

Phosphoglyceride crystal deposition disease mimicking a malignant tumor

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ABSTRACT

A 45-year-old woman who had undergone surgical repair for an atrial septal defect at the age of 7 years presented with multiple anterior mediastinal masses. Positron-emission tomography (PET) with 2-[¹⁸F]fluoro-2-deoxy-D-glucose (FDG) revealed high uptake in the masses. The findings were interpreted as mediastinal malignant tumors with dissemination. Biopsy was performed, and the histological diagnosis was phosphoglyceride crystal deposition disease without neoplastic changes. Although phosphoglyceride crystal deposition disease is rare, it should be recognized as a potential interpretive pitfall that mimics a malignant tumor in FDG-PET findings in a patient after cardiac surgery.

1. Introduction

Phosphoglyceride crystal deposition disease is defined as deposition of crystals of the phospholipid phosphoglyceride. This disease tends to occur at the sites of invasive procedures, including surgical sites [1,2]. We herein report a 45-year-old-woman presenting with multiple anterior mediastinal masses that were diagnosed as phosphoglyceride deposits. We also conducted a literature review of clinical and imaging findings for phosphoglyceride crystal deposition disease. The imaging findings for phosphoglyceride crystal deposition disease are generally limited availability. It is an extremely rare disease, but clinicians should consider it as a differential diagnosis for masses generated at surgical sites. In this report, we describe the clinical and imaging features of the disease.

2. Case presentation

A 45-year-old Japanese woman was referred with a strange feeling in her left shoulder. She had a history of surgical repair of an atrial septal defect at the age of 7 years. The levels of serum tumor markers (carcinoembryonic antigen and carbohydrate antigen 19-9) were within normal limits. No eyelid ptosis or multiple visions were observed. A negative result was obtained for the acetylcholine receptor antibody test. Contrast-enhanced computed tomography (CT) showed 2 masses with partial calcification, located in the anterior mediastinum. The 2 masses showed homogeneous enhancement. They measured 9 × 6 × 4 cm and 2.5 × 1.5 × 2.0 cm (Fig. 1a, b). On magnetic resonance imaging (MRI), a T1-weighted image (T1WI) demonstrated a

well-defined isointense mass (Fig. 2a, b). A T2-weighted image (T2WI) demonstrated a mixture of isointense and hyperintense areas (Fig. 2c, d).

Positron-emission tomography (PET) with 2-[¹⁸F]fluoro-2-deoxy-D-glucose (FDG) images revealed uptake in the 2 masses (Fig. 3a, b). The maximum standardized uptake values (SUV) of the 2 lesions were 26.0 and 13.6. Other signs of abnormal uptake suggesting a malignant lesion were not observed.

The findings were interpreted as mediastinal malignant tumors with dissemination. After obtaining informed consent, we performed a biopsy on the larger mass, under CT guidance. Histologically, the biopsy specimen showed a foreign body granuloma featuring deposition of many small crystals and foreign-body giant cells. Under polarized light, the deposited materials appeared as string-like crystals and appeared to be refractive (Fig. 4).

Immunohistochemistry identified histiocytes and multinucleated giant cells, which were positive for vimentin and CD68. Based on these findings, the tumors were diagnosed as resulting from phosphoglyceride crystal deposition. Because there was no evidence of neoplasia, the patient refused to permit resection of the masses. She did not receive any further treatment. Two years later, the size of the masses had not changed, and there was no exacerbation of her symptoms.

3. Imaging protocol

3.1. CT imaging protocol

CT of the chest were performed using a 64-detector row CT machine

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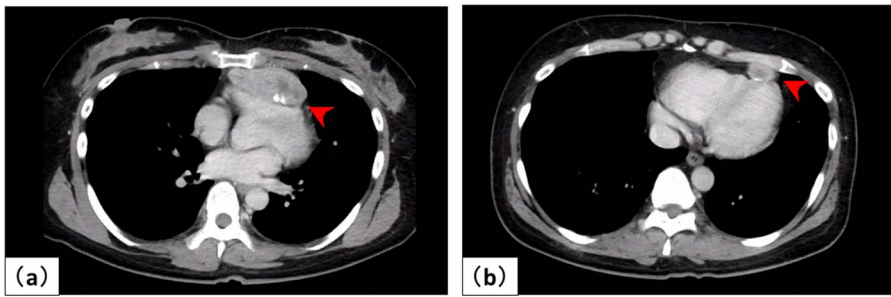


Fig. 1. A 45-year-old woman presenting with multiple anterior mediastinal masses. (a, b) On contrast-enhanced computed tomography (CT), the masses demonstrated homogeneous enhancement with partial calcification (arrowheads).

