Clinical Case Report

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Necessity of adjuvant postoperative radiotherapy for diffuse pigmented villonodular synovitis of the knee

A case report and literature review

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Abstract

Rationale: Pigmented villonodular synovitis (PVNS) is an idiopathic, proliferative disorder lesion of synovial tissue, which is regarded as a benign disease, but has a local invasion. Up to now, these are no consensus about the etiology and pathogenesis of PVNS. Because of the lack of typical clinical features, misdiagnosis and delayed diagnosis are not uncommon, magnetic resonance imaging (MRI) can assist diagnosis and histopathological examination is recognized as the gold standard for the final diagnosis. Because this disease is so rare, there is no standard treatment. Surgical resection of the lesion is considered the preferred treatment, but postoperative recurrence is a problem that cannot be ignored. Postoperative radiotherapy is necessary, especially for patients with diffuse PVNS of the knee.

Patient concerns: A 27-year-old female teacher presented with 3 years chronic pain of the right knee, and progressive swelling aggravated for 1 week. The range of motion of the knee was limited.

Diagnoses: Clinical and laboratory examination failed to provide definitive diagnosis. Imaging can assist in diagnosis, and pathology is the gold standard. Erythrocyte sedimentation rate (ESR), antihemolytic streptococcus O (ASO), and rheumatoid factors (RF) were all negative. Joint puncture revealed giant cell tumor of the synovial membrane. PVNS was confirmed by postoperative pathology. The characteristic T2 weighted low signal of MRI suggests the recurrence of PVNS.

Interventions: The patient underwent 2 stages of treatment: open synovectomy was performed in the first place and postoperative external radiotherapy was not considered. After 2 years of disease-free remission, she was diagnosed with a recurrence of the disease by MRI. Further, arthroscopic total synovectomy of the right knee was performed and external beam radiotherapy was carried out after the operation.

Outcomes: Up to now, the patient was followed up for 3 years without any sign of recurrence.

Lessons: Adjuvant postoperative radiotherapy can improve the local control rate, it is a reliable treatment method for diffused PVNS.

Abbreviations: ASO = antihemolytic streptococcus O, CT = computed tomography, DR = digital radiography, ESR = erythrocyte sedimentation rate, MRI = magnetic resonance imaging, PVNS = pigmented villonodular synovitis, RF = rheumatoid factors.

Keywords: pigmented villonodular synovitis, radiotherapy, surgery

1. Introduction

Pigmented villonodular synovitis (PVNS) is a rare, benign proliferative disorder lesion of synovial tissue that most often affects large joints. There is no difference between genders. Younger patients seem predominantly affected, 30 or 40 years old is the most common.[1] Typically, PVNS is almost always monoarticular, while multiarticular disease in children have been reported.[2] Although it is classified as a benign condition, it has local invasiveness. Untreated PVNS can rapidly lead to irreversible joint destruction. Granowitz et al[3] subdivided this disease into 2 forms: localized and diffused. Both of these forms are similar histologically, but there are great differences in biological behavior, treatment principles, and prognosis.

So far, it is still the key to cure PVNS by complete surgical resection of the diseased synovial membrane, but there is a higher risk of recurrence after the operation, especially in diffuse PVNS. According to reports, the recurrence rate is between 8% and 56%.[4,5] For patients with suspected or proven residual PVNS, surgery combined with external radiation therapy is reliable.[6,7] Adjuvant postoperative external beam radiotherapy can improve the local control rate.

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2. Patient information

A 27-year-old female teacher of Han nationality presented with 3 years chronic pain of the right knee, and gradually increasing with swelling was observed 1 week later. By asking about her medical history, she denied any previous illness and denied a history of familial genetic disease. For the past 3 years, she has not been systematically treated to relieve pain symptoms mainly through oral analgesics (specifically unknown) and hot compress and acupuncture, with good results and bad results.

3. Clinical findings

Through checking, swelling in patient is obvious in above patella of the right knee and touching the local cable. Skin temperature and color are normal, no obvious tenderness and rebound pain. The floating patella test was negative. The lateral extrusion test was negative. The drawer test was negative. The range of motion of the knee was limited. Erythrocyte sedimentation rate (ESR), anti-hemolytic streptococcus O (ASO), and rheumatoid factors (RF) were all negative