Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.2259-18
Intern Med 58: 1907-1912, 2019
http://internmed.jp

【 CASE REPORT 】

Pulmonary Thromboembolism Caused by Calcification in the Inferior Vena Cava of a Japanese Adult

Satoshi Ikeda[1], Seiji Koga[1], Yuki Yamagata[1], Yuji Koide[1], Hiroaki Kawano[1], Hiroshi Mukae[2] and Koji Mamemura[1]

Abstract:
A 45-year-old Japanese man was referred to our hospital with chest and back pain with a duration of two days. Contrast-enhanced computed tomography (CT) showed a large calcified lesion in the inferior vena cava (IVC), thrombus with calcification in the pulmonary arteries of the left lower lobe, and an infiltrative shadow in the left lower lobe. He was diagnosed with pulmonary thromboembolism (PE) and pneumonia. Calcification in the IVC was not evident on any CT images obtained six and eight years earlier. This patient was identified to be an extremely rare case of PE associated with IVC calcification that developed during adulthood.

Key words: calcified thrombosis, inferior vena cava, pulmonary thromboembolism, Japanese

(Intern Med 58: 1907-1912, 2019)
(DOI: 10.2169/internalmedicine.2259-18)

Introduction

Calcified lesions in the inferior vena cava (IVC) are rare. Calcified thrombus in the IVC was originally identified in two children, and it has since been primarily found in pediatric populations (1). Silverman et al. described four children aged from birth to 12 years who had calcified thrombi of the IVC. These characteristically appeared as bullet-shaped formations on abdominal X-rays (2). However, few reports have so far described IVC calcification contributing to pulmonary thromboembolism (PE) in adults, especially in Japan. We herein describe a 45-year-old Japanese man with PE derived from IVC calcification that had developed within the last six years.

Case Report

A 45-year-old man was referred to our hospital with a two-day history of chest and back pain. He had a history of acute appendicitis 6 and 8 years ago, and underwent an appendectomy 6 years previously. Upon admission, his vital signs were as follows: pulse, 66 bpm; blood pressure, 152/94 mmHg; temperature, 36.6℃; arterial oxygen saturation on pulse oximetry, 98% on room air. A coarse crackle at the left lower lung was auscultated, but edema was not evident at the extremities. Table shows that laboratory findings indicated inflammation [white blood cells (WBC), 9,000/μL; C-reactive protein (CRP), 8.01 mg/dL], elevated biliary enzymes (total bilirubin, 2.5 mg/dL; alkaline phosphatase, 340 U/L; lactate dehydrogenase, 240 U/L) as well as elevated D-dimer (2.1 μg/mL) and fibrin degradation products (8.2 μg/mL). Chest X-rays revealed an infiltrative shadow in left lower lung field (Fig. 1, left), but no cardiomegaly (cardiothoracic ratio, 49%). Electrocardiography showed a sinus rhythm of 66/min and an S1Q3T3 pattern (Fig. 1, right). Echocardiography revealed a normal left ventricular function (ejection fraction, 67%) and no overt right ventricular overload, namely a tricuspid valve regurgitation pressure gradient of 21 mmHg with IVC diameters of 20 and 8 mm at inspiration and expiration, respectively. Contrast-enhanced computed tomography (CT) demonstrated a calcified lesion (77×16 mm) in the IVC without collateral circulation (Fig. 2), and thrombus with calcification in the pulmonary arteries of the left lower lobe (Fig. 3), but with no calcification in the deep veins of lower legs. An infiltrative shadow

[1]Department of Cardiovascular Medicine, Nagasaki University Graduate School of Biomedical Sciences, Japan and [2]Department of Respiratory Medicine, Unit of Translational Medicine, Nagasaki University Graduate School of Biomedical Sciences, Japan
Received: October 12, 2018; Accepted: January 18, 2019; Advance Publication by J-STAGE: March 28, 2019
Correspondence to Dr. Satoshi Ikeda, sikeda@nagasaki-u.ac.jp

