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Pigmented Villonodular Synovitis of The Knee Joint: Diagnosis, Management and Summary of Tenosynovial Giant Cell Tumors: A Rare Case Report

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Abstract

Introduction: Pigmented villonodular synovitis (PVNS) is a rare, benign, but potentially locally aggressive and recurrent condition characterized by synovial proliferation and hemosiderin deposition inside the joints, tendon sheaths, and bursae. It usually affects the large joints such as hip, knee, and ankle. Localised pigmented villonodular synovitis {PVNS} of the knee is rare diagnosis, with clinical signs and symptoms mimicking meniscal damage or other common knee injuries.

Case Presentation: We report a case of PVNS of the knee joint in a 39-year-old female which was treated by arthroscopic subtotal synovectomy as a first stage surgery after which patient was planned for total synovectomy and postoperative radiotherapy. This case highlights the clinical presentation of this rare disorder and emphasizes its consideration as a differential diagnosis in our setup when dealing with non-traumatic persistent knee pain and swelling.

Conclusion: Pigmented villonodular synovitis demonstrates a locally destructive process but is rarely fatal. PVNS is primarily a disease of quality of life as it

can lead to difficulty with activities of daily living and an overall decrease in quality of life. The clinical presentation of one case found in our region is described. Patients usually present with insidious onset joint swelling associated with pain that mimics joint effusion. Joint pain subsequently supervenes, but the swelling is disproportionate to the degree of pain. The pain is mild and of insidious onset, and it progressively worsens and frequently is accompanied by decreased range of motion and sometimes locking of the joint. We recommend that PVNS should be included as a differential diagnosis when evaluating a young adult with non-traumatic persistent knee pain and swelling

Keywords: Villonodular, Synovitis, Synovectomy, Mri, Radiotherapy

Introduction

Pigmented villonodular synovitis (PVNS) is a rare proliferative disease of synovial membranes, with characteristics of villonodular synovial hyperplasia and hemosiderin deposition[1]. It primarily affects people in their third to fourth decade of life, while it can affect both young people and the elderly. It is typically linked to t(1;2)(CSF-1;COL6A3) chromosomal translocation, which causes colony stimulating factor (CSF1) to be overexpressed. PVNS is classified into two types based on the biological behavior. These are diffuse and localized, and although they have the same histological characteristics, their therapy and prognosis are different[2]. It is distinguished by the development of tendon papillae and follicles, as well as hyperplasia and pigment (hemosiderin) deposition in the joints. At present, the standard treatment for pigmented villonodular synovitis has been surgical excision with total synovectomy of the affected joint[2]. If left untreated, the affected joint can become severe deformity, degenerative articular change, and articular destruction and finally lead to the risk of arthrodesis or amputation[2]. This thing leads to the need for early recognition of the clinical presentation and using imaging diagnosis to make an early and accurate diagnosis.

Especially, due to the low incidence rates, PVNS often is misdiagnosed with other diseases of synovial membranes leading to late diagnosis and severe articular destruction. Magnetic resonance imaging (MRI) plays an important role in early diagnosis and improving treatment outcomes, protecting joint function as well as the quality of life. In imaging diagnosis, MRI is the most appropriate imaging modality for detection and assessment of disease extent, biopsy guide, and PVNS treatment[1]. The preferred therapy for severe, extra-articular diffuse PVNS is open arthrotomy and complete synovectomy, whereas arthroscopic resection is mostly advised for localized PVNS[7]. The scope of diffuse PVNS makes it challenging to control, particularly when adjacent structures are implicated. The incidence of recurrence varies between 14% and 55%, even after the pathogenic tissue has been surgically removed[5].

In this article, we describe a case of diffuse PVNS in a 39- year-old female who was not properly diagnosed after going to several hospitals within 8 months. The patient was treated in several hospitals with the diagnosis of right knee effusion but the symptoms became worsened. When coming to our hospital, the patient underwent imaging examinations of the right knee joint including ultrasound, and MRI. The features found on imaging suggested the diagnosis of diffuse PVNS. Therefore, we report this case to emphasize the diffuse PVNS lesions, and we would like to share our experience in diagnosing PVNS and differentiating it from other lesions of the knee joint, and appropriate

management protocol and measures to prevent recurrence.

Case Report

A 39-year-old female presented in our unit with three years history of right knee pain and swelling. She reported generalized right knee pain of insidious onset which progressively increased in severity. The swelling gradually increased over a period of time and was associated with difficulty in walking and standing. The swelling was diffuse and nodular in consistency, measuring 17 centimeter(cm) into 11 centimeter(cm) in size. The overlying skin was normal with no signs of inflammation. There was no instability of the knee joint on physical examination. No other joint was involved. She denied any history of trauma, weight loss, anorexia or fevers. Review of the respiratory, cardiovascular, gastrointestinal, genitourinary and nervous systems was essentially normal. Her past medical and family history were unremarkable.

