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BRIEF REPORT Open Access

A case of phosphoglyceride crystal deposition disease in the maxilla

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Abstract

Background Phosphoglyceride crystal deposition disease (PCDD) is a rare disorder in which phosphoglyceride crystals accumulate in soft tissues and bones. It tends to occur years after surgery, trauma, or repeated injections.

Case presentation An 81-year-old woman was referred to our department because of swelling of the left maxillary gingiva. The left maxillary second molar had been extracted more than 10 years earlier. Surgical biopsy was performed, and histopathological findings indicated a foreign body granuloma. The patient underwent tumorectomy, during which we found a yellowish tumor. The pathologic findings were the characteristic crystal deposition, fibril-like crystals, and giant cells around the crystals. Gold hydroxamic acid staining revealed positivity for the crystals. The final pathological diagnosis was PCDD. The patient had no further symptoms and no disease recurrence.

Conclusions It is relatively easy to diagnose PCDD from the characteristic histopathological findings; however, it may be overlooked by pathologists who are unaware of the disease. T2-weighted magnetic resonance imaging of PCDD in the jawbone has depicted low intensity, a finding that differs from those of ordinary cancers and odontogenic tumors. The oral cavity often undergoes surgical procedures, and PCDD may form, and grow.

Keywords Phosphoglyceride crystal deposition disease, Jawbone, Histopathology, MRI, Foreign body granuloma

Introduction

Phosphoglyceride crystal deposition disease (PCDD) is a rare disorder in which phosphoglyceride crystals accumulate in soft tissues and bones, but not in the joints [1–15]. Histopathological study reveals a foreign body granuloma–like appearance and depositions of asteroid-shaped crystals that together form a string-like fibrillar phosphoglyceride crystal. Phosphoglyceride crystals are refractive under polarized light, and gold hydroxamic acid (GHA) staining yields positive results [2, 5, 16, 17]. PCDD often develops on past injection scars or surgical scars, which suggests an association with surgery [1–15]. We report a case of PCDD in the left maxilla; to date, only one other case of PCDD in the oral cavity has been reported [2].

Case report

In a dental office, swelling of the left maxillary gingiva was found in an 81-year-old woman, and she visited our hospital for medical examination and treatment. She had no family medical history of note; her medical history included right bundle branch block, appendectomy at the age of 15 for acute appendicitis, left mastectomy at the age of 47 for breast cancer, and posterior laminoplasty

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for cervical myelopathy at the age of 80. She also had no history of smoking or alcohol consumption. The left maxillary second molar had been extracted more than 10 years earlier, and a mass (25 × 21 mm) extended from the distal part of the left maxillary first molar to the maxillary tubercle; the surface mucosa was intact (Fig. 1A). No bilateral cervical lymph node swelling was observed.

Panoramic radiography depicted bone resorption in the left maxilla, and the border between the lesion and the maxillary sinus was unclear (Fig. 1B). Computed tomography (CT) showed both a tumor (17 mm in diameter) with well-defined soft tissue density and a bone-like structure within the maxilla that corresponded to the position of the left maxillary second molar. Compressive bone resorption was evident around the tumor, but we found no destructive invasion of the pterygoid process or the surrounding tissue. At the floor of the maxillary sinus, we observed a compressive dome-shaped bulge and a thin sinus wall; however, we did not find tumor extension into the maxillary sinus (Fig. 2A, B). Magnetic resonance imaging (MRI) revealed isointensity of the mass with muscle on T1-weighted images and hypointensity on T2-weighted images; the internal properties were relatively uniform, and the enhancement effect was faint and uniform (Fig. 2C, D). Laboratory studies revealed elevated levels of cholesterol (total cholesterol: 295 mg/dL; high-density lipoprotein: 86 mg/dL; low-density lipoprotein: 183 mg/dL), lactate dehydrogenase (250 U/L), fasting blood glucose (114 mg/dL), and D-dimer (3.4 μL/mL).