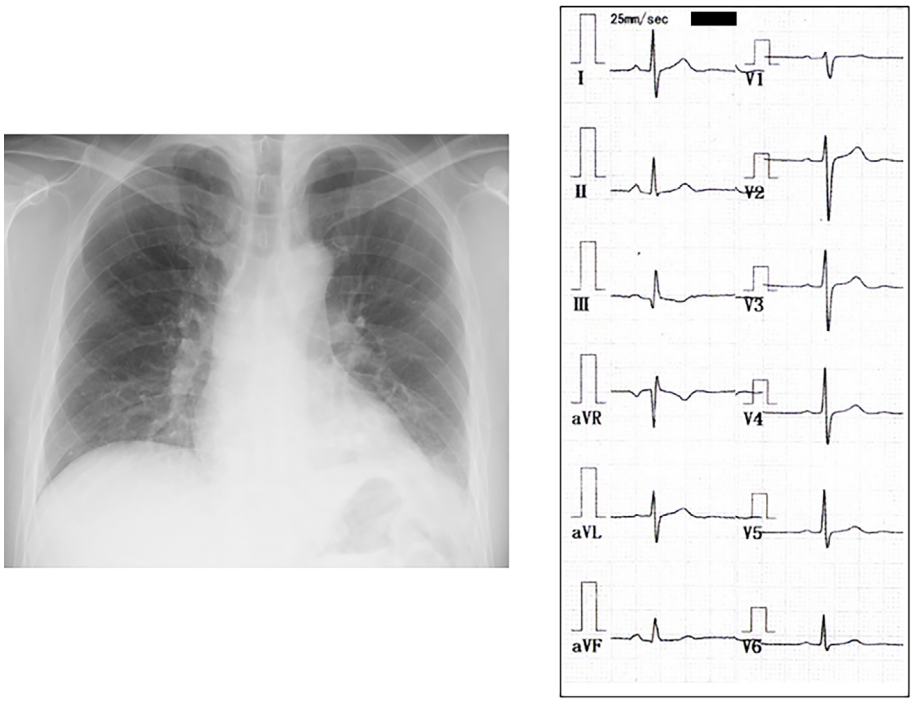

Figure 1. **Chest X-ray (left) and electrocardiography (right) findings on admission.**

was also observed in the left lower lobe (Fig. 3). He was diagnosed with PE and pneumonia and was immediately treated with antibiotics and intravenous unfractionated heparin, then a direct oral anticoagulant (DOAC). We examined the factors associated with thrombophilia, such as deficiencies of protein C, protein S and antithrombin III, antiphospholipid syndrome, connective tissue diseases and homocysteine; however, these findings were normal (Table). The parameters of the calcium metabolism, namely serum calcium, phosphate and intact parathyroid hormone (PTH), were also within the normal ranges (Table). The treatment relieved his symptoms, decreased the WBC, C-reactive protein (CRP) and D-dimer values, and he was discharged on hospital day 24. Six months of anticoagulant therapy improved the PE, but the calcification in the pulmonary artery of the left lower lobe and the IVC persisted (Fig. 4). The patient has remained free of recurrent PE under a DOAC under careful observation for approximately 2 years. Notably, abdominal CT 6 and 8 years earlier did not reveal calcification in the IVC (Fig. 5).

Discussion

The present report describes a Japanese adult male with PE associated with IVC calcification that had developed over the last 6 to 8 years.