Examination findings: The general physical examination was unremarkable, except for the presence of a right sided antalgic gait. Local examination of the left knee revealed generalized swelling and increased local temperature. The knee had active range of motion of 0° - 60°. Neurovascular status was normal.

Radiographs of the left knee were obtained which showed no bony abnormality (Figure1). A magnetic resonance imaging (MRI) scan revealed a large joint effusion seen predominantly in the suprapatellar recess as well as in the lateral and medial femoral recesses appearing hyperintense on T2-weighted images. Diffuse synovial thickening was seen which appeared hypointense on T1 as well as hypo on T2-weighted and susceptibility images, and the synovium appeared hypertrophied. A multilobulated lesion was seen in continuity with the synovium in the anteromedial, anterolateral, and patella-femoral joint space. Few internal septae were seen. All these features were consistent with the diagnosis of pigmented villonodular synovitis.

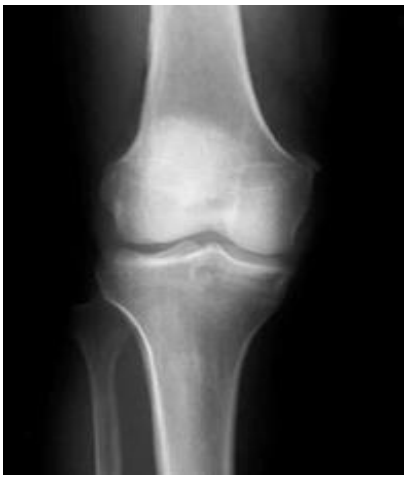

Figure 1: X-ray knee

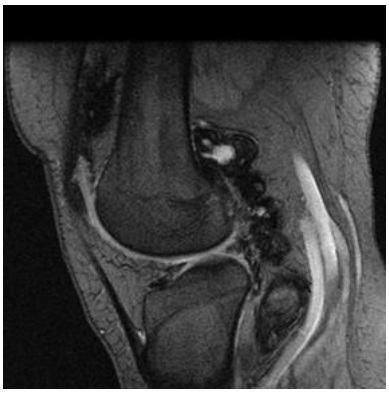

Figure 2A: Saggital image

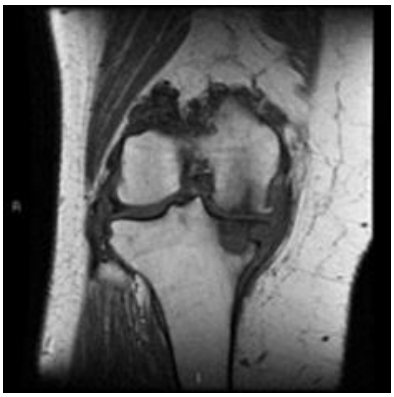

Figure 2B: Coronal image

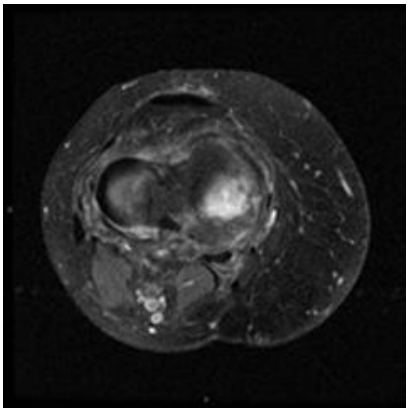

Figure 2C: Axial image.

The MRI imaging showed diffuse irregular thickening of the synovium, slightly hypointense in T1W, hypointense in T2W due to hemosiderin deposition, strong enhancement of the synovium after contrast-agent infusion, with knee effusion (Figs. 2A, 2B,2C). We made the diagnosis of diffuse pigmented villonodular synovitis (diffuse PNVS) of the right knee joint. - Complete blood count was normal. ESR was 25mm/hr. Rheumatoid factor, alkaline phosphatase, calcium and phosphate levels were normal.

