



CASE REPORT

Retroperitoneal hemorrhage due to ruptured artery induced by median arcuate ligament syndrome in patients with COVID-19: A case series

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Abstract

Background: Median arcuate ligament syndrome describes a clinical presentation associated with direct compression of the celiac artery by the median arcuate ligament. Decreased blood flow from the celiac artery and increased flow from superior mesenteric artery causes blood flow in the pancreatic arcade to increase, and aneurysms can form. We report our experience with six cases of retroperitoneal hemorrhage induced by median arcuate ligament syndrome in patients during the COVID-19 period.

Case Presentation: The time from the onset of COVID-19 to that of abdominal pain in the patients ranged from 3 to 9 days. None of the patients required oxygen for COVID-19. We used contrast-enhanced computed tomography to diagnose retroperitoneal hemorrhage and formation of a visceral pseudoaneurysm or aneurysm due to median arcuate ligament syndrome. Five patients underwent transcatheter arterial embolization. One patient suffered complications of duodenal stenosis and another suffered portal vein thrombosis.

Conclusions: Retroperitoneal hemorrhage associated with median arcuate ligament syndrome is rare. However, it might be triggered by COVID-19 disease, resulting in arterial disruption and hemorrhage.

KEYWORDS

COVID-19, MALS, retroperitoneal hemorrhage

INTRODUCTION

Median arcuate ligament syndrome (MALS) describes the clinical presentation associated with direct compression of the celiac artery by the median arcuate ligament (MAL). In a retrospective database analysis of contrast-enhanced computed tomography (CE-CT) performed for various indications, radiologic evidence of celiac artery compression by the MAL was present in about 3% of cases. To the authors' knowledge, no agreement by group consensus

regarding the diagnosis of MALS exists. Despite this, patient presentation and radiologic signs appear to be generally consistent across the literature.¹ Decreased blood flow from the celiac artery and increased flow from the superior mesenteric artery (SMA) cause an increase of blood flow in the pancreatic arcade that results in the formation of aneurysms in the pancreaticoduodenal arcade, splenic artery, and celiac artery.² The lethality of MALS is that rupture of the aneurysm formed induces retroperitoneal hemorrhage.

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There is scarce data on the relationship between coronavirus disease 2019 (COVID-19) and retroperitoneal hemorrhage induced by a ruptured visceral aneurysm due to MALS. Here, we report six cases of retroperitoneal hemorrhage caused by MALS that was potentially associated with COVID-19.

CASE REPORT

There were 1490 COVID-19 patients admitted to Kansai Medical University Medical Center from January 2020 to September 2022. Six patients (0.4%) of them had retroperitoneal hemorrhage due to MALS. The number of cases was 1/41 (2.4%) in the first wave when wild strains were prevalent, 1/254 (0.4%) in the fifth wave when mainly delta strains, 1/376 (0.3%) in the sixth wave when mainly omicron strains (BA.1 and BA.2), 3/289 (1.0%) in the seventh wave when mainly omicron strains (BA.5). (Table S1) The six cases included four males and two females aged from 41 to 74 years. None had been diagnosed as having MALS previously and developed retroperitoneal hemorrhage following the sudden appearance of abdominal pain during their COVID-19 disease period. We used CE-CT scanning to diagnose retroperitoneal hemorrhage and aneurysm formation due to MALS. The diagnosis of MALS was based findings of kinking of the proximal celiac artery and a characteristic hooked appearance with poststenotic dilatation in the parasagittal reconstruction of the CE-CT images.

The number of days from the onset of COVID-19 to that of retroperitoneal hemorrhage ranged from 3 to 9 days. None of the patients required oxygen for COVID-19, and only one showed symptoms of pneumonia. The median values of laboratory data on admission were CRP: 2.7 mg/

dL, FDP-D dimer: 2.5 µg/mL, and IL-6: 8.8 pg/mL. All patients underwent angiography, the findings of lesion artery (location/morphology) from angiography were as follows, No.1 (IPDA/aneurysm), No.2 (DPA-IPDA/dilatation and meandering), No.3 (DPA-AIPDA/pseudoaneurysm and dilatation), No.4 (AIPDA/beaded and aneurysm), No.5 (PIPDA/pseudoaneurysm) and No.6 (DPA-SPDA/pseudoaneurysm). Five underwent transcatheter arterial embolization (TAE), four with coils and one with imipenem/cilastatin (this use of embolic substances not covered by insurance has been authorized by our hospital's ethics committee). In the case (No.1), there was almost thrombosed aneurysm in angiography, we selected temporary embolic substance IPM/CS, not permanent embolic substance. The case (No.2) was not so many hemorrhages in the CECT on the arrival, so we selected standby angiography. In the angiography at 13th day from onset of stomachache, pseudoaneurysm seen on CECT on arrival was had disappeared. So, we performed only angiography not TAE. Elective radical MAL resection was performed in two patients. The median follow-up period was 18 months, with none of the patients experiencing rebleeding during follow-up. Two complications were induced by retroperitoneal hemorrhage, duodenal stenosis in one patient and portal vein thrombosis in another (Table 1). A typical case is presented below.