Calcification of the IVC is rare. Most previous reports of IVC calcification describe pediatric, rather than adult populations (1-5). Indeed, our literature review uncovered fifteen publications that describe adult patients (6-20). Among them, IVC calcification was associated with PE in two. Chetwood et al. described a 49-year-old male with recurrent PE and IVC calcification who did not have a remarkable medical history or risk factors for thromboembolic disease (7). Ahmed et al. described a 65-year-old male patient who presented with recurrent deep vein thrombosis (DVT) and PE with IVC calcification (17). Calcification in the 49-year-old male was found in the lumen and on the entire circumferential wall of the IVC, similar to the findings of our patient, and from the left to the posterior wall of the IVC in the patient described by Ahmed et al. The recurrent PE might have been caused by thrombosis attached to the calcification in both of these patients. However, images of PE in the former patient were not published and only a lung prefusion image was included in the description of the latter. In addition, the patient described by Ahmed et al. had DVT in the right common femoral vein, suggesting that DVT could directly migrate and embolize in the pulmonary arteries. On the other hand, our patient had PE with calcification in the left lower lung lobe, indicating that the PE was derived from the IVC calcification. Few reports have so far described IVC calcification among Japanese individuals. To our knowledge, only a single case report from a Japanese institution has described intravenous leiomyomatosis with calcification from the right atrium to the left internal iliac vein (11). The present Japanese male patient had an extremely rare adult onset of IVC calcification associated with PE.

The suggested etiology of such calcification includes adrenal hemorrhage, abdominal neoplasm, coagulopathy, dehydration, sepsis, birth asphyxia, maternal diabetes and congenital abnormalities of the IVC (2, 10). Among these, adrenal hemorrhage, congenital disorders and coagulopathy were ruled for our patient (Table and Fig. 4). We finally considered organized thrombosis, neoplasm and exogenous mate-