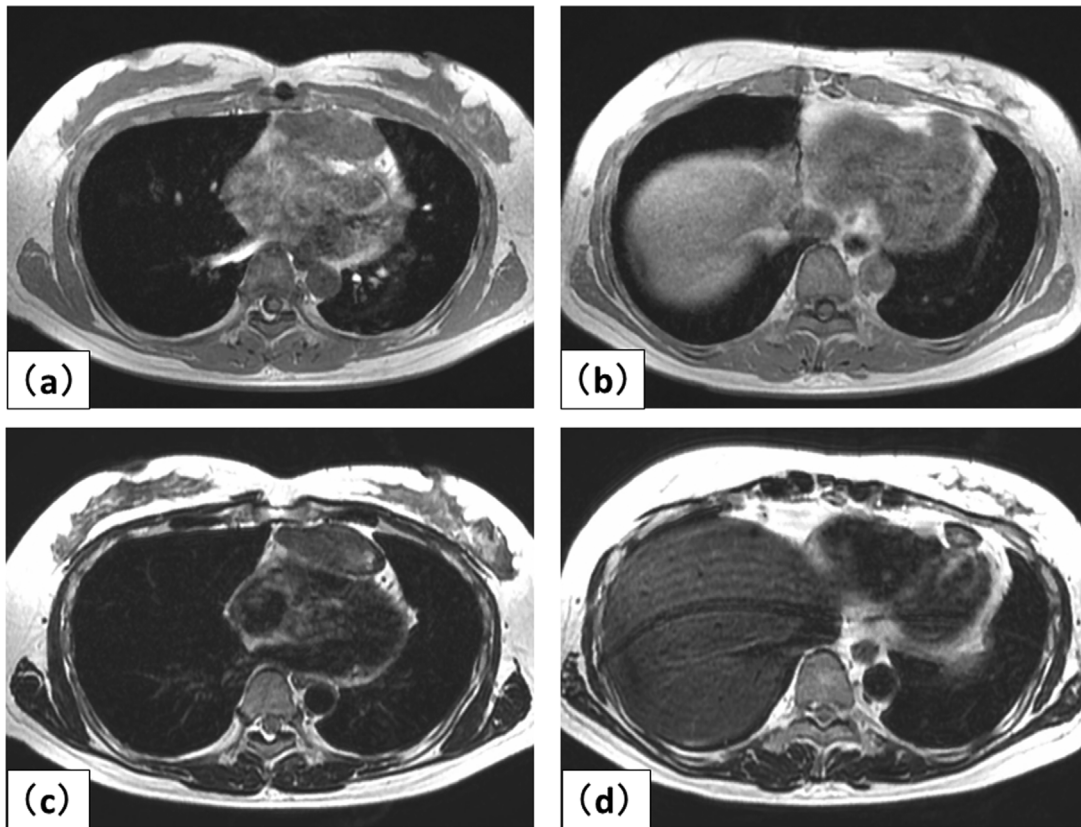


Fig. 2. Magnetic resonance imaging (MRI) findings. (a) A T1-weighted image (T1WI) demonstrated a well-defined isointense mass. (b) A T2-weighted image (T2WI) demonstrated a mixture of isointense and hyperintense areas.

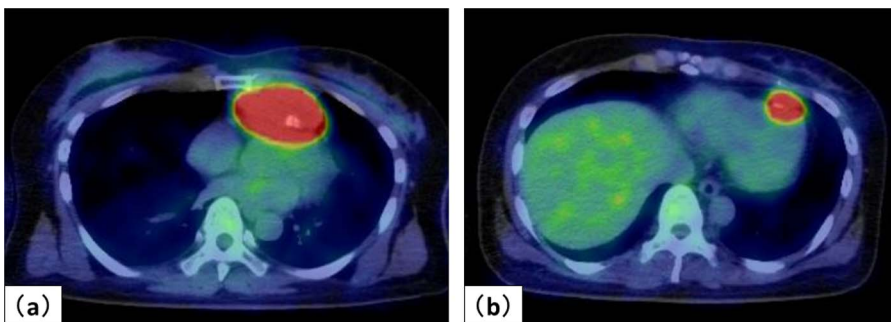


Fig. 3. FDG-PET images showed uptake in the 2 masses. The maximum standardized uptake value (SUV) of 2 lesions were (a) 26.0 and (b) 13.6.

(Aquilion 64, Toshiba Medical System, Tokyo, Japan). Contrast-enhanced CT has been performed after an intravenous bolus injection of 100 ml nonionic iodinated contrast media (iopamidol, 300 mg I/ml; Iopamiron, Bayer Yakuhin, Tokyo, Japan) at a rate of 3 ml/s. Scanning was initiated approximately 60 s after the initiation of the bolus injection of contrast media. Scanning parameters as follows: tube voltage, 120 kV; tube current, 250 mAs; rotation time, 0.358 s; field of view,

400 mm; reconstruction interval, 1 mm; slice thickness, 0.8 mm.