A 56-year-old male with no specific past medical history was diagnosed as having COVID-19 at a clinic. On Day 2 of sickness, he had abdominal pain and visited our hospital. We diagnosed retroperitoneal hemorrhage, a pseudoaneurysm in the pancreaticoduodenal arcade, and MALS by CE-CT. On Day 3 of sickness, the pseudoaneurysm in the posterior inferior pancreaticoduodenal artery was embolized with coils. He was discharged on Day 5, but he returned to our hospital on Day 13 day after becoming ill complaining

TABLE 1 Summary of the data of the 6 patients.

No.	Age/sex	COVID-19 severity	Wave/main strain of pandemic in Japan	SARS-CoV-2							Pangolin lineage	Vaccination frequency	Anti-viral drug	Comorbidities	Laboratory data on arrival CRP (mg/dL)
				Viral load of nasopharyngeal PCR (copies/µL)	SNP PCR assays				SNP						
					Possible variants	L452R	N501Y	E484K	G339D						
1	59/M	Mild	1/wild	NA	NA	NA	NA	NA	NA	NA	0	Favipiravir	Cerebral infarction	5.5	
2	50/M	Moderate	5/delta	118,575,560	B.1.617.2 (+)	(-)	(-)	NA	NA	B.1.617.2	0	Remdesivir	HT, HL	0.8	
3	74/F	Mild	6/BA.1, BA.2	1,021,907	BA.1 or BA.2	(-)	NA	NA	NA	NA	2	Nothing	HT	0.4	
4	41/M	Mild	7/BA.5	13,586	BA.5	(+)	NA	NA	(+)	NA	3	Nothing	HU, HL	6.2	
5	56/M	Mild	7/BA.5	NA	NA	NA	NA	NA	NA	NA	3	Nothing	None	2.1	
6	52/F	Mild	7/BA.5	161,394	BA.5	(+)	NA	NA	(+)	BA.5	0	Remdesivir	None	3.3	

Abbreviations: AIPDA, anterior inferior pancreaticoduodenal artery; CRP, C-reactive protein; DPA, dorsal pancreatic artery; HL, hyperlipidemia; HT, hypertension; HU, hyperuricemia; IL-6, interleukin-6; IPDA, inferior pancreaticoduodenal artery; IPM/CS, imipenem/cilastatin; MAL, median arcuate ligament; NA, not available; PCR, polymerase chain reaction; PIPDA, posterior inferior pancreaticoduodenal artery; SNP, single nucleotide polymorphism; SPDA, superior pancreaticoduodenal artery; TAE, transcatheter arterial embolization.

of vomiting. CT scan revealed that the retroperitoneal hematoma had shrunk compared to the first time, but that the hematoma was compressing the descending portion of duodenum. Upper gastrointestinal endoscopy showed no mucosal necrosis of the duodenum and the circumferential stenosis of the descending portion. We diagnosed duodenal stenosis due to retroperitoneal hematoma by the findings of CT scan and endoscopy. He was treated by fasting and decompression by gastric tube. He was started on a diet on Day 26 of sickness and was discharged on Day 34. Follow-up angiography and CT scan performed 6 days later confirmed no abnormalities at the embolization site. Thereafter, we followed him with CE-CT, and there has been no recurrence of aneurysm or retroperitoneal hemorrhage for 20 months (Figure 1).

DISCUSSION

To our knowledge, there are no reports of retroperitoneal hemorrhage from a ruptured artery formed by MALS in patients with COVID-19, so this may be the first report. Retroperitoneal hemorrhage associated with MALS was observed in 0.4% of COVID-19 admissions. By the epidemic wave, the incidence ranged from 0% to 2.4%, with the highest rate in the first wave (2.4%), when wild strains were prevalent, and the second highest rate in the seventh wave (1.0%), when mainly BA.5. For the very small number of cases in the periods, we couldn't mention differences in incidence by strain. However, there were some reports on ruptured aneurysm, pseudoaneurysm and shunt associated with COVID-19: intracerebral hematoma induced by cerebral aneurysm and pseudoaneurysm, severe hemoptysis bronchial requiring TAE, delayed forming bronchial