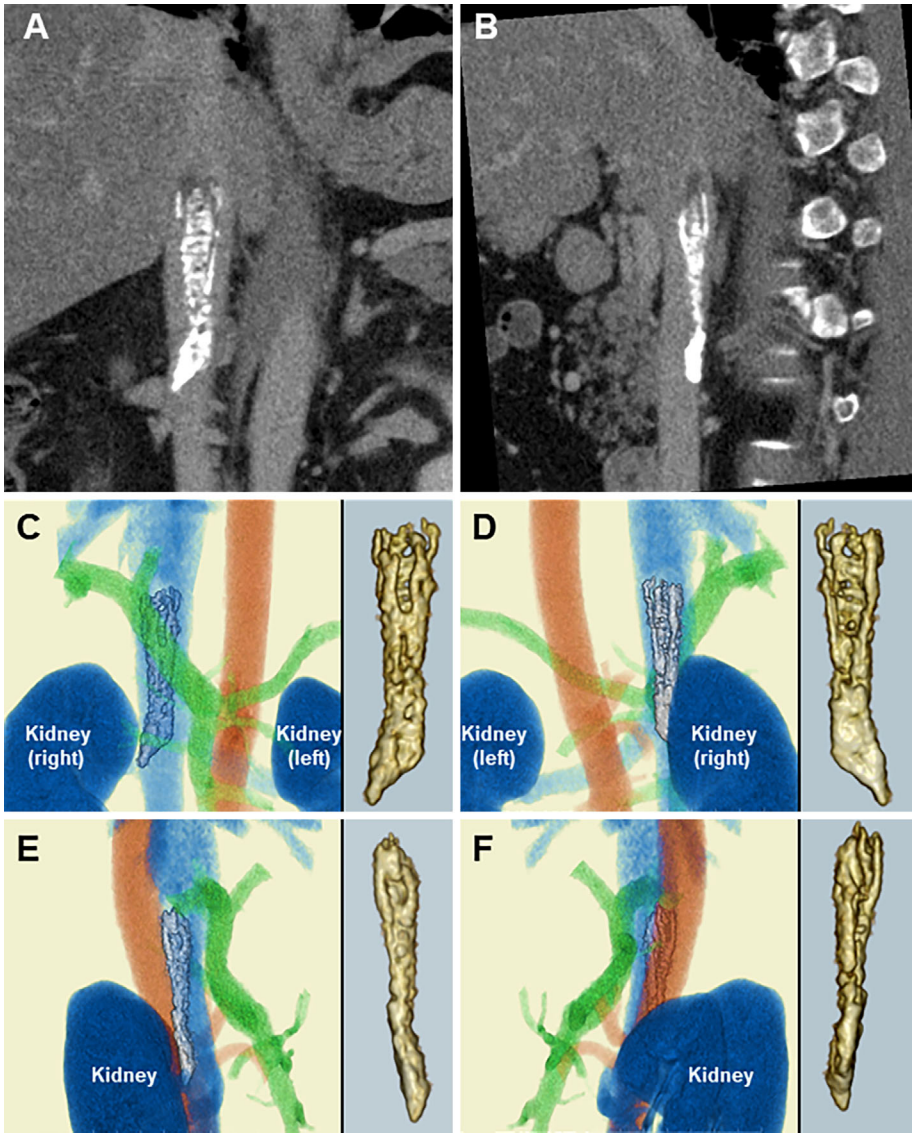

Figure 2. **Contrast-enhanced computed tomography findings of calcification in the inferior vena cava. Front (A) and left (B) views of IVC calcification in CT images. Three-dimensional images of IVC (blue vessel), portal vein (green vessel), abdominal aorta (red vessel) and IVC calcification in front (C), back (D), right (E), and left (F) views. CT: computed tomography, IVC: inferior vena cava**

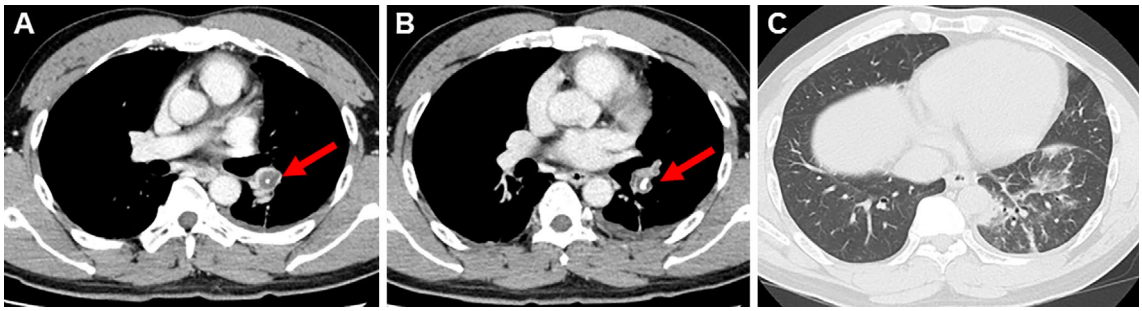

Figure 3. **Contrast-enhanced computed tomography findings of pulmonary thromboembolism and pneumonia. CT images of PE with calcification in the pulmonary arteries (A and B) and infiltrative shadows in left lobe (C). Red arrows, calcification in pulmonary arteries. CT: computed tomography, PE: pulmonary thromboembolism**

rial as possible etiologies. Exogenous material was suspected judging from the shape of the IVC calcification (Fig. 2), but our patient had never experienced surgery requiring intravenous manipulation. Contrast-enhanced mag-

Table. Laboratory Data on Admission.