A biopsy was performed, and the histopathological findings suggested a foreign body granuloma and no malignancy. Therefore, because of the clinical diagnosis of a left maxillary tumor, the patient underwent tumorectomy, under general anesthesia. An incision was made under the periosteum, and the mucoperiosteal flap was peeled off and turned over. A similar mucoperiosteal flap was formed on the palatal side, revealing the tumor. The floor bone of the maxillary sinus was missing, but the maxillary sinus mucosa remained. The cortical bone was missing in the removed cavity, and the bone marrow was exposed. The remaining cavity was filled with a buccal fat pad. The wound was fixed with sutures, and a relaxing incision was made on the buccal periosteum, after which the wound was closed with sutures. Three months after the operation, the patient was doing well, with no evidence of recurrence.

Macroscopic examination of the resected sample revealed a mass 2.4 × 2.2 cm in size, and the cut surface was muddy-looking and yellowish (Fig. 3A, B). The tumor contained calcification in some areas. Histological study revealed a foreign body granuloma just below the gingiva, extending to the deep tissue. In the granuloma, crystals with a fibril-like structure radially arranged in a circle were deposited. Numerous foamy histiocytes and foreign body–type giant cells surrounded the crystals (Fig. 3C, D). The crystals were refractive under white light from a polarizing microscope (Fig. 3E), but this finding was not present in the decalcified tissue specimen. Immunohistochemical examination with CD68 staining revealed positivity for foreign body–type multinucleated giant cells, and GHA staining revealed positivity for the crystal structure (Fig. 3F). The final histopathological diagnosis was PCDD.

Discussion

PCDD was first reported in 1992 by Kubo et al., [1] who showed that the deposited crystals were a kind of phosphate ester or ether, and Miura et al., using microscopic infrared spectrometry, and microsampling mass spectrometry, reported that the crystalline substance was phosphoglyceride and that it was bound with calcium as a counterion [2, 5]. PCDD lesions tend to develop at sites of invasive procedures, including injection scars, and surgical scars [1–15]. PCDD is considered to be a local disorder of lipid metabolism that occurs mainly in damaged soft tissues, in which foreign body granulomas form with deposition of phosphoglyceride crystals [2].

On the basis of radiographic imaging and CT before the operation in this case, we suspected odontogenic tumors, including malignancy. However, T1-weighted MRI showed that the tumor had the same signal intensity as muscle, and T2-weighted MRI showed uniform hypointensity, which were not consistent with the findings in common odontogenic tumors and cancers [18–20]. Typically, head and neck lesions that appear hypointense on T2-weighted images include calcified or osseous lesions, granulomatous lesions, fibrous lesions, mucus-, or protein-containing lesions, hemosiderin-containing lesions, melanin-containing lesions, thyroglobulin-containing lesions, rapid blood flow, and air-filled spaces [21]. We suggest that the differential diagnosis of such tumors include granulomatous lesions such as central giant cell granuloma, odontogenic fibroma, malignant melanoma, hematopoietic tumors such as malignant lymphoma and multiple myeloma, and metastatic tumors.

In the resected specimen from our patient, the cut surface was yellowish-white. Histological examination revealed a foreign body granuloma with the deposition of quasi-circular crystals arranged in a fibril-like structure radiating from the center from just below the epithelium to the deep tissue. The histopathological features were relatively characteristic of and similar to those in previous reports of PCDD. GHA staining can help identify phosphoglyceride on sections by histochemically demonstrating the reduction of hydroxamic acid produced from phosphoglyceride by alkaline hydroxylamine in reaction to gold ions [2, 5, 16, 17]. As a result of GHA staining in