artery pseudoaneurysm, and hepatic artery.³⁻⁶ The forming arterial lesion (aneurysm, pseudoaneurysm etc.) with COVID-19 might be explained by the following mechanism. SARS-CoV-2 has been reported to infect vascular endothelial cells and induce inflammation and damage within them. Angiotensin II (AII) is also reported to cause vascular inflammation, and SARS-CoV-2 infection increases AII levels.⁷ There are reports that increased concentrations of AII in vivo are involved in the formation of aneurysms.⁸ In this case series, five of the six cases had COVID-19 of mild severity, and the laboratory data did not suggest severe microvascular disease or cytokine storm. Therefore, we guess that pseudoaneurysm causing retroperitoneal hemorrhage was likely to have followed aneurysm, beaded, meandering, and dilated aneurysms formed by COVID-19 and MALS. We reported that about 1% of outpatients having abdominal symptoms with mild COVID-19 suffered retroperitoneal hemorrhage due to a ruptured pseudoaneurysm formed by the MAL.⁹ Thus, it might not be so rare that retroperitoneal hemorrhage caused by this mechanism occurs in patients with COVID-19.

One case (No.5) had duodenal stenosis after TAE for retroperitoneal hemorrhage. We estimated that the cause of the delayed duodenal stenosis was increased external compression due to fibrosis of the hematoma, as there were no abnormal mucosal findings on endoscopy and retroperitoneal hematoma was shrinking compared with the first. Hemostasis with TAE as the initial treatment for ruptured aneurysms is known to be useful. We performed angiography as initial treatment in all cases, and TAE by coils in four cases. Though we experienced two cases that didn't recur without TAE by permanent embolization, TAE should be performed when the angiography shows aneurysm or pseudoaneurysm, since complications such as duodenal stenosis and portal vein thrombosis

FDP/D-dimer (mg/dL)	IL-6 (pg/mL)	Days from COVID-19 onset to abdominal pain	Days from abdominal pain to angiography	Angiographic findings in artery with lesion		Procedure for hemorrhage	MAL dissection (months post onset)	Complication post retroperitoneal hemorrhage	Follow-up time post onset (months)	Recurrence of retroperitoneal bleeding
				Location	Morphology					
3.8	NA	9	3	IPDA	Aneurysm	TAE (IPM/CS)	No	None	6	No
0.3	17.6	3	13	DPA ~ IPDA	Dilatation and meandering	Only angiography	Yes/2	None	19	No
3.6	5.1	No symptoms (COVID-19)	7	DPA ~ AIPDA	Pseudoaneurysm and dilation	TAE (coil)	Yes/7	None	23	No
1.1	9.8	3	4	AIPDA	Beading and aneurysm	TAE (coil)	No	None	15	No
1.3	7.7	2	2	PIPDA	Pseudoaneurysm	TAE (coil)	No	Duodenal stenosis	17	No
4.3	NA	3	3	DPA ~ SPDA	Pseudoaneurysm	TAE (coil)	No	Portal vein thrombosis	19	No

