limitations of biopsy specimens, MNAC is easy to misdiagnose when the morphology is close to that of SCC. When tumours show papillary and squamous epithelial growth patterns by biopsy, it is necessary to carefully observe whether they have adenoid structures and examine them by immunohistochemistry to avoid misdiagnosis.

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Phosphoglyceride crystals deposition disease: a rare pseudosarcomatous growth with peculiar predilections

To the Editor,

Phosphoglyceride crystals deposition disease (PCDD) is an exceedingly rare disease with striking resemblance to

sarcoma radiologically and clinically. There have been only 13 reported cases so far. Interestingly, all these cases were exclusively reported from Japan (Table 1). There is no apparent reason for this peculiar country predilection. There are no gender predilection, congenital abnormalities, metabolic disorders, or familial history associated with the disease. The affected patients ranged from 37 to 76 years of age. Our case illustrates Malaysia's first reported case of PCDD.

Herein we report a case of a 69-year-old Malay man, who presented with a slow growing mass over the medial aspect of his right calf for the previous 4–5 years. He recalled a traumatic laceration 10 years ago by a bamboo stalk at the same site. His blood uric acid level was found to be normal (325 µmol/L). Radiological findings were suggestive of a peripheral nerve sheath tumour; however, malignancy could not be excluded because there was no clear evidence of fat plane demarcation with the gastrocnemius and soleus muscles (Fig. 1). Thus, a wide excision was performed with part of the soleus muscle, paratenon of Achilles tendon and periosteum removed. Intraoperative features also revealed a malignant appearing mass measuring 10 cm in diameter with necrotic tissue anterior to the mass, and adherence to the adjacent fascia and periosteum.

Macroscopically, the mass was lobulated and appeared confined to the subcutaneous layer. It had a soft tan to yellowish cut surface with haemorrhagic areas. Microscopically, the mass was well circumscribed by a thick fibrous capsule, containing lobules of foreign body granuloma. These lobules were separated by fibrous septae of varying thickness. The foreign body granulomas were composed of numerous round eosinophilic fibrillary crystals, surrounded and engulfed by sheets of foreign body type multinucleated giant cells (Fig. 2). These crystals showed spectacular corona-shaped string-like reflective particles when examined under polarised light. The crystals and surrounding macrophages showed negative periodic acid–Schiff (PAS) staining, while CD68 immunohistochemistry showed retained staining within the macrophage's cytoplasm and membrane. The patient was discharged well and given long-term follow-up at his nearest local clinic.

The diagnosis of PCDD is mainly based on the characteristic histological features as seen in our patient's microscopy findings. Occasional asteroid bodies may also be seen. The crystals typically do not dissolve during the usual formalin fixation and paraffin embedding process, and they are usually so soft that thin sections could be performed without decalcification.

Miura *et al.*¹ in 2000 reported that these crystals show diffuse, strong, purple-black staining with gold hydroxamic acid method and focal weak staining can be seen with von Kossa's method and Berlin blue stain.

The actual aetiology of PCDD remains unknown; however, there is an association with previous injury in all cases. Initially, PCDD was attributed to a discontinued drug containing vitamin E, named Nibenal, that was in use in Japan from the year 1950–1960. The drug was made from ethanolic extraction of bovine liver. It was used repeatedly in bilateral arm intramuscular injections by a patient in the Miura *et al.*¹ paper as treatment for chilblain. She later developed bilateral brachial muscle PCDD. However, this was proven to be not related as subsequent reported patients with PCDD were not exposed to the drug.²

