Pigmented villonodular synovitis: a retrospective study of seventy five cases (eighty one joints)

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Abstract

Purpose Pigmented villonodular synovitis (PVNS) is a relatively rare, benign proliferation lesion of the synovium of large joints, but there is not much information available about the disease's aetiology, clinical history, differential diagnosis, treatment, and long-term effects. We conducted a study to analyse these aspects of PVNS.

Methods We reviewed all clinical data for 75 patients with PVNS (81 joints) who were treated either by synovectomy alone or synovectomy plus arthroplasty.

Results In all cases, the diagnosis of PVNS was confirmed by pathological examination. The ratio of males to females was 27:48, and the average age of patients was 46 years (range, 15–80 years). Lesions were located in the knee, hip, or ankle, and pain and swelling were the main symptoms. Of 75 patients, 42 had a history of trauma to the involved joint. Forty-one patients (43 joints) underwent synovectomy alone, and 34 patients (38 joints) underwent synovectomy and arthroplasty together. Of the 75 patients, 61 had full follow-up data. Twelve patients had recurrent lesions detected by pathological examinations; four patients had

more than two recurrences. Moreover, five patients developed PVNS after arthroplasty.

Conclusions PVNS occurs most often in middle-aged women and most frequently involves the knee, followed by the hip and ankle. The disease's etiology is varied and unclear. Surgical excision alone or with arthroplasty is an effective treatment, but there is a high rate of recurrence.

Introduction

Pigmented villonodular synovitis (PVNS) usually affects the larger joints, such as the hip, knee, and ankle joints, and often is intra-articular and infiltrative. Although the lesion is aggressive and sometimes recurs, it has always been considered a benign proliferation of the synovium. The few published reports about PVNS [1] have focused on the clinical [2] and radiological characteristics of the disease. Because such reports have provided little information about the disease's aetiology [3], clinical history, differential diagnosis via pathological examination, treatment, and long-term effects, we investigated these aspects. Our hospital is one of the major centres in China for the treatment of bone disease, making it possible for us to have access to enough patients with PVNS to constitute a study population.

Patients and methods

Patients

Our study was a systematic single-centre retrospective analysis. All 75 patients with PVNS treated at our hospital between 2000 and 2010 constituted our study population. All patients underwent radiological examination of affected joints, and PVNS was diagnosed in all by pathological examination. In addition, all patients underwent surgery.

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Data collection

All clinical data were collected from the electronic files for patients with PVNS. Follow-up data were obtained from hospital charts and, if necessary, by a phone call. For the patients we could not contact by telephone, we considered the most recent follow-up visit to be their final visit.

Imaging

All patients except those undergoing arthroplasty were examined with magnetic resonance imaging (MRI) before their first surgical treatment.

Treatment

Treatment was either surgical synovectomy alone or synovectomy plus arthroplasty. Surgery was performed by arthroscopy or arthrotomy. Relapse was defined as the need for a second or third surgery, and diagnosis was made by pathological examination.

Results

Patients

There were 75 patients (81 joints) with PVNS in our study (Table 1), with the disease occurring significantly more frequently in females than in males (48:27; 64 %). The average age of patients was 46 years (range, 15–80 years). Only a few cases involved patients younger than 20 years; most involved patients in their fourth decade of life. The knee (37 joints; 63 %) was the most frequent site of PVNS, followed by the hip (17 joints; 23 %) and the ankle (four joints; 5 %). Only one case involved the joints of the hand. There were more patients with PVNS on the right side of the body (40; 53.3 %) than on the left (29; 38.7 %), especially in males. There were six patients who had two joints with PVNS either at the same time or at different times. The symptoms at diagnosis were pain and/or swelling, which limited joint function in most cases. Patients had pain in 68 cases, swelling in 55 cases, and limited joint action in 61 cases. The mean delay from first clinical symptoms to diagnosis was 55 months but was dramatically shorter in males (11.5 months) than in females (91 months). In 42 cases, there was a clear history of joint trauma lasting 7–71 months. PVNS was diffuse in 67 joints (89.3 %) and localized in eight (10.7 %). Haemarthrosis was confirmed in 12 cases by fine-needle paracentesis before surgery. In another 16 cases, faintly yellow fluid was found in the involved joints. In three of those cases, the faintly yellow fluid became haemarthrosis at a later stage. In 12 cases,

there were osteophytes or bone spurs in the joints affected by PVNS. MRI demonstrated PVNS in 53 cases. Articular cartilage was destroyed to varying degrees in 72 cases, and in 35 cases a bone lesion caused by PVNS was detected both by MRI and during surgery.