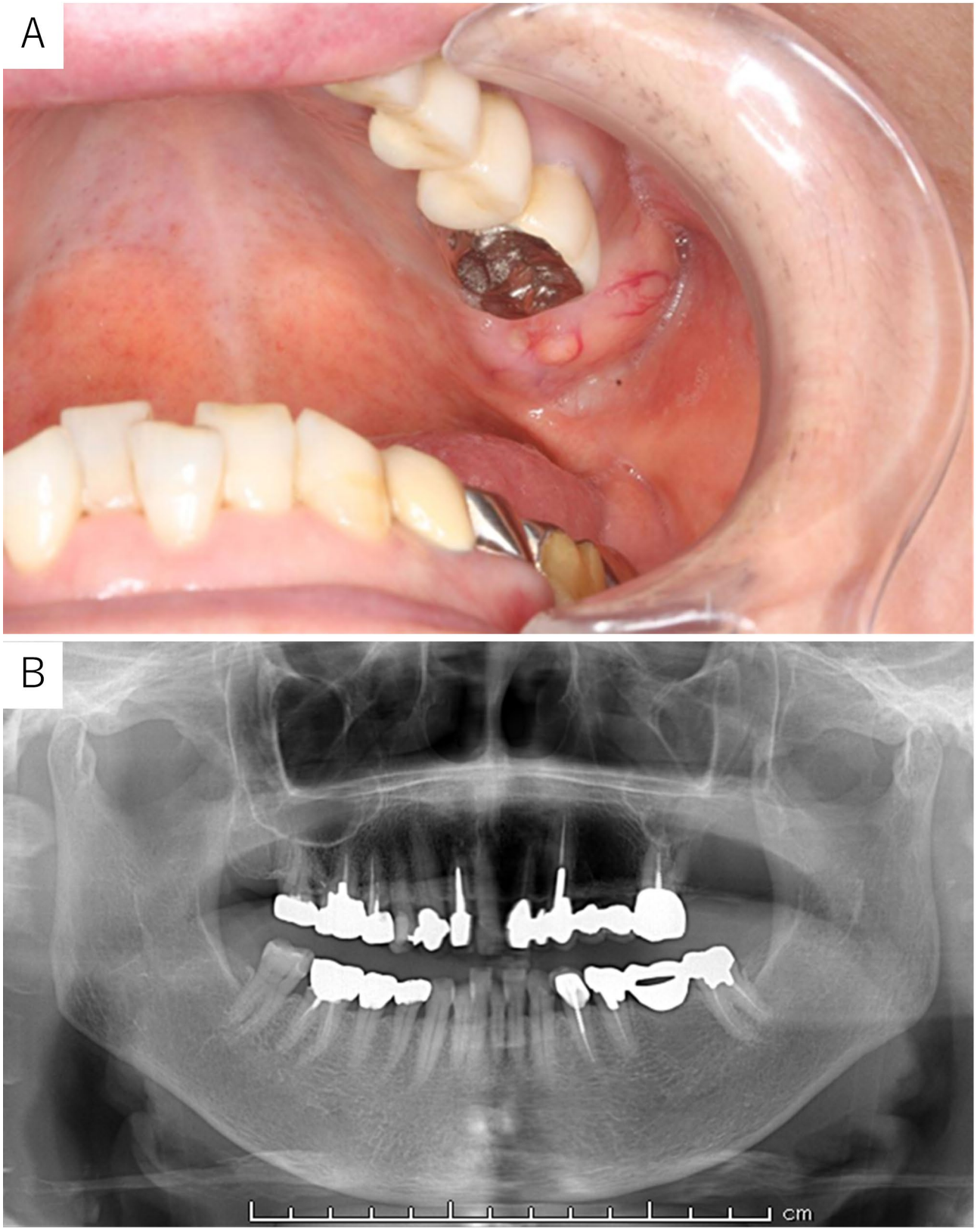

Fig. 1 (**A**) Intraoral photograph, taken at first visit, of a mass on the left upper jaw, covered with normal mucosa. (**B**) Panoramic radiograph showing well-defined bone loss from the mesial side of the first molar in the left maxilla; the border between the lesion and the maxillary sinus was unclear

