal	Pancytopenia Decreased HB level from 14.1 to 7.3 gm%	WBC:5 x10^3/mm^3	WBC:3.7 ($x10^3$/mm^3) HB: 7.8 g/dl PLT:149 ($x10^3$/mm^3)	HB: 9.5g/dl
INR	NA	NA	NA	Normal	NA	Normal	NA	Normal	Normal
CRP mg/dl	NA	NA	4.4	48	86.6	NA	300.4	368.1	NA
D-dimer ng/ml	NA	NA	NA	6910	259	Normal	NA	NA	NA
Management	NA	NA	LMWH	Splenectomy & resection of ischemic bowel loop	Heparin drip for 24h then shift to Enoxaparin 1mg/kg twice daily	Supportive	Emergent laprotomy & splenectomy	Splenic artery embolization	Emergent laparotomy & splenectomy was done
Outcome	NA	NA	Improved	Improved	Improved	NA	Died (severe sepsis, multi organ failure, PE)	Improved	Improved

DM: Diabetes mellitus, OSA: Obstructive sleep apnea, MI: myocardial infarction, PE: pulmonary embolism, LMWH: low molecular weight heparin, NA: Not available.