Imaging

MRI showed diffuse thickening of the synovium and low-intensity areas on both T₁- and T₂-weighted imaging in diffuse PVNS. The villonodular tissue was clearly visible. With MRI, it was possible to see the presence of hemosiderin in the tissue. Many of the lesions expanded to the adjacent tissues because of synovial proliferation and hydrarthrosis. The articular cartilage of even the deep bone was destroyed and the synovium extended into the adjacent soft tissues in 35 of the 67 joints with diffuse PVNS. In all cases, the joint space had narrowed. There were one or more nodular hypointensity signals in the joints with localized disease. There were no noteworthy abnormalities in most joints in the early phase, but there was bone erosion in the late phase in some joints (Fig. 1). CT was useful for showing the degree of bone erosion. MRI was not used in patients who had undergone arthroplasty.

Surgical treatment

All 75 patients (81 joints) with PVNS were treated with surgical or arthroscopic synovectomy alone or underwent arthroplasty at the same time (Fig. 2, Table 2). Of those, 41 patients (43 joints) underwent synovectomy alone and 34 patients (38 joints) underwent synovectomy and arthroplasty at the same time.

Histology

In all 75 patients, diagnosis was made by pathological examination. Macroscopically, the specimen consisted of pieces. The surface was brown and was covered with nodules and both long and short papillae. Below the surface, the tissue was pale yellow (Fig. 3). Histologically, the surface of the tissue was composed of synoviocytes with brown pigment in the cytoplasm. Below the surface, there were numerous foamy cells and multinucleated giant cells stained with haemosiderin. The diagnosis was PVNS (Fig. 4).

None of the 75 patients had postoperative complications or infection. Of those, 60 kept all appointments for follow-up care and were monitored for a mean of 41 months. At a later stage, 28 patients had slight pain or swelling in the involved joints; MRI showed that these patients had joint effusion. In 21 of those patients, the effusion had resolved by the next follow-up visit. By a mean of 35 months after surgery, recurrent lesions were found on MRI in 17 joints

Table 1 Clinical characteristic of 75 patients with pigmented villonodular synovitis

Characteristic	Male	Female	Total
Gender	27 (36 %)	48 (64 %)	75
Mean age (years)	44	47	46
Age distribution (years)			
10–19	2	0	2 (2.7 %)
20–29	5	9	14 (18.7 %)
30–39	5	8	13 (17.3 %)
40–49	5	15	20 (26.7 %)
50–59	4	2	6 (8 %)
60–69	1	8	9 (12 %)
70–80	5	6	11 (14.6 %)
Anatomical distribution			
Knee	18 (1)	34 (4)	52 (69.4 %)
Hip	6 (1)	12	18 (24 %)
Ankle	3	1	4 (5.3 %)
Hand	0	1	1 (1.3 %)
Side			
Left	7	22	29 (38.7 %)
Right	17	23	40 (53.3 %)
Both sides	2	4	6 (8 %)
Mean time elapsed from disease onset to diagnosis (months)	11.5	91	54
Disease form			
Diffuse	27	40	67 (89.3 %)
Localized	1	7	8 (10.7 %)
Symptoms at diagnosis			
Pain	26	46	72 (96 %)
Joint effusion	12	16	28 (37.3 %)
Swelling	13	16	29 (38.7 %)
Osteophyte or bone spur	6	6	12 (16 %)
Mean duration of follow-up (months)	42	39	40
Recurrence	6; two had a third recurrence and surgery	6; two had a third recurrence and surgery	12 (16 %); four had a third recurrence and surgery (53 %)

with diffuse PVNS. Among those 17 joints, 12 had prosthesis loosening of varying degrees and underwent surgery a second time because of recurrent PVNS diagnosed on pathological examination. Among those 12 joints, four had another recurrence of PVNS at a mean of 17 months after the second operation. They underwent a third operation and then radiotherapy; and they have not had more recurrences (Table 2).