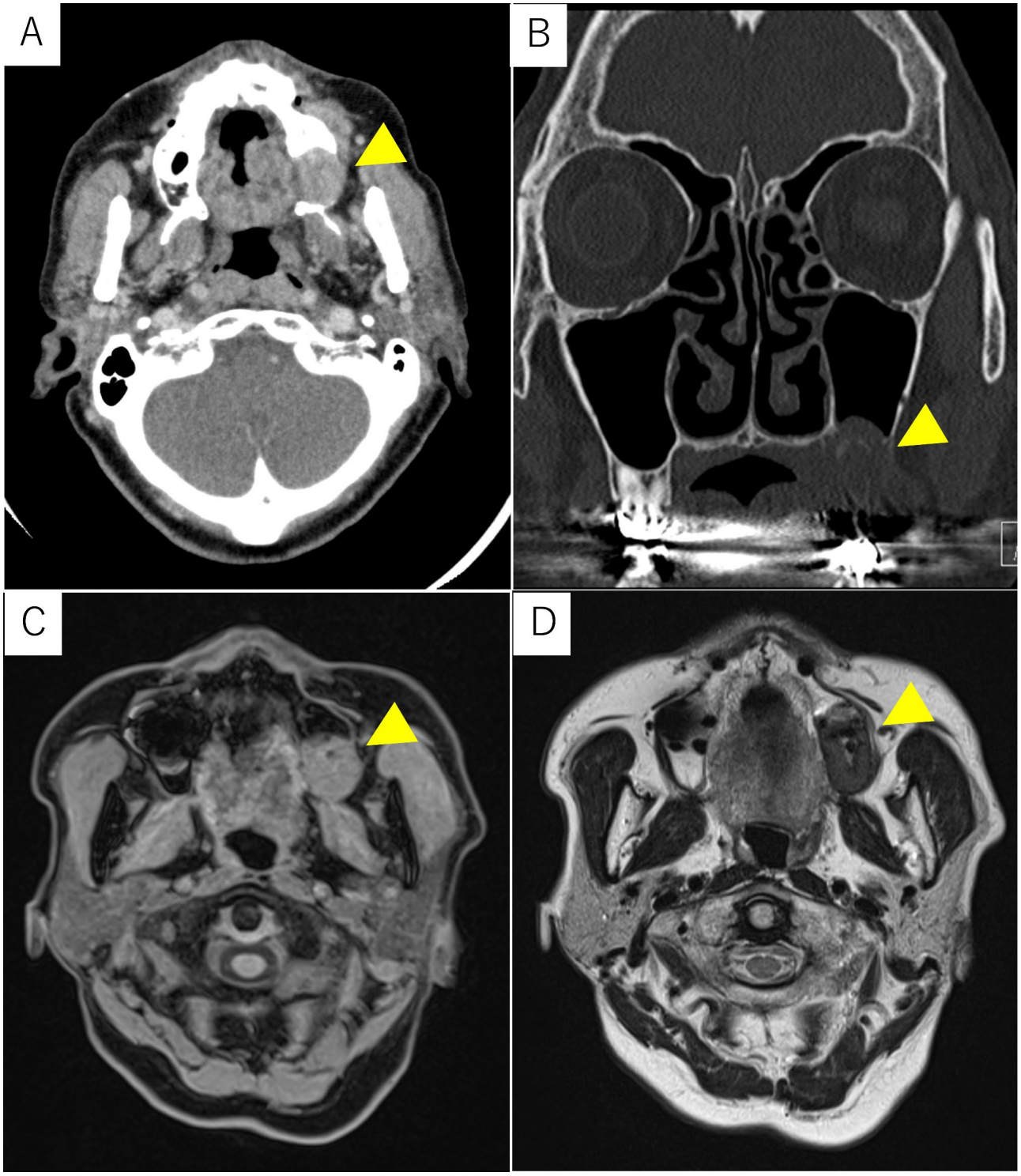

Fig. 2 (**A**, **B**) Computed tomography of the presenting solid mass (arrow head) in the left maxillary bone. (**A**) Bone resorption caused by tumor compaction. (**B**) Compressive dome-shaped bulging and thinning of the inferior wall of the maxillary sinus, observed from the left maxillary alveolar area. (**C**, **D**) Magnetic resonance imaging. (**C**) T1-weighted image of an occupying lesion with well-defined borders and isointensity with muscle. (arrow head) (**D**) The lesion exhibited low signal in a T2-weighted image. (arrow head)