Blood count		Biochemistry		Coagulation	
Red blood cell	546×10⁴ /μL	Total protein	8.4 mg/dL	PT-INR	1.07
Hemoglobin	16.1 g/dL	Total bilirubin	2.5 mg/dL	APTT	26.9 sec
Hematocrit	45.3 %	Aspartate aminotransferase	20 U/L	D-dimer	2.1 μg/mL
White blood cell	9,000 /μL	Alanine aminotransferase	31 U/L	FDP	8.2 μg/mL
Platelet	11.4×10⁴ /μL	γ-glutamyl transpeptidase	49 U/L	Antithrombin-III	110 %
		Alkaline phosphatase	340 U/L	Protein C	109 %
Serology		Lactate dehydrogenase	240 U/L	Protein S	124 %
C-reactive protein	8.01 mg/dL	Blood urea nitrogen	10 mg/dL	Antibody/others	
		Creatinine	0.92 mg/dL	Lupus anticoagulant	1.14
Blood gas analysis		Na	139 mmol/L	Anti-CLβ2GPI antibody	1.2 U/mL
PaO_2	73.5 mmHg	K	3.9 mmol/L	Antinuclear antibody	<20×
$PaCO_2$	37.8 mmHg	Cl	104 mmol/L		
HCO_3	24.7 mmol/L	Ca	9.6 mg/dL	Homocysteine	11.3 nmol/mL
SaO_2	96.1 %	P	3.7 mg/dL	intact PTH	33.6 pg/mL

PT-INR: prothrombin time international normalized ratio, APTT: activated partial thromboplastin time, FDP: fibrin degradation products, Anti-CLβ2GPI antibody: anti-cardiolipin β2-glycoproteinI complex antibody, intact PTH: intact parathyroid hormone

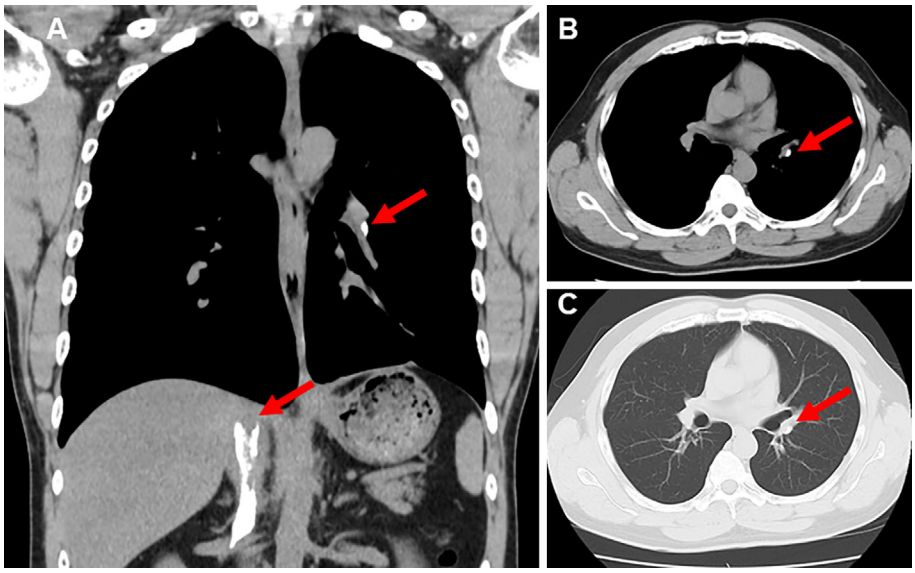

Figure 4. Computed tomography findings of calcification in the inferior vena cava and pulmonary artery at six months after developing pulmonary thromboembolism. Coronal section (A), and transverse section with mediastinal (B) and pulmonary window setting (C). Red arrows, calcification in IVC and pulmonary arteries. IVC: inferior vena cava

netic resonance imaging ruled out a malignant neoplasm around the IVC calcification. Therefore, we concluded that the calcification was organized thrombosis. The following have been considered as possible etiologies of thrombosis within the IVC: generalized or focal infection, tumors in the region of liver and IVC, and anomalies of the IVC (2). Our patient had two episodes regarding infection, the pneumonia associated with this presentation and a previous occurrence of appendicitis. The pneumonia was transient and thus too short to generate a large organized thrombosis. The appendicitis was also a transient and focal infection far from the site of the organized thrombosis. Therefore, the relationship between these infections and organized thrombosis is unclear. In addition, none of the other etiologies were deemed to be relevant to our patient. Ultimately, the etiology of the calcification in the present patient remains unknown because he declined to undergo invasive examinations or surgical resection.

