Immunohistochemical analyses to determine pathogenesis of tenosynovitis with psammomatous calcification in the wrist: A case report

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Abstract. Tenosynovitis with psammomatous calcification is an extremely rare clinicopathological condition, which is characterized histopathologically by the presence of numerous psammomatous calcifications surrounded by a granulomatous reaction comprising a mixture of histiocytes and fibroblasts. The pathogenesis of this disease remains unclear, although an association with repetitive tendinous injury has been proposed. The present study describes the details of a case in an elderly Japanese female, and, to the best of our knowledge, the first known immunohistochemical analysis of the mechanism underlying psammomatous calcification formation. A 66-year-old Japanese woman presented with pain in the right wrist. The lesion was surgically resected. Histopathological examination revealed a well-circumscribed lesion composed of psammomatous calcification. The calcification was surrounded by histiocytes, and a few multinucleated giant cells and fibroblastic spindle cells. Immunohistochemical study revealed that these histiocytes were positive for cluster of differentiation 163, and the histiocytes and spindle cells surrounding the psammomatous calcification expressed bone morphogenetic protein-1 (BMP-1). Tenosynovitis with psammomatous calcification is hypothesized to be a distinctive subtype of idiopathic calcifying tenosynovitis involving an unusual reactive or degenerative process. BMP-1 has been demonstrated to be involved in the regulation of hard tissue mineralization, and its expression has been suggested to be associated with psammoma formation in papillary thyroid cancer. To the best of our knowledge, the case report within the present study suggested for the first time that BMP-1 expression was associated with development of psammomatous calcification in this condition.

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Introduction

Tenosynovitis with psammomatous calcification is an extremely rare clinicopathological condition. Since it was first described by Gravanis and Gaffney in 1983 (1), only a few additional cases have been examined in the English language literature (2-5). This variant of calcifying tenosynovitis or calcific tendonitis is characterized histopathologically by the presence of numerous psammomatous calcifications surrounded by a granulomatous reaction comprising a mixture of histiocytes and fibroblasts (2-5). Recently, Michal *et al* (6) investigated a large case series of this disease, and confirmed that the disease exhibited a tendency to affect the fingers or toes of young to middle-aged women, and appeared to be associated with trauma and/or repetitive activity. They concluded that tenosynovitis with psammomatous calcification is a distinctive trauma-associated subtype of idiopathic calcifying tenosynovitis.

However, the pathogenesis of tenosynovitis with psammomatous calcification remains unclear. Although an association of this disease with repetitive tendinous injury has been described previously (2,6), other studies have described cases without a history of trauma (3,4). Bone morphogenetic protein (BMP)-1, also known as procollagen C-peptidase, is a multifunctional protein regulating of hard tissue mineralization (7). BMP-1 expression has been suggested to be associated with ectopic ossification (8) and psammoma formation in papillary thyroid cancer (9). The present study described a case report of tenosynovitis with psammomatous calcification that occurred in the wrist of an elderly female, and the immunohistochemical analysis of the mechanism of psammomatous calcification formation, particularly association with BMP-1 expression.

Case report

A 66-year-old Japanese female presented with pain in the right wrist. She had a history of De Quervain's disease and infliximab use for ulcerative colitis, but no history of trauma to the

wrist. Radiographic imaging demonstrated a calcified lesion in the palmar side of the right wrist, around the lunar and capitate bones. The lesion was surgically resected following a clinical diagnosis of ectopic bone formation.

Samples were fixed in 10% formalin at room temperature for 24 h and paraffin-embedded specimens (60˚C, 4 h) of the resected lesion were processed for routine histological examination and immunohistochemical analyses. Immunohistochemical analyses were performed using autostainers (XT System Benchmark; OptiView DAB Universal Kit, Roche Diagnostics) and Autostainer link 48 (Envision FLEX; cat. no. K8000; Dako; Agilent Technologies). The primary antibodies used were a mouse monoclonal antibody against α-smooth muscle actin (α-SMA; clone name, 1A4; 20 min at room temperature; Dako; Agilent Technologies), a rabbit polyclonal antibody against BMP-1 (cat. no. ab205394; 32 min at room temperature; Abcam) and a mouse monoclonal antibody against CD163 (clone name, 10D6; 32 min at room temperature; Leica Microsystems, Ltd). Light microscopic examination of 3-μm H&E-stained (hematoxylin, 3 min and eosin, 5 min at room temperature) sections (magnification, x12.5, x100 and x400) revealed a well-circumscribed lesion with a central cystic cavitation (Fig. 1A), and the notable feature of numerous psammomatous calcifications (Fig. 1B). These calcifications were surrounded by histiocytes, and a few multinucleated giant cells and fibroblastic spindle cells (Fig. 1C). Neither foamy cells nor siderophages were observed within the lesion.