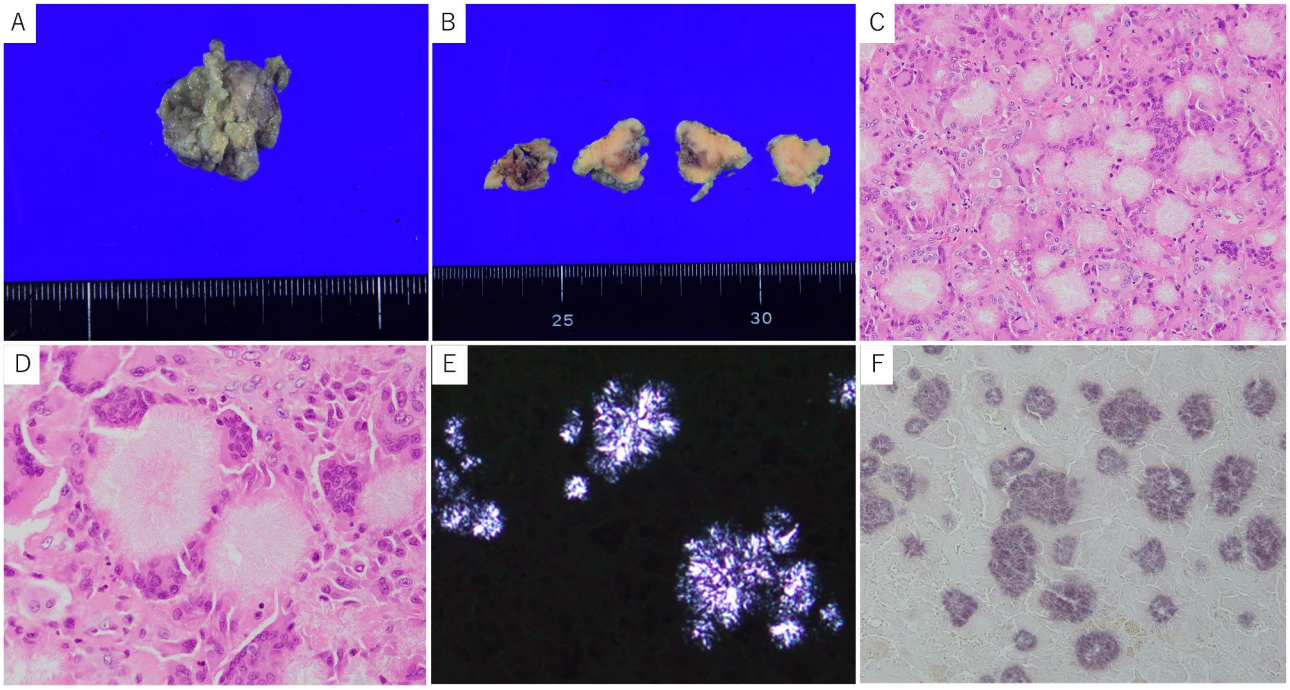

Fig. 3 (**A**, **B**) Gross appearance of the resected tumor. The cut surface of the tumor was yellowish (**B**). (**C**, **D**) Histological appearance of the resected tumor at low-power magnification (**C**) and high-power magnification (**D**). A foreign body granuloma with deposition of quasi-circular crystals had a fibril-like structure radiating from the center. (**E**) The deposited crystals were asteroid-shaped and exhibited refractive properties under a polarized light microscope. (**F**) The deposited material showed positive staining in dark purple by gold hydroxamic acid

this case as well, the crystals turned purple-black; therefore, we deduced that the crystals were phosphoglyceride.

To the best of our knowledge, 18 cases of PCDD have been reported so far (Table 1) [1–15]. One patient was Malaysian, and all the others were Japanese. The median age was 59.5 years, and the male-to-female ratio was 1:1.6. The site of onset was not specific, but most cases developed over surgical or nonsurgical wounds. Only one case of onset in the oral cavity has been reported [2]. The mean time from invasive procedure to onset was 29.8 years, and in most cases, this interval was 10 years or longer. In treatment of PCDD, surgical resection was performed in 12 cases, and 6 cases were nonsurgically monitored. One case of two recurrent lesions at the same site has been reported [4]. Other reports indicated that the size of the lesions did not change significantly, even in follow-up cases. Deaths from this disease have not been reported. In some cases of PCDD, a large mass forms, which may be diagnosed clinically as a malignant tumor. In addition, positron emission tomography/CT studies have revealed fluorodeoxyglucose (FDG) accumulation in lesions in multiple cases, and the maximum standardized uptake value of tumors caused by phosphoglyceride crystal deposition is extremely high, ranging from 13.6 to 42.9 [6, 8–10, 13, 15]. Because FDG also accumulates at inflammatory sites, such accumulation may be triggered by the inflammation associated with phosphoglyceride deposition [9].