In conclusion, we herein described a Japanese male who developed PE caused by a calcification in the IVC that might have been an organized thrombosis acquired during adulthood. This condition is extremely rare, and the patient is likely to require long-term anticoagulant therapy.

The authors state that they have no Conflict of Interest (COI).

Acknowledgement

We would like to thank Yoshiaki Fukushima, a radiological

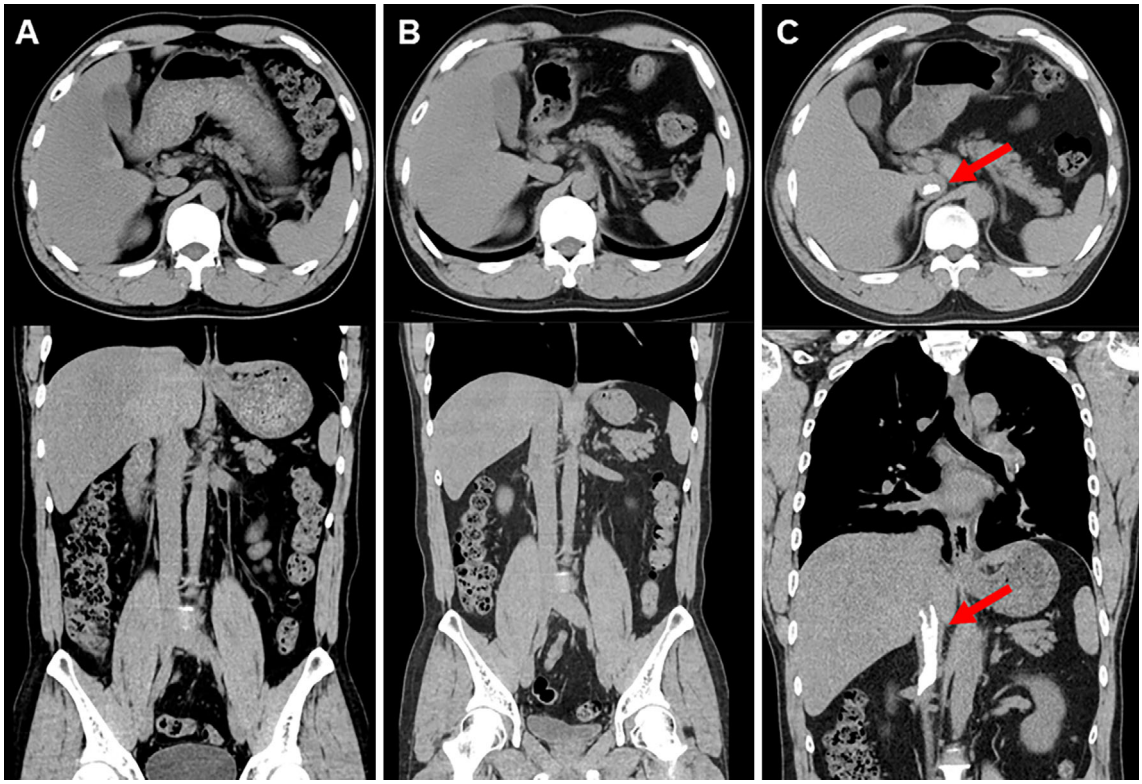

Figure 5. **Computed tomography findings of calcification in the inferior vena cava. Images acquired eight (A) and six (B) years before, and at the onset of pulmonary thromboembolism (C). Upper and lower panels, transverse and coronal images, respectively. Red arrows, calcification in IVC. IVC: inferior vena cava**

technologist, for his assistance in constructing the 3-D CT images.

