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Phosphoglyceride crystal deposition disease requiring differential diagnosis from malignant tumors and confirmed by Raman spectroscopy: a case report

Phosphoglyceride crystal deposition disease

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Abstract

BACKGROUND

Phosphoglyceride crystal deposition disease is a rare acquired disease, phospholipid crystals depositing onto bone and soft tissue long after surgery, trauma, and repeated injections.

CASE SUMMARY

A 60-year-old-womanwas referred to our department because of multiple abdominal masses after open splenectomy for idiopathic thrombocytopenic purpura 29 years before. All of the masses showed marked FDG uptake on ^{18}F-FDG PET scan, and were strongly suspected to be malignant tumors. Surgical biopsies were performed, and the abdominal masses were aligned vertically three in a row along the tissue layers cut in the patient's previous surgery. Pathological finding of the specimen showed foreign body granuloma consisting of histiocytes and multinucleated giant cells accumulating around needle-like crystals. The crystals were confirmed as phosphoglyceride by Raman spectroscopy, and she was diagnosed as having the phosphoglyceride crystal deposition disease. To our knowledge, this is the first report of phosphoglyceride crystal deposition diagnosed by the Raman spectroscopy.

CONCLUSION

We made a definitive diagnosis of PCDD in a patient who had tumors with marked FDG uptake on PET-CT by incisional biopsy and composition analysis using Raman spectroscopy, a method that has not been previously reported for the diagnosis of PCDD.

Key Words: Phosphoglyceride crystal deposition disease; Raman spectroscopy; Positron emission tomography; crystals with a foreign body granuloma; scar of surgery; case report

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Core Tip: Here, we report a case of phosphoglyceride crystal deposition disease with extremely high uptake on 18F-fluorodeoxyglucose-positron emission tomography, that we successfully diagnosed by the Raman spectroscopy, and excluded malignant tumor.

INTRODUCTION

In phosphoglyceride crystal deposition disease (PCDD), which is a rare acquired disease regarded as a type of lipid metabolism disorder, phospholipid crystals deposit onto bone and soft tissue and histiocytes and giant cells accumulate around these deposits to form foreign body granulomas [1, 2]. PCDD frequently occurs at sites of scar of trauma, surgery, and repeated injections. In previous reports, phosphoglyceride was characterized by the gold hydroxamic acid method, X-ray microanalysis, and microstamping mass spectrometry[1]. Clinically, ^{18}F-fluorodeoxyglucose-positron emission tomography (^{18}F-FDG PET) scan showed a maximum standardized uptake value ranged from 13.6 to 26.0 [3, 4]. Here, we report a case of PCDD with extremely high uptake on ^{18}F-FDG PET, that we successfully diagnosed by the Raman spectroscopy, and excluded malignant tumor.

CASE PRESENTATION

Chief complaints

On upper gastrointestinal endoscopy as part of a routine health checkup, the extrinsic compression at the greater curvature of the upper stomach was found. Abdominal CT

History of present illness

On upper gastrointestinal endoscopy as part of a routine health checkup, the extrinsic compression at the greater curvature of the upper stomach was found. Abdominal CT (Figure 1(a), (b)) showed a 50x40x48mm mass protruding outward from the greater curvature of the upper staomach. Contrast enhancement of the mass was observed in the arterial phase. Three masses protruding from the abdominal wall into the peritoneal cavity were also observed that measured 28x16x18 mm, 55x42x36 mm, and 55 x44x55 mm and had irregular margins. All of these masses had internal calcification and contrast enhancement. ^{18}F-FDG PET scan (Figure 2) showed a maximum standardized uptake value (SUV) of 34.19 within a 5-cm mass protruding toward the serosa at the greater curvature of the stomach. The abdominal masses also had high FDG uptake (SUV max: 37.71). And the left axiallary lymph node also had high FDG uptake (SUV max: 3.51) and suspected lymph node metastasis. Blood tests showed a low platelet count of 49x10^3/μL, normal tumor markers including sIL-2R (258 U/mL). She was therefore referred to the Department of Gastrointestinal Surgery for definitive diagnosis. We had a high index of suspicion for malignant tumors, thus performed incisional biopsy.

History of past illness

The patient was a 60-year-old woman being treated with prednisolone 1 mg orally for idiopathic thrombocytopenic purpura (ITP) at the Department of Hematology of our hospital. She had undergone open splenectomy for ITP 29 years before and had been treated with steroids since then.

Personal and family history

No special instruction

Physical examination

The tumor can be palpated by palpation of the abdomen. In addition, it is not considered as a special place.

