[CASE REPORT]

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

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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

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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°C; 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 (77x16 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...
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 PTH, were also within the normal ranges (Table). The treatment relieved his symptoms, decreased the WBC, 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 AK 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 perfusion image was included in the description of the latter. In addition, the patient described by Ahmed AK 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-
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).

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**Table. Laboratory Data on Admission.**

| Blood count       | Biochemistry                | Coagulation            |
|-------------------|----------------------------|------------------------|
| Red blood cell    | Total protein: 8.4 mg/dL    | PT-INR: 1.07           |
|                   | Total bilirubin: 2.5 mg/dL  | APTT: 26.9 sec         |
|                   | Aspartate aminotransferase: 20 U/L | D-dimer: 2.1 μg/mL   |
|                   | Alanine aminotransferase: 31 U/L | FDP: 8.2 μg/mL       |
|                   | γ-glutamyl transpeptidase: 49 U/L | Anti-thrombin-III: 110 %|
|                   | Alkaline phosphatase: 340 U/L | Protein C: 109 %      |
|                   | Lactate dehydrogenase: 240 U/L | Protein S: 124 %      |
|                   | Blood urea nitrogen: 10 mg/dL | Antibody/others       |
|                   | Creatinine: 0.92 mg/dL      | Lupus anticoagulant: 1.14 |
|                   | Na: 139 mmol/L              | Anti-CLβ2GPI antibody: 1.2 U/mL |
|                   | K: 3.9 mmol/L               | Antinuclear antibody: <20x |
|                   | Cl: 104 mmol/L              |                        |
|                   | Ca: 9.6 mg/dL               | Homocysteine: 11.3 nmol/mL|
|                   | 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

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**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

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

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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.