The origin of PCDD has not been elucidated, but tissue damage, and focal lipid metabolism disorders are thought to be causes. However, no association with other diseases has been found, and the disease is thought to be confined to the site where invasive procedures were performed [2]. Initially, the cause of PCDD was suspected to be Nibenal, alcohol extract from bovine liver injection, which was administered in Japan from 1950 to 1960 [2]. Since then, the disease has been reported in patients who had not been treated with that drug, and one case was also reported in Malaysia; therefore, that hypothesis is unfounded [1–15]. Another hypothesis is that local inflammation causes local impairment of phosphoglyceride metabolism. It is believed that local inflammation impairs phosphoglyceride metabolism in macrophages; undegraded crystals then accumulate in and around macrophages, which results in the formation of foreign body granulomas [5]. The interval between the surgical invasion and the onset of this disease is several decades or more; thus, it takes many years for crystal deposits within small macrophages to accumulate and enlarge to form masses. Miura et al., using electron microscopy, demonstrated the accumulation of phosphoglyceride crystals in the lysosomes of macrophages [2, 5]. The degradation of phosphoglycerides by acid phospholipase A1 and A2 is inhibited by calcium. Large amounts of calcium generated during surgical invasion and inflammation during wound healing are thought to reduce the phagocytic

Table 1 Summary of reported phosphoglyceride crystal deposition disease

Patient No.	Authors	Country	Year	Age	Sex	Number of tumors	Location	Trauma or post-operative past history	Interval after trauma or operation (years)	Maximum tumor diameter (cm)	The gold hydroxamic acid staining	Other
1	Kubo et al. [1]	Japan	1992	58	M	Single	Buttock	NA	NA	11	ND	X-ray microanalysis, infrared absorption spectra analysis
2	Miura et al. [2] and Nishimura et al. [3]	Japan	2000	62	F	Multiple	Oral soft tissue at right maxilla, mandible	After dental procedure	8	1-11	Positive	Infrared spectrophotometry, mass spectrometry, and X-ray microanalysis
							Bilateral brachial muscle	After multiple vitamin E injection at bilateral arm for chilblain	NA			
							Abdomen	Post-appendectomy	19			
							Spine	After lumbar anesthesia	45	NA		
3	Yachida et al. [4]	Japan	2002	51	M	Multiple	Para-gastric	Post-gastrectomy	33	3.5	Positive	
4	Miura et al. [5]	Japan	2004	58	M	Single	Abdomen	Post-gastrectomy	40	'Infant head size'	Positive	Infrared spectrophotometry, mass spectrometry, and X-ray microanalysis
5				64	F	Single	Abdomen	Post-gastrectomy	35	4	Positive	
6				64	F	Single	Scapular bone	NA	NA	10	Positive	
7	Shoji et al. [6]	Japan	2007	37	M	Single	Anterior mediastinum	Ventricular septal defect repair	35	6	ND	FDG-PET(SUVmax16.9)
8	Yamada et al. [7]	Japan	2015	50	F	Multiple	Pelvic	Caesarean delivery	26	10	ND	
9	Nakahara et al. [8]	Japan	2018	57	M	Single	Abdomen	Post-appendectomy	40	10	ND	FDG-PET(SUVmax41)
10	Tokue et al. [9]	Japan	2018	45	F	Multiple	Anterior mediastinum	Atrial septal defect repair	38	9	ND	FDG-PET(SUVmax26.0),(SUVmax13.6)
11	Sato et al. [10]	Japan	2020	42	M	Single	Left ventricular	Atrial septal defect repair	38	4.5	ND	FDG-PET(SUVmax42.9)
12	Omar et al. [11]	Malaysia	2021	69	M	Single	Leg	Injury	10	10	ND	
13	Nakamura et al. [12]	Japan	2021	84	F	Multiple	Uterine adnexa	Simple hysterectomy	44	4.5	Positive	
14	Isida et al. [13]	Japan	2021	59	F	Single	Rib bone	Patent ductus arteriosus repair	NA	4	Positive	FDG-PET (SUVmax21.8)
15				85	F	Single	Ovary	Post-appendectomy	NA	16	Positive	
16	Takeuchi et al. [14]	Japan	2022	72	F	Single	Right atrium	Atrial septal defect repair and tricuspid valvuloplasty	26	4	Positive	
17	Ohkura et al. [15]	Japan	2022	60	F	Multiple	Upper stomach, Abdomen	open splenectomy for idiopathic thrombocytopenic purpura	29	5.5	ND	FDG-PET(SUVmax34.2) (SUVmax37.7), Raman spectroscopy
18	Saitou et al. (present case)	Japan	2023	81	F	Single	Left maxilla	After tooth extraction	>10	2	Positive	