Discussion

Our retrospective study is the one of few large series of patients with PVNS affecting mainly large joints that has been reported in the literature. We found that PVNS occurs mainly in middle-aged adults, with no difference between the sexes regarding age distribution. Almost the same

percentage of patients in every decade, excluding the fourth decade, had PVNS. There were few cases of PVNS in patients who had not reached adulthood.

Few cases of PVNS involving small joints have been reported [4]. In our study, there was only one case of PVNS involving the hand; the other 74 cases (80 joints) involved the knee, hip, and ankle joints.

Most of our patients were female. Joint pain and swelling were the main clinical symptoms, as with other joint diseases. All of the patients had had PVNS for a long time before they first underwent surgery, with females waiting longer than males. We speculate that the females tended to tolerate the clinical symptoms of PVNS longer than the males did.

There is no consensus about the etiology of PVNS. Some researchers have debated whether PVNS is inflammatory or

Fig. 1 Magnetic resonance image showing the right knee of a 56-year-old woman with pigmented villonodular synovitis that destroyed the articular cartilage and the deep bone

neoplastic in origin [5]. Others have suggested trauma-induced haemorrhage as an etiology [6]. In our study, 42 patients had a clear history of trauma before PVNS was diagnosed, and 12 patients with bloody fluid in the involved joints had an osteophyte or bone spur. However, some patients had bloody fluid in the involved joints for no obvious reason, and some had joint fluid that was bloody at the first evaluation and then was slightly yellow at a later evaluation, which could not have been explained by trauma.

Fig. 2 Radiographs of the knee prosthesis after concurrent synovectomy and arthroplasty in the same patient as in Fig. 1

All of the suggested aetiologies could cause synovium proliferation in involved joints directly or indirectly. We also had five cases of PVNS involving patients with a history of arthroplasty.

The mechanism of bone erosion in PVNS is still under debate. Some researchers believe that pressure within involved joints increases because of synovial overgrowth. Others believe that perhaps the synovium releases a substance that causes bone erosion. Whatever the cause, bone erosion results in joint destruction [7].

MRI was useful for the diagnosis of PVNS except in cases with specificity. The ability to determine the form of PVNS before surgery was helpful for the surgeon in choosing the most appropriate surgical technique. Haemosiderin deposits were an important feature for differentiating PVNS from other types of proliferative synovitis [8]. MRI did detect synovial hyperplasia, but it did not have enough sensitivity to allow accurate diagnosis even when haemosiderin deposits were present. MRI did not make it possible to distinguish synovial hyperplasia from other types of proliferative synovitis, rheumatic arthritis, or tuberculous arthritis. However, MRI effectively indicated bone lesions, articular cartilage lesions, and osteophytes in the joint cavity, which is helpful in determining whether arthroplasty is necessary. Therefore, we consider MRI to be useful in the diagnosis of PVNS and in determining the choice of surgical modalities, although pathological examination is needed in addition to MRI to accurately distinguish PVNS from rheumatoid arthritis, degenerative osteoarthritis, synovial haemangioma, and other disorders [9].

We were also able to detect hydrarthrosis with MRI. The colour of the fluid in the involved joint cavity was variable. It was dark red in some patients and slightly yellow in other patients, and it sometimes differed in the same patient at different phases of the disease when checked by paracentesis before surgery.

Surgery is usually considered the best therapy for PVNS, although no standard technique has been defined. Whether done arthroscopically or through an open arthrotomy, the therapy of choice is synovectomy with excision of the lesion for localized PVNS, and total synovectomy for diffuse PVNS. In our study, we performed both open surgical synovectomy and arthroscopic synovectomy, with the choice of modalities depending on the form of the disease and the location of the lesion. Our follow-up data showed a higher disease recurrence rate for open surgical arthrotomy than for arthroscopic procedures. We believe that this occurred because some lesions in the mini spaces in the involved joints could be excised via arthroscopy but not via arthrotomy [10].