References

1. Singleton EB, Rosenberg HS. Intraluminal calcification of inferior vena cava. Am J Roentgenol Radium Ther Nucl Med **86**: 556-560, 1961.
2. Silverman NR, Borns PF, Goldstein AH, Greening RR, Hope JW. Thrombus calcification in the inferior vena cava. Am J Roentgenol Radium Ther Nucl Med **106**: 97-102, 1969.
3. Kassner EG, Baumstark A, Kinkhabwala MN, Ablow RC, Haller JO. Calcified thrombus in the inferior vena cava in infants and children. Pediatr Radiol **4**: 167-171, 1976.
4. Gammill SL, Nice CM Jr. Calcification in the inferior vena cava. Radiology **92**: 1288-1290, 1969.
5. Chen R, Deng X, Luo J, Huang P. Calcified inferior vena cava and right atrial myxoma in an 18-month-old male: a case report. Medicine (Baltimore) **97**: e11073, 2018.
6. Kale SB, Raghavan J. Calcified right atrial mass. J Card Surg **27**: 361, 2012.
7. Chetwood A, Saweirs M, Davies AH. A calcified lesion within the inferior vena cava presenting as recurrent pulmonary emboli. J Vasc Surg **53**: 204-245, 2011.
8. Leclerc A, Lapebie FX, Thuillier F, Lacroix P. [Calcified bullet thrombus of the inferior vena cava and left renal vein in an adult]. J Mal Vasc **41**: 294-297, 2016 (in French, Abstract in English).
9. Vaideeswar P, Karunamurthy A, Patwardhan AM, Hira P, Raut AR. Cardiac calcified amorphous tumor. J Card Surg **25**: 32-35, 2010.
10. Hinrichs CR, Singer A, Maldjian P, Abu-Judeh H, Dadarwala A. Inferior vena cava thrombosis: a mechanism of posttraumatic adrenal hemorrhage. AJR Am J Roentgenol **177**: 357-358, 2001.
11. Tanaka YO, Jikuya T, Iijima T, Sakakibara Y, Itai Y. Intravenous leiomyomatosis diagnosed by plain radiographs. Clin Radiol **57**: 1037-1040, 2002.
12. Kareem H, Devasia T, Nayak K, Agarwal S. Unexplained extensive calcification of the venae cavae extending into the right atrium causing partial obstruction of the tricuspid valve. BMJ Case Rep 2014.
13. Cagnoli L, Viglietta G, Madia G, et al. Acute bilateral renal vein thrombosis superimposed on calcified thrombus of the inferior vena cava in a patient with membranous lupus nephritis. Nephrol Dial Transplant **5** (Suppl 1): 71-74, 1990.
14. McWilliams RG, O'Connor PJ, Chalmers AG. Case report: extensive calcified thrombus of the inferior vena cava. Clin Radiol **51**: 660-662, 1996.
15. Yaghmai V, Baker SR. Extensive calcification in the inferior vena cava in an adult. AJR Am J Roentgenol **161**: 676-677, 1993.
16. Katz D, Melsom R. Calcification of the inferior vena cava. J Comput Assist Tomogr **6**: 637-639, 1982.
17. Ahmed AK, Finocchi V, Al-Agib S. Inferior vena cava calcification, a possible link with recurrent deep venous thrombosis and pulmonary embolism: a case study and review of literature. BJR Case Rep **4**: 20180018, 2018.
18. Madia G, Tonti R, Viglietta G, Cagnoli L, Maffi AM, Pantani P. [A calcified thrombus of the vena cava inferior in lupus nephropathy]. Radiol Med **79**: 251-254, 1990 (in Italian).
19. Kopp W, Tolly E, Ebner F. [Calcification of the inferior vena cava imitates an aortic aneurysm]. Rofo **143**: 592-593, 1985 (in German).
20. Luong S, Miller JA. Calcifications and narrowing of the inferior vena cava. A study using duplex Doppler ultrasound. JDMS **7**: 154-156, 1991.

The Internal Medicine is an Open Access journal distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view the details of this license, please visit (https://creativecommons.org/licenses/by-nc-nd/4.0/).

Ⓒ 2019 The Japanese Society of Internal Medicine