Laboratory examinations

Blood tests showed a low platelet count of $49x10^3/\mu L$, normal tumor markers including sIL-2R (258 U/mL). She was therefore referred to the Department of Gastrointestinal Surgery for definitive diagnosis.

Imaging examinations

On upper gastrointestinal endoscopy as part of a routine health checkup, the extrinsic compression at the greater curvature of the upper stomach was found. Abdominal CT (Figure 1(a), (b)) showed a 50x40x48mm mass protruding outward from the greater curvature of the upper staomach. Contrast enhancement of the mass was observed in the arterial phase. Three masses protruding from the abdominal wall into the peritoneal cavity were also observed that measured 28x16x18 mm, 55x42x36 mm, and 55 x44x55 mm and had irregular margins. All of these masses had internal calcification and contrast enhancement. ^{18}F-FDG PET scan (Figure 2) showed a maximum standardized uptake value (SUV) of 34.19 within a 5-cm mass protruding toward the serosa at the greater curvature of the stomach. The abdominal masses also had high FDG uptake (SUV max: 37.71). And the left axiallary lymph node also had high FDG uptake (SUV max: 3.51) and suspected lymph node metastasis.

FINAL DIAGNOSIS

Phosphoglyceride crystal deposition disease

TREATMENT

We had a high index of suspicion for malignant tumors, thus performed incisional biopsy. Intraoperative findings showed an incision of approximately 5 cm was made along the scar from the previous pararectal incision. The dissected tissues were hard and elastic.

OUTCOME AND FOLLOW-UP

After that, there was no particular change, and the patient was being followed up at the outpatient department.

DISCUSSION

We encountered a patient with PCDD who had multiple masses spread across skin incision scars and areas within the peritoneal cavity caused by splenectomy 29 years before. We initially suspected the masses were malignant tumors because of marked FDG uptake and performed incisional biopsy. Finally, we pathologically diagnosed as foreign body granulomas with crystal, and confirmed it by the Raman spectroscopy. To our knowledge, this is the first reported case of using Raman spectroscopy to diagnose PCDD.

Regarding on ^{18}F-FDG PET scan, FDG uptake in two previous reported cases with PCDD [3, 4], uptake ranged from 13.6 to 26.0. Our patient had even higher uptake, ranging from 34 to 37, in all of her many masses. So, malignant tumors such as sarcomas were the first differential diagnosis considered. However, marked FDG uptake is also observed in benign conditions such as granulomas and aggregations of inflammatory cells can show FDG uptake similar to that of cancer cells [5]. Nevertheless, it is necessary to make a definitive diagnosis by excision or biopsy whenever ^{18}F-FDG PET-CT shows lesion with marked FDG uptake in order to rule out malignancy first.

Histopathologically, PCDD is characterized by the formation of foreign body granulomas through accumulation of large numbers of histiocytes and multi-nucleated giant cells around crystals. Yamada *et al*[6] found that crystals ranged from 50 to 150 μm in diameter and appeared as pink ovals or blue aggregates on hematoxylin-eosin staining, forming corona-like circles. Although phosphoglycerides were not only crystals depositing in soft tissue, many substances were reported such as monosodium urate, calcium pyrophosphate dihydrate, calcium oxalate, and cholesterol esters[1]. The simplest way to prove phosphoglycerides was spraying acetic acid to the tissue and

observing oxygen production, but it was not so specific. The gold hydroxamic acid method, X-ray microanalysis, and microstamping mass spectrometry were another methods to confirm phosphoglycerides, but they took a great deal of time. The more simple and precise methods to analyze phosphoglycerides was warranted.

In this case, we used Raman spectroscopy for composition analysis of the crystals. Raman spectroscopic analysis was not required pre analytical sample preparation, non-destructive, non-contact, high-resolution, and three-dimensional method. The principle of Raman spectroscopy is as follows. When a substance is irradiated with light, interactions between the light and the substance result not only in reflection, refraction, and absorption of light, but also in a phenomenon called scattering. Two types of light scattering are Rayleigh scattering (elastic scattering), where scattered light has the same wavelength as incident light, and Raman scattering (inelastic scattering), where the scattered light has a wavelength different from that of incident light due to molecular vibrations. Light produced by Raman scattering is extremely weak (10^{-6} times dimmer) compared with that produced by Rayleigh scattering. The Raman spectra produced by this faint diffracted light are used to analyze the molecular structure of substances. As described in the Results section, we definitively determined the composition of crystals by their Raman spectra.

CONCLUSION

We made a definitive diagnosis of PCDD in a patient who had tumors with marked FDG uptake on PET-CT by incisional biopsy and composition analysis using Raman spectroscopy, a method that has not been previously reported for the diagnosis of PCDD.

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PRIMARY SOURCES

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