After obtaining written informed consent from the patient, she was submitted to surgery. An arthroscopic Sub-total synovectomy was done to the knee joint. The arthroscopic excision of synovium is done followed arthroscopic debridement. Intraoperatively, a brownish nodular synovium was found which again was suggestive of PVNS (Figure3). Samples of the synovium, nodular tissue and fluid were taken for both histology and bacteriology. The excised synovium was sent for histopathological examination which showed tissue fragments with mild autolytic changes, showing several villous structures and nodules lined by a single layer of cuboidal cells and underlying areas showing edema , hyalinization , numerous scattered mononuclear cells and chronic inflammatory cells , several hyalinized vascular channels, pseudo alveolar space and hemosiderin laden macrophages are identified . No atypical cells and mitotic activity seen. All these features are consistent with Pigmented Villonodular Synovitis/Tenosynovial Giant Cell Tumor, Diffuse type.

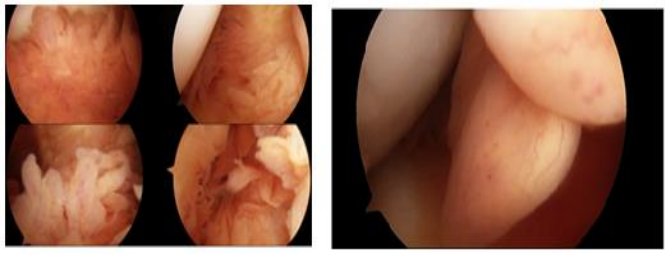

Figure 3: Intra operative images

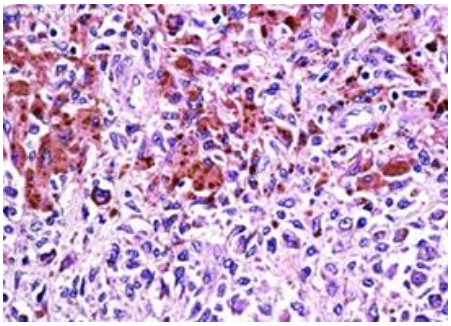

Figure 4: Histology

Postoperatively, the patient was started on passive knee flexion and extension exercises for 15 days and made to walk after that. Now patient was referred to cancer hospital for radiotherapy for radiotherapy. . Four weeks following the surgery, the patient received adjuvant postoperative external radiation to increase local control rates and decrease recurrence. Using the three-dimensional conformal radiation (3DCRT) approach, the patient got a 38 Gy regimen administered five times a week in 19 fractions at a rate of 2.0 Gy/fraction. The greatest range of knee joint movements that could be accomplished was -5º of extension to 90º of flexion, about two months after the surgery and a few days after the final radiation session. The MRI showed no notable changes eighteen months after the treatment ended. A maximum range of 0º extension and 110º flexion was attained 3 months after surgery. Imaging and clinical

orthopaedic assessment did not show a disease recurrence. The patient had no functional restrictions and was asymptomatic.

Discussion

Pigmented villonodular synovitis (PVNS) refers to a subtype of tenosynovial giant cell tumors that diffusely affect the soft tissue lining of joints and tendons. PVNS most commonly affects the knee, hip, and ankle joints and is insidious in onset, with symptoms often being present for years before diagnosis.[1,2] Furthermore, PVNS is more aggressive compared to the other major subtype of tenosynovial giant cell tumors, giant cell tumor of the tendon sheath (GCT-TS). According to a 1980 report, PVNS affects roughly 9.2 new people per million in the United States each year.[1] Even after treatment, the recurrence rate of PVNS ranges from 14 to 55%.[2]Pigmented villonodular synovitis has been shown to have neoplastic components. Translocations of chromosome 1p13 are present in the majority of PVNS cases with the endpoint effect of overexpressing colony-stimulating factor 1 (CSF1). As CSF-1 becomes overexpressed, clusters of aberrant cells form to create focal areas of soft tissue hyperplasia in the synovial cells lining joints.[3]

Due to its slow onset, the median time of definitive diagnosis from the onset of symptoms to definitive diagnosis has been shown to be 18 months.[4] There is conflicting data regarding the gender distribution of pigmented villonodular synovitis. Some studies suggest that male and female genders are affected at equal rates,[3] while others suggest females are slightly more predisposed, but only in the context of localized disease.[5,6] Pigmented villonodular synovitis has been consistently shown to have a lower incidence in pediatric populations. As a result, it gets more frequently misdiagnosed in children[7].