In some cases, arthroplasty was necessary. Disease of the knee joint does not always require total knee replacement, but certainly replacement is a reasonable solution when

Table 2 Synovectomy by anatomical site

Site	Side	Number of joints (no. with second recurrence and surgery; no. with third recurrence and surgery)				
		Surgery	Arthroscopy	Arthroplasty	Localized	Diffuse
Knee	R	4 (3; 1)	10 (1)	10 (1; 1)	2	22 (5; 2)
	B	4	6 (1)	10 (1)	Knee	B
	L	3 (2)	16 (1)	4 (1)	1	22 (4)
Hip	R	2 (1; 1)		10 (1; 1)	2	10 (2; 2)
	B			2 (1)		2 (1)
	L			5	2	3
Ankle	R	2		1		3
	L	1			1	
Hand	L	1				1
Total		13 (6; 2)	30 (2)	38 (4; 2)	8	73 (12; 4)

B bilateral, L left, R right

sufficient bone has been damaged. Hip surgery appears to have a high rate of failure in terms of restoration of normal function and often requires total joint replacement [11]. A higher percentage of our patients underwent hip joint replacement than knee replacement.

In current treatment approaches, radiotherapy is recommended as an adjunct to total synovectomy for preventing recurrences when there is residual tumour or as second-stage treatment in recurrences. Surgeons should watch for local complications, such as postradiation fibrosis, swelling, and wound-healing problems, along with risks to bone graft incorporation if it is necessary later [12]. Malignant transformation after radiotherapy is a worrisome adverse effect, especially in young patients. In reports of malignant PVNS, there is often a history of radiotherapy [13].

Imatinib mesylate, which is the oncogene-targeted drug used to treat chronic myeloid leukemia and gastrointestinal stromal tumours, may be useful for PVNS [14]. To avoid

multiple recurrences, some authors have treated local recurrences of PVNS with anti-tumour necrosis factor- α [15].

The reported rate of recurrence varies [16]. In our study, 17 patients had recurrent PVNS, diagnosed on the basis of MRI findings and/or clinical symptoms. It is possible, however, that some cases represented not recurrences but rather the usual proliferation of the synovium after surgery. Among those 17 patients, 12 underwent a second procedure and three underwent a third procedure. Thus, it could be said that there were two recurrence rates: one for MRI and one for pathology. In part, the cause might have been how recurrence was defined. The recurrence rate was higher in patients with recurrent disease than in patients in whom the disease was diagnosed for the first time.

PVNS has been reported to have a high recurrence rate, but it rarely becomes cancerous or metastasizes [13]. Although the literature suggests that a malignant form exists, there is no evidence to support the idea that it arises from or is the same as the benign disorder. It is not clear what the

Fig. 3 Nodular and papillary masses (partial specimen) with haemosiderin staining caused by pigmented villonodular synovitis of the knee joint in the same patient as in Fig. 1. Note the effect on the synovium capsule wall

Fig. 4 Histological image from the same patient as in Fig. 1 showing the nodular and papillary structure and the presence of synovial cells, histiocytes, and hyperplasia, with haemosiderin in the cytoplasm (hematoxylin and eosin; original magnification $\times 40$)

best complementary therapy is. If the lesion recurs locally, radiotherapy and isotopic synoviorthesis may be helpful.

Our study showed that PVNS occurs mainly in middle-aged adults and has a variable etiology. Arthroplasty has not been mentioned as a possible aetiology until recently. We found that the knee was the most frequent location for lesions, followed by the hip and the ankle, and that pain and joint effusion were the most frequent clinical symptoms. Haemarthrosis was more frequent than slight yellowing of synovial fluid in patients with hydrarthrosis. MRI is very useful for diagnosis, for planning the extent of synovectomy, for choosing surgical technique, and for follow-up examinations. Complete surgical removal of localized lesions, or total synovectomy, is still the first line of treatment. Isotopic synoviorthesis or radiotherapy may be useful, especially for patients who undergo incomplete synovectomy and those with recurring disease. Both MRI and pathological examination show that PVNS has a high recurrence rate.

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