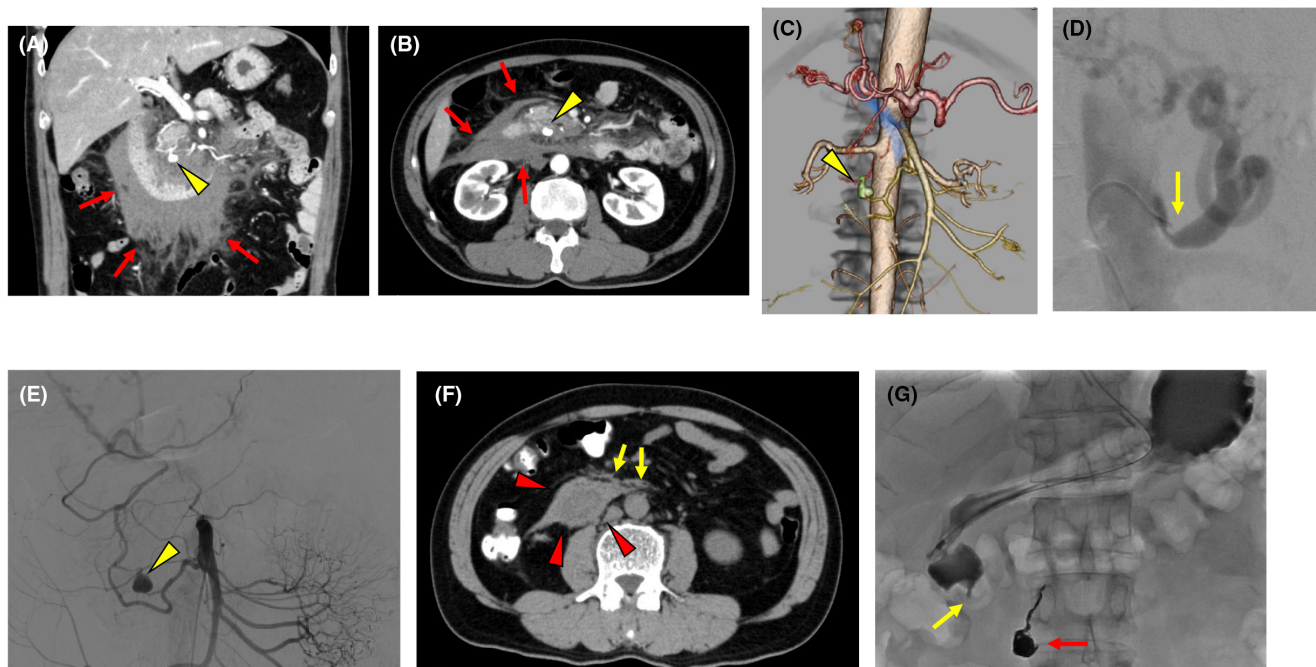


FIGURE 1 Images of retroperitoneal hemorrhage induced by visceral aneurysm rupture formed by median arcuate ligament syndrome in case 5. (A–C) Axial, coronal, and 3D computed tomography (CT) images on Day 2 of sickness show evidence of retroperitoneal hemorrhage (red arrows) with pseudoaneurysm of the inferior pancreaticoduodenal artery (yellow arrowhead). (D) Celiac artery angiographic image on Day 3 of sickness reveals the almost occluded celiac arterial root and post-stenotic dilation (yellow arrow). (E) Superior mesenteric artery angiography on the Day 3 image reveals a pseudoaneurysm of the inferior pancreaticoduodenal artery (yellow arrowhead). (F) Axial CT image on Day 13 reveals retroperitoneal hematoma (red arrowheads) and duodenal compression (yellow arrows). (G) Upper gastrointestinal series image on Day 13 reveals disruption in the duodenum (yellow arrow) and the coil placed for the pseudoaneurysm of the inferior pancreaticoduodenal artery (red arrow).

may occur due to hematoma enlargement. Whether radical resection of the MAL should be performed is controversial. Some reports indicate that new aneurysms almost never develop without radical MAL resection and that MAL resection is not mandatory.¹⁰ Two of the first three cases (No. 1–3) were performed elective MAL dissection. Through the subsequent three cases (No. 4–6), we began to consider the possibility that this rare retroperitoneal hemorrhage associated with the vasculopathy of COVID-19. Though the follow-up period was short, imaging studies after recovery from COVID-19 showed that no new lesions appeared and that the lesions had disappeared or improved. Therefore, we chose the policy of follow-up carefully in the latter three cases, assuming that the risk of bleeding decreases as recovering from COVID-19. All six cases including those for which TAE was not performed have progressed without rebleeding. However, the follow-up period after bleeding in the present patients was very short, so it could not be determined to necessary to perform MAL resection in most of them.

CONCLUSION

We reported six cases of retroperitoneal hemorrhage due to a ruptured aneurysm formed by MALS in association with COVID-19. Retroperitoneal hemorrhage caused by MALS is rare, but it might be triggered by COVID-19 and can result

in arterial disruption and hemorrhage. In COVID-19 patients presenting with abdominal pain, a CT scan may be necessary to rule out this syndrome.

ACKNOWLEDGMENTS

The authors thank Rise Japan LCC for carefully proofreading the manuscript.

CONFLICT OF INTEREST STATEMENT

Dr. Yasuyuki Kuwagata is an Editorial Board member of AMS Journal and a co-author of this article. To minimize bias, they were excluded from all editorial decision-making related to the acceptance of this article for publication.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

Approval of the research protocol: None.

Informed consent: Written informed consent was obtained from the patients for publication of this study and accompanying images. The documentation for informed consent is available from the corresponding author on request.

Registry and registration no. of the study/trial: N/A.

Animal studies: N/A.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Okuno N, Maruyama S, Wada D, Komemushi A, Shimazu H, Kanayama S, et al. Retroperitoneal hemorrhage due to ruptured artery induced by median arcuate ligament syndrome in patients with COVID-19: A case series. *Acute Med Surg*. 2024;11:e70015. <https://doi.org/10.1002/ams2.70015>