Table 1 Clinical summary of all reported PCDD cases

Authors	Country	Year	Age, years	Gender	No. lesions	Location of lesion	Initial trauma	Interval after initial trauma	Maximum tumour diameter
Kubo <i>et al.</i> ³	Japan	1992	58	Male	Single	Buttock	Not stated	Not stated	11 cm
Miura <i>et al.</i> ¹	Japan	2000	62	Female	Multiple, recurrent	Oral soft tissue at right maxilla Bilateral branchial muscle Abdomen Spine	After dental procedure After multiple vitamin E injection at bilateral arm for chilblain Post-appendicectomy Post anaesthesia	8 years	11 cm
Yachida <i>et al.</i> ²	Japan	2002	51	Male	Multiple	Para-gastric	Post-gastrectomy for gastroduodenal ulcer disease	19 years 33 years	3.5 cm
Miura <i>et al.</i> ¹⁰	Japan	2004	58	Male	Single	Abdomen	Post-gastrectomy	40 years	'Infant head size'
			64	Female	Single	Abdomen	Post-gastrectomy	35 years	4 cm
			64	Female	Single	Scapular	Not stated	Not stated	10 cm
Nishimura <i>et al.</i> ⁴	Japan	2005	76	Female	Multiple	Spine	After lumbar anaesthesia	45 years	Not stated
Shoji <i>et al.</i> ⁶	Japan	2007	37	Male	Single	Anterior mediastinum	Ventricular septal defect repair	35 years	6 cm
Yamada <i>et al.</i> ⁵	Japan	2015	50	Female	Multiple	Pelvic	Caesarean delivery	26 years	10 cm
Nakahara <i>et al.</i> ¹¹	Japan	2018	57	Male	Single	Abdomen	Post-appendectomy	40 years	10 cm
Tokue <i>et al.</i> ⁷	Japan	2018	45	Female	Multiple	Anterior mediastinum	Atrial septal defect repair	38 years	9 cm
Sato <i>et al.</i> ⁸	Japan	2020	42	Male	Single	Left ventricular apical mass	Atrial septal defect repair	38 years	4.5 cm
Miki <i>et al.</i> ⁹	Japan	2020	48	Female	Single	Anterior mediastinum	Ventricular septal defect repair	40 years	9 cm
Our case	Malaysia	2021	69	Male	Single	Leg	Injury	10+ years	10 cm

A proposed hypothesis in the same article¹ postulates that a local inflammation initiates localised disturbance of phosphoglyceride (PG) metabolism. PGs are a class of phospholipids (PLs), which are the major component of all the lipid membranes in the human body. Like any other PLs, some portions of PG are insoluble and undegraded in aqueous media as they are partly hydrophobic. Those undegraded portions are kept in the macrophages' lysozyme for slow degradation. However, very rarely, due to the localised disturbance of lysozyme's PG metabolism, the undegraded material starts to accumulate in and between the macrophages leading to a nidus formation.

The proposed hypothesis is supported by the identification of localised reduction in lysozyme staining intensity using Lysozyme, Luxol fast blue and PAS stains.¹ There was also reduction in the staining intensity of macrophages using CD68 and S100 stains within the lesion, as compared to the staining intensity in bone marrow macrophages, indicating the presence of a localised reduction of the macrophages' phagocytic abilities.¹ However, our case only showed negative PAS staining, while the CD68 staining was retained within the lesion's macrophages.

The accumulation of PG crystals within the lysozyme's membrane in electron microscopy examination by Miura *et al.*¹ strengthens the hypothesis, as the lysozyme's enzymatic degradation process by phospholipase A1 and A2 enzymes occurs within the lysozyme's membrane.

The undegraded PG tend to bind with calcium as a counter ion in an acidic inflammatory microenvironment. This acts as an inhibitory rather than a stimulatory factor to the lysozyme's activities, causing the size of the nidus to amplify slowly with time. This is compounded by further recruitment of the chronic

inflammatory cells. Miura *et al.*¹ and Kubo *et al.*³ in the earliest paper in 1992 proved this theory as they yielded phosphorus and calcium peaks through X-ray microanalysis, infrared spectrophotometry and microsampling mass spectrometry.

The postulation of this time-consuming foreign body type chronic inflammatory process is highlighted by the fact that almost all patients had an average interval of more than 10 years from their initial injury, as seen in our case.