Light microscopic analyses of immunohistochemistry (magnification, x400) revealed that these histiocytes were positive for CD163 (Fig. 1D). A small number of α-SMA-positive spindle cells were also detected, and the histiocytes and spindle cells surrounding the psammomatous calcification expressed BMP-1 (Fig. 1E). Based on these features, a final diagnosis of tenosynovitis with psammomatous calcification was made.

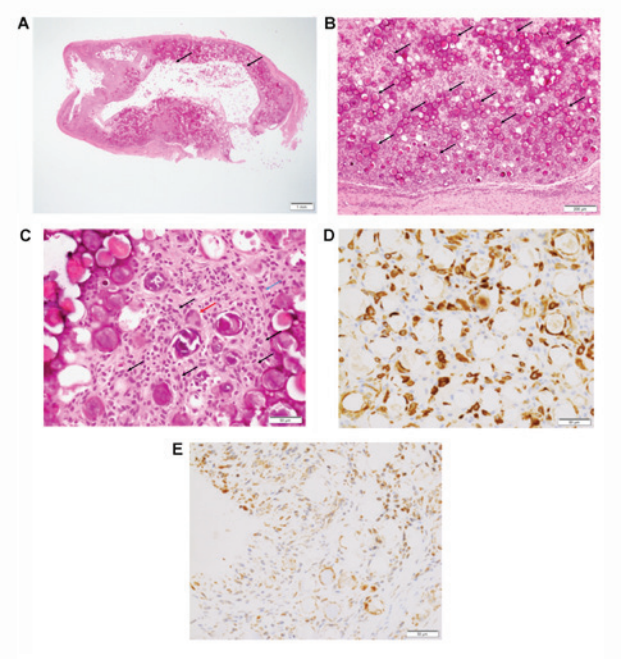

Figure 1. Histopathological and immunohistochemical features of the surgically resected wrist lesion. (A) A well-circumscribed lesion with central cystic cavitation (indicated by arrows), visualized using H&E staining (magnification, x12.5; scale bar, 1 mm). (B) Numerous psammomatous calcifications are observed (indicated by arrows), visualized using H&E staining (magnification, x100; scale bar, 200 μm). (C) Histiocytes (indicated by black arrows) and spindle cells (indicated by the blue arrow) are present around the calcification. A multinucleated giant cell is also visible (indicated by the red arrow), visualized using H&E staining (magnification, x400; scale bar, 50 μm). (D) Cluster of differentiation 163-positive histiocytes are present around the calcification (magnification, x400; scale bar, 50 μm). (E) Bone morphogenetic protein-1 expression is noted in the histiocytes and spindle cells around the calcification (magnification, x400; scale bar, 50 μm).

Discussion

In the present report, a case of tenosynovitis with psammomatous calcification was described. In addition, to the best of our knowledge, this was the first time immunohistochemical analysis was used to identify the potential mechanism of psammoma formation. Table I summarizes the clinicopathological features of the case in the present study, and those of previously described cases. As demonstrated, this disease affects patients with a median age of 44 years (14-83 years), with a female predominance (male:female ratio, 4:30), particularly in young to middle-aged women. Of the patients examined previously and in the presents study, 12 of 25 had a history of trauma or repetitive activity. The majority of cases occurred in the hand, in particular in the finger, or the foot, and the most common complaint was a painful mass. A previous study involving the largest case series revealed these aforementioned clinicopathological features of tenosynovitis with psammomatous calcification (6), which is believed to be a distinct clinicopathological condition involving an unusual reactive or degenerative process in the chronically traumatized tendon and peritendinous tissue (2,6). However, the underlying molecular mechanism of development of this disease remains unclear.