NA, not available; ND, not done

activity of macrophages, which results in local disturbances in phosphoglyceride metabolism [2, 5]. In other words, it is thought that local inflammation during wound healing triggers the deposition of phosphoglyceride crystals over a long period of time.

In our patient, phosphoglyceride crystal deposition was at the site of a tooth extraction that had been performed more than 10 years earlier. However, no suggestion of PCDD was noted in clinical or imaging findings at the time of appendicitis, breast cancer, or cervical spine surgery. Although hyperlipidemia was observed in this case, no association between hyperlipidemia, and PCDD has been documented so far. In the single other case of PCDD in the oral cavity, the lesion was one of several throughout the patient's body; however, the detailed status of oral lesions and imaging findings were not described [2]. Surgical treatments such as surgical periodontal therapy and tooth extraction are often performed in the oral cavity. Although PCDD is very rare, it is possible that other cases in the oral cavity have been overlooked because it usually occurs at sites of local invasion, such as surgery, and trauma. PCDD develops over a long time, but when tumor formation is observed in the oral cavity of a patient who has undergone surgical procedures, PCDD should be included in the differential diagnosis, in addition to malignant tumors.

Conclusion

In this case, PCDD occurred in the maxilla at the site of a tooth extraction. Although it is relatively easy to diagnose PCDD from the characteristic histopathological findings, it may be overlooked by pathologists who are unaware of the disease. In addition, PCDD in the jawbone was suggested to exhibit a characteristic T2-weighted MRI finding of low intensity, which differs from MRI findings in ordinary cancers and odontogenic tumors. The oral cavity often undergoes surgical procedures such as surgical periodontal treatment and tooth extractions, and PCDD, although rare, can develop.

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Author contributions
All authors reviewed the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Competing interests
The authors declare no competing interests.

Declarations of interest
None.