PCDD is often single, with a homogenous yellowish-white to yellowish-brown surface as seen in our case. The lesion occurs at sites typical for intramuscular injections, anaesthetic injections and post-operative sites. However, multiple lesions have occurred, such as in the case reported by Nishimura *et al.*⁴ in which the patient presented with multiple lesions surrounding the spine 45 years after an anaesthetic procedure, while Yamada *et al.*⁵ reported a case of multiple pelvic lesions 26 years after a caesarean section. Lesions within the soft tissue surrounding the viscera have also been reported, such as the case in Yachida *et al.*² where multiple para-gastric lesions were seen in a patient 33 years post-gastrectomy for gastroduodenal ulcer disease, while other authors reported lesions occurring many years post-cardiac surgery within the pericardium and on the wall of the heart.^{6–9} Our case is the first ever occurrence in the extremities with a history of traumatic laceration.

The lesions are usually localised to the injured sites, measuring more than 10 cm. The cases reported by Kubo *et al.*³ Yamada *et al.*⁵ and Miura *et al.*¹⁰ in their other small case series in 2004 also showed central necrosis and haemorrhage simulating a malignancy. Furthermore, PCDD also shows the ability to grow larger and adhere to adjacent structures as seen in our case.

Fig. 1 Magnetic resonance imaging of right lower limb revealed a well defined lobulated solid lesion within the posterior medial aspect of distal right leg, measuring 6.0×4.9×11.5 cm.

Previous authors also concluded in their case reports that PCDD does not show any relation to the joint space as compared to other crystal deposition diseases.^{5,8} The other crystals show different characteristics as compared to PG crystals and no other crystals commonly seen in the human body are known to show the characteristic oxygen gas formation with reaction to 30% acetic acid such as PG crystals.¹

Radiologically, there is high uptake of fluorodeoxyglucose (FDG) in the positron emission tomography scan as reported by Tokue *et al.*,⁹ simulating a high-grade sarcoma or an aggressive benign tumour. However, they concluded that, being a glucose analogue, FDG is also known to be taken up by inflamed tissue such as in PCDD.

The mainstay treatment of PCDD is localised excision surgery.^{5,6,11} However, some patients were subjected to more extensive surgery, as described by Miura *et al.*¹ in which the patient underwent multiple resections and extensive surgeries, and Nakahara *et al.*¹¹ where the patient underwent exploratory laparotomy instead of laparoscopic surgery, mainly because a malignancy could not be safely ruled out clinically and radiologically.

Most of the previous cases showed a favourable outcome, such as cases reported by Nishimura *et al.*⁴ and Miki *et al.*⁹ which showed no recurrence after one year follow-up post-resection. A case by Shoji *et al.*⁶ with an inoperable lesion within the heart and a case by Tokue *et al.*,⁷ in which the patient refused surgery also showed no change in tumour size during the latest follow-up. However, an earlier case by Miura *et al.*¹ showed recurrent multisystemic lesions with evidence of accumulation within the bone marrow, while a case by Yamada *et al.*⁵ twice showed recurrence of the lesion at the same site after 4 year intervals from each resection. Miki *et al.*⁹ recommended lifelong radiological surveillance in view of the detection of a slowly enlarging

Fig. 2 Numerous round shaped eosinophilic fibrillary crystals, surrounded by sheets of foreign body type multinucleated giant cells with scattered epithelioid histiocytes and lymphocytes. Examination under polarised light showed corona-shaped string-like reflective particles. (A) Haematoxylin and eosin stain and (B) higher power. (C) Polarised microscopy and (D) higher power.

lesion within the heart during the 3 year follow-up of their case.

In summary, although a rare entity, PCDD should be included in the differential diagnoses, particularly when there is history of previous injury. A higher index of suspicion for PCDD may help to avoid unnecessary extensive surgeries. More studies are needed to evaluate whether surveillance alone is sufficient or additional anti-inflammatory drugs are needed to help the affected patients, particularly patients with recurrent and multisystemic forms of disease.

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