3.2. MR imaging protocol

MRI was performed using the 1.5-T superconductive system (Avanto; Siemens Medical Systems, Erlangen, Germany) with an eight-channel body matrix coil and a spine matrix coil. T1WI was acquired

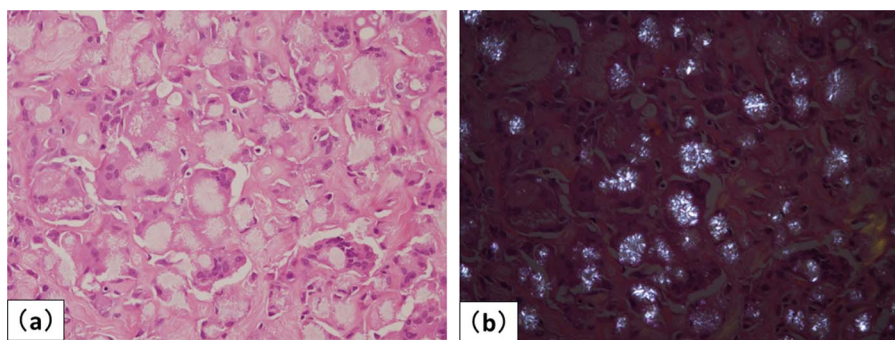


Fig. 4. (a) Histologically, the biopsy specimen showed a foreign body granuloma featuring deposition of many small crystals and foreign-body giant cells (Hematoxylin and eosin staining, original magnification 200 \times). (b) Under polarized light, the deposited materials demonstrated string-like crystals and appeared to be refractive.

using a breath-hold gradient-echo sequence with the following parameters: repetition time(TR)/echo time(TE), 750/10, msec; matrix, 320 \times 70%; field of view (FOV), 400 mm \times 65%; slice thickness, 5.0 mm. T2WI was acquired under breath-holding and the parameters were as follows: TR/TE, 2250/90 ms; matrix, 320 \times 70%; FOV, 400 mm \times 65%; slice thickness, 5.0 mm.

3.3. FDG PET/CT imaging protocol

The patient fasted for 6 h before receiving an intravenous injection of 18 F-FDG (5 MBq/kg). FDG PET/CT scans were obtained using Biograph 16 (Siemens Medical Solutions; Knoxville, TN, USA) scanners, with a 700-mm FOV and a slice thickness of 3.27 mm. The CT was acquired to correct PET transmission using the following parameters: 140 kV and 120–240 mAs to produce 128 \times 128 matrix images. The patient was scanned in the arms-down position, from head to thigh. Shallow breathing was advised to avoid motion artifacts and minimize misregistration of CT and PET images. Intravenous contrast material was not administered for CT scanning. After the CT scan, the PET data were acquired, and acquisition time was 3 min per bed position. CT images were reconstructed using the conventional filtered back-projection method. Axial full width at half-maximum at 1 cm from the center of the FOV was 6.3 mm.

4. Discussion

Phosphoglyceride crystal deposition disease is characterized by phosphoglyceride crystals deposited as tumors in soft tissue or bone, with no relation to the joint. Phosphoglycerides are a class of phospholipids, including lecithin and cephalin. They are a major component of cell membranes. Phosphoglyceride crystal deposition disease is considered a lipid metabolic disorder, occurring predominantly in injured soft tissues, forming foreign body granulomas [1,2]. In our case, the phosphoglyceride crystal deposition was located on a surgical wound relating to myocardia.

The histologic findings for phosphoglyceride crystal deposition disease are known to include clustering of macrophages around the crystals and formation of foreign body granulomas. The crystals are 50–150 μ m in diameter, appearing as oval pink or blue aggregates on hematoxylin and eosin staining, arranged in corona-like circles [3]. On polarized light microscopy, the fibrillar crystals appear refractive [3]. The crystals do not dissolve in the usual specimen creation process, but characteristically dissolve in acetic acid, with oxygen gas formation. They also dissolve easily in high-pH solvents, and stain positively for phosphoglycerides in the gold hydroxamic acid method [1–3]. Immunohistochemistry shows macrophages accumulating around the numerous crystal deposits, which show weak focal positivity for pan-macrophage marker (CD68), and faint positivity for lysozymes and S-100 protein [1,2,4].