BMP-1, also known as procollagen C-peptidase may convert a variety of precursor proteins, including procollagen and dentin matrix protein, into active forms, resulting in their involvement in cell adhesion and the regulation of hard tissue mineralization (7). Therefore, the present study focused on the association between psammomatous calcification of this lesion and BMP-1 expression. From the data in the present study, the expression of BMP-1 in histiocytes and spindle cells surrounding the psammomatous calcification was clearly observed. This suggests that the expression of BMP-1 may be associated with the development of psammomatous calcification.

In conclusion, the present study described a typical case of tenosynovitis with psammomatous calcification and reviewed its clinicopathological characteristics. The results suggested that the expression of BMP-1 in the histiocytes and spindle cells surrounding the psammomatous calcification may be associated with development of this condition.

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Table I. Clinicopathological features of tenosynovitis with psammomatous calcification.

Author, year	Case no.	Age, years	Sex	Location	Primary complaint	History of trauma or repetitive activity	(Refs.)
Gravanis and Gaffney, 1983	1	54	Male	Right pectoralis minor tendon	NA	NA	(1)
	2	28	Female	Left ring finger, PIP joint	Swelling	NA	(1)
Shon and Flope, 2010	3	16	Female	Right foot peritendinous tissue	Painful mass	Yes	(2)
	4	19	Female	Right foot peritendinous tissue	Point tenderness	Yes	(2)
	5	40	Female	Right thumb	Painful mass	Yes	(2)
	6	63	Female	Right flexor carpal tendon	Persistent pain	Yes	(2)
	7	67	Female	Right ring finger	Painful mass	Yes	(2)
	8	83	Female	Right middle finger	Painful mass	Yes	(2)
Robb *et al*, 2012	9	52	Female	Left knee	Persistent pain	No	(3)
Kawata *et al*, 2014	10	35	Male	Left middle finger, PIP joint	Painful swelling	No	(4)
Fox *et al*, 2017	11	14	Male	Right ring finger	Pain, intermittent locking	No	(5)
Michal *et al*, 2018	12	16	Female	Right foot	NA	Yes	(6)
	13	17	Female	Left great toe	Pain	Yes	(6)
	14	18	Female	Left IV finger	Nerve tingling	Yes	(6)
	15	19	Female	Right foot MTP joint	Pain	NA	(6)
	16	25	Female	Right toe MTP joint	Pain and edema	Yes	(6)
	17	33	Female	Right IV MCP joint	Swelling with pain	No	(6)
	18	33	Female	Right IV finger PIP joint	Pain	No	(6)
	19	38	Female	Left III finger PIP joint	None	Yes	(6)
	20	40	Female	Right IV finger PIP joint	Pain and edema	No	(6)
	21	41	Female	Right II finger	Pain	No	(6)
	22	44	Female	V finger PIP joint	None	No	(6)
	23	44	Female	Right big toe	None	No	(6)
	24	44	Female	Right IV finger	NA	NA	(6)
	25	47	Female	Left finger	NA	NA	(6)
	26	49	Female	Right hand	NA	NA	(6)
	27	49	Female	Left big toe	Pain and edema	Yes	(6)
	28	49	Female	Right III finger	Pain	No	(6)
	29	50	Female	Left thumb	Pain	NA	(6)
	30	52	Female	Left knee	Pain	No	(6)
	31	59	Male	Left IV finger	NA	NA	(6)
	32	63	Female	Right II finger	NA	NA	(6)
	33	75	Female	Right elbow	Pain	No	(6)
Present study		66	Female	Right wrist	Pain	No	-

MCP, Metacarpophalangeal; MTP, Metatarsophalangeal; NA, not available; PIP, Proximal interphalangeal.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

CM and MI were responsible for the conception and design of the study. CM, MI, YH, TT and KT were involved in the acquisition and analysis of the data. CM and MI drafted the manuscript. The final version of the manuscript was read and approved by all authors.

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki, and written consent was obtained from the patient.

Patient consent for publication

Written informed consent for publication was obtained from the patient.

Competing interests

The authors declare that they have no competing interests.

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