Synovial fluid analysis in pigmented villonodular synovitis most often has a dark brown or hemorrhagic color[8]. Microscopic workup reveals an assortment of mononuclear cells, macrophages with extensive hemosiderin stores, and multinucleated osteoclast-type giant cells[9]. Specifically, hemosiderin deposits result from the episodic nature of the disease. As repeated bleeding into the joint occurs, hemoglobin breaks down to form large deposits of iron in surrounding tissues. The resulting hemosiderin-laden parenchyma is a direct reflection of recurrent hemarthrosis in patients with PVNS.[8,10]

The tumor of pigmented villonodular synovitis is slow-growing, and, early on in the disease course, the patient presents with unexplained painless swelling in the affected joint[6]. As the tumor expands, however, pain and swelling add to cause moderate to severe range of motion limitations in the affected area[6,9]. As the disease progresses, recurrent hemarthrosis leads to worsening joint stiffness and moderate to severe joint destruction[11]. A single joint presentation is the most common, but rarely PVNS can present polyarthropically[7]. Since the onset of symptoms in PVNS is insidious, patient history often includes an extensive workup for other causes of joint pain.[12] Pigmented villonodular synovitis typically occurs in the large joint of the upper and lower extremities. Most commonly, the disease affects the knee in the patellofemoral compartment at the infrapatellar fat pad[6].

Clinicians typically pigmented villonodular synovitis through a combination of several radiographic modalities. Initial X-ray studies show signs of soft tissue

swelling in addition to boney erosion around the affected joint[9]. MRI imagining is the most sensitive imagining study. Classically, MRI demonstrates joint effusion, hemosiderin deposits, expansion of the synovium, and boney erosion. Routine blood markers for inflammation, including erythrocyte sedimentation rate and C reactive protein, are not elevated in the majority of patients, despite the clinical appearance of soft tissue swelling[4,6]. Several authors have suggested a link between a prior joint injury and the development of PVNS, but this correlation has not been proven to be consistent across investigators[9,13]. Incidental hemarthrosis from aspiration of a chronically inflamed joint can also provide an important diagnostic clue[8].

The gold standard of treatment for pigmented villonodular synovitis has traditionally been surgical excision with total synovectomy of the affected joint, either with an open or arthroscopic approach[14]. While both of these methods have a similar reccurrence rate of PVNS post-surgery, the arthroscopic procedure has consistently demonstrated better functional and range of motion outcomes for the patient[15]. However, even after surgery, PVNS has a recurrence rate of up to 50%, prompting investigators to explore additional treatment options[6]. When used as monotherapy, external beam radiation has demonstrated local control of up to 95.1% when dosed from 30 Gy to 50 Gy[16]. Radiation therapy has also been shown to reduce PVNS recurrence post-surgical synovectomy significantly[16]. The elucidation of the CSF-1 pathway has lead to the investigation of multiple systemic therapies, including monoclonal antibodies and tyrosine kinase inhibitors. Amongst these agents, emactuzumab and PLX3397 show promise[6]. Emactuzumab is a monoclonal antibody that directly binds the CSF-1 receptor on the surface of macrophages, thus reducing or eliminating the effects of aberrant CSF-1 production. In a recent phase 1 trial, 26 out of 28 patients with PVNS had an objective response to treatment with emactuzumab[6]. PLX3397, which works by blocking molecular endpoints of CSF-1, demonstrated not only a well-tolerated side effect profile but also a clinical response in 52% of patients[6]. Most recently, the use of pexidartinib, a CSF-1 receptor antagonist, was approved by the FDA in August 2019 for use in patients with extensive disease who are not likely to benefit from surgical intervention[17].The differential diagnosis include Rheumatoid arthritis, septic joints, hemarthrosis, and other neoplasia can all mimic the clinical features of pigmented villonodular synovitis upon clinical inspection[7]. Even with ideal radiographic and diagnostic studies, pigmented villonodular synovitis can get misdiagnosed as a ganglion, schwannoma, or hemangioma[18].

Conclusion

Pigmented villonodular synovitis demonstrates a locally destructive process but is rarely fatal. PVNS is primarily a disease of quality of life as it can lead to difficulty with activities of daily living and an overall decrease in quality of life. The clinical presentation of one case found in our region is described. Patients usually present with insidious onset joint swelling associated with pain that mimics joint effusion. Joint pain subsequently supervenes, but the swelling is disproportionate to the degree of pain. The pain is mild and of insidious onset, and it progressively worsens and frequently is accompanied by decreased range of motion and sometimes locking of the joint. We recommend that PVNS should be included as a differential diagnosis when evaluating a young adult with non-traumatic persistent knee pain and swelling.

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Abbreviations:

1. PVNS-Pigmented villonodular synovitis.
2. MRI-Magnetic resonance imaging.

3. CM-Centimeter.
4. T1W-T1 Weighted.
5. T2W-T2 Weighted.
6. ESR-Erythrocyte Sedimentation Rate.
7. 3DCRT-Three-Dimensional Conformal Radiation.
8. CSF1-Colony-Stimulating factor 1.
9. Gy-Gray.