We performed an English literature review by searching for articles on phosphoglyceride crystal deposition disease, published up to November 2017 on PubMed. The clinical features and imaging findings

for phosphoglyceride crystal deposition disease are shown in Table 1. In all cases, phosphoglyceride crystal deposition disease occurred at sites susceptible to invasion due to a previous injury [1–7]. Phosphoglyceride crystal deposition disease sometimes forms large masses, which could be misdiagnosed as malignant tumors. In our case, the crystal formation at the site of invasion took many years to grow into a tumor-like lesion and become symptomatic. To our knowledge, there is no case of multiple masses of the anterior mediastinum as seen in our case. The etiology and pathogenesis of this disease are unknown. No sex predilection, congenital abnormalities, or family history of metabolic disorders have been identified in connection with this disease entity. Deposition sites are characteristically postoperative sites or intramuscular injection sites.

FDG-PET images of phosphoglyceride crystal deposition disease are not widely known. Only 2 reports, including our case, on FDG-PET imaging features of phosphoglyceride crystal deposition disease have been published in the English-language literature [4]. In the previous report, the entire mass showed FDG uptake, and the maximal standardized uptake value was very high, as in our case [4].

FDG-PET imaging is used in clinical oncology because it allows for functional imaging of various types of tumors. Generally, high-grade sarcomas and aggressive benign lesions have higher SUVs than benign lesions. However, the use of FDG-PET imaging for tumor diagnosis is limited by the fact that FDG, a glucose analog, is taken up not only by tumor cells but also by macrophages, granulation tissue, and inflamed tissue [8].

In previous reports, phosphoglyceride crystal deposition disease tends to show aggregation of macrophages around the crystals and formation of foreign-body granulomas [1–4]. As in our case, a giant cell is a mass formed by the union of several macrophages. These reactions are suggested to trigger positive FDG uptake. As malignant tumors also show higher uptake of FDG in the same way, we must be careful not to mistake phosphoglyceride crystal deposits for malignant tumors.

In phosphoglyceride crystal deposition diseases, surgical removal is usually performed, but in our case the patient refused to permit resection of the masses. There was no change in size at the last follow up, but careful future follow-up will be necessary.

In conclusion, although phosphoglyceride crystal deposition disease is extremely rare, it should be considered in the differential diagnosis of anterior mediastinum masses in patients with a past history of cardiac surgery.

Authors' contributions

HT and ME contributed to the treatment of the patient. HT collected the clinical data. HT and ME prepared and analyzed the pathological data. HT drafted the manuscript. All authors helped in the manuscript drafting. All authors have read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

Table 1
Clinical features and imaging findings for phosphoglyceride crystal deposition disease.

No.	Author	Age/Sex	Past history	Age of operation	Location	Tumor size (cm)	Shape	CT	MRI	FDG (max-SUV)
No. 1	Kubo [5]	58/M	intramuscular injection	NS	left buttock muscle	11 × 10 × 6	irregular	low-density area in the center	low intensity on T1WI	NS
No. 2-1	Miura [1]	62/F	dental treatment appendectomy intramuscular injection	32 32 32	right mandible laparotomy scar bilateral brachial muscle	NS 1–11 × 6 NS	lobulate	heterogeneously enhanced in the periphery, low-density area in the center	high intensity on T2WI low intensity on T1WI	NS NS
No. 2-2	Nishimura [6]	76/F	lumbar anesthetic	32	vertebral bodies (Th12, L4)	NS	irregular	osteolytic changes	low intensity on T1WI high intensity on T2WI	NS
No. 3	Yamada [3]	50/F	cesarean delivery	24	pelvic	10	lobulate	NS	contained a hemorrhagic component; central solid part exhibited a low intensity on T2WI	NS
No. 4	Shoji [4]	37/M	repair for a ventricular septal defect	2	anterior mediastinum	6	irregular	heterogeneously enhanced, partial calcification	NS	16.9
No. 5	Yachida [7]	51/M	gastrectomy	18	upper abdominal soft region	3.5	lobulate	heterogeneously enhanced	NS	NS
No. 6	Miura [2]	58/M	gastrectomy	18	abdominal soft region	infant's head size	NS	NS	NS	NS
No. 7	Miura [2]	64/F	NS	NS	scapular bone	10	NS	NS	NS	NS
No. 8	Our case	45/F	repair for an atrial septal defect	7	anterior mediastinum	9 × 6 × 4 2.5 × 1.5 × 2.0	lobulate	heterogeneously enhanced, partial calcification	isointense on T1WI, mixture of iso- and hyper- intense areas on T2WI	26.0 13.6

CT: computed tomography; MRI: magnetic resonance imaging; FDG: 2-[18F]fluoro-2-deoxy-D-glucose; SUV: standardized uptake value; NS: Not shown; T1WI: T1-weighted MRI; T2WI: T2-weighted MRI. Nos. 2-1 and 2-2 refer to the same patient.

Consent for publication

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

Ethics approval and consent to participate

The ethical approval has been received by our hospital concerning the publication of this manuscript and any accompanying images.

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