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References

1. Kubo K, Manabe J, Matsumoto S, et al. Unusual huge intramuscular granuloma with calcium phosphate crystal deposition in the buttock. Acta Pathol Jpn. 1992;42:508–11. https://doi.org/10.1111/j.1440-1827.1992.tb03097.x.
2. Miura K, Fukuda H, Mineta H, et al. Phosphoglyceride crystal deposition disease. Pathol Int. 2000;50:992–8. https://doi.org/10.1046/j.1440-1827.2000.01138.x.
3. Nishimura A, Kasai Y, Takegami K, Uchida A. Phosphoglyceride crystal deposition disease in the spine: A case report. J Spinal Disord Tech. 2005;18:112–5. https://doi.org/10.1097/01.bsd.0000127701.37593.03.
4. Yachida S, Fukushima N, Nakanishi Y, et al. Case report: phosphoglyceride crystal deposition disease presenting as multiple paragastric masses. Dig Dis Sci. 2002;47:1413–8.
5. Miura K, Han G, Kondo S, Ohhashi H, Tsutsui Y. Phosphoglyceride (PG) crystal deposition disease: a novel acquired disease in which PG crystals are deposited in injured soft tissue and bone with phospholipid metabolism disturbance. Pathol Int. 2004;54:881–9. https://doi.org/10.1111/j.1440-1827.2004.01776.x.
6. Shoji F, Yoshino I, Kometani T, Yamamoto H, Maehara Y. Phosphoglyceride crystal deposition disease originating from the myocardium. J Thorac Cardiovasc Surg. 2007;134:508–9. https://doi.org/10.1016/j.jtcvs.2007.04.007.
7. Yamada Y, Nishioka K, Kajihara H, Noguchi T, Naruse K, Horie K. A case of phosphoglyceride crystal deposition disease in the pelvic soft tissues recurring after initial surgery. Case Rep Obstet Gynecol. 2015;2015:751582.
8. Nakahara O, Baba H. Phosphoglyceride crystal deposition disease in the abdominal wall: a case report. Surg Case Rep. 2018;4:120. https://doi.org/10.1186/s40792-018-0516-2.
9. Tokue H, Ebara M, Takahashi R, Tokue A, Tsushima Y. Phosphoglyceride crystal deposition disease mimicking a malignant tumor. Eur J Radiol Open. 2018;5:16–9. https://doi.org/10.1016/j.ejro.2018.01.004.
10. Sato T, Konishi T, Wakasa S, Oyama-Manabe N, Anzai T. Phosphoglyceride crystal deposition disease as a rare tumour after cardiac surgery. Eur Heart J. 2020;41:2596. https://doi.org/10.1093/eurheartj/ehaa289.
11. Omar N, Mohd Yusof MAM, Kwan Min VL, Lee Kwan Min V, Bakrin IH, Awang M, Abdul Muthalib FA. Phosphoglyceride crystals deposition disease: a rare pseudosarcomatous growth with peculiar predilections. Pathology. 2022;54:830–3. https://doi.org/10.1016/j.pathol.2021.10.007.
12. Nakamura T, Fujiwara M, Hara K, Kurosawa K, Miyazaki T. Phosphoglyceride crystal deposition disease involving adnexa Uteri: a case report with histogenetic consideration. Pathologica. 2021;113:442–8. https://doi.org/10.32074/1591-951X-193.
13. Ishida A, Fujimoto M, Yamada Y, Takei Y, Sakamoto A, Miura K, Minamiguchi S, Haga H. Phosphoglyceride crystal deposition disease in a rib bone and ovary mimicking malignancy: A report of two cases including a previously undescribed cystic case. Pathol Int. 2021;71:860–2. https://doi.org/10.1111/pin.13169.
14. Takeuchi K, Tanaka H, Kawamori H, Ohta E, Suzuki M, Shimoura H, Izawa Y, Kodama Y, Hirata K. Severe functional tricuspid stenosis due to phosphoglyceride crystal deposition disease in right atrium. JACC Case Rep. 2022;4:230–5. https://doi.org/10.1016/j.jaccas.2021.09.024.
15. Ohkura Y, Uruga H, Shiiba M, Ito S, Shimoyama H, Ishihara M, Ueno M, Udagawa H. Phosphoglyceride crystal deposition disease requiring differential diagnosis from malignant tumors and confirmed by Raman spectroscopy: A case report. World J Clin Cases. 2022;10:8304–11. https://doi.org/10.12998/wjcc.v10.i23.8304.
16. Adams CWM, Davison AN. The histochemical identification of Myelin phosphoglycerides by their ferric hydroxamates. J Neurochem. 1959;3:347–51. https://doi.org/10.1111/j.1471-4159.1959.tb12641.x.
17. Gallyas F. The histochemical identification of phosphoglycerides in Myelin. J Neurochem. 1963;10:125–6. https://doi.org/10.1111/j.1471-4159.1963.tb11472.x.
18. Kurabayashi T, Ohbayashi N, Sakamoto J, Nakamura S. Usefulness of MR imaging for odontogenic tumors. Odontology. 2021;109:1–10. https://doi.org/10.1007/s10266-020-00559-z.

19. Widmann G, Henninger B, Kremser C, Jaschke W. MRI sequences in head and neck radiology - state of the Art. Fortschr Röntgenstr. 2017;189:413–22.
20. Lenz M, Greess H, Baum U, Dobritz M, Kersting-Sommerhoff B. Oropharynx, oral cavity, floor of the mouth: CT and MRI. Eur J Radiol. 2000;33:203–15. https://doi.org/10.1016/S0720-048X(99)00143-6.
21. Kato H, Kawaguchi M, Ando T, Kaneko Y, Hyodo F, Matsuo M. Hypointense head and neck lesions on T2-weighted images: correlation with histopathologic findings. Neuroradiology. 2020;62:1207–17. https://doi.org/10.1007/s00234-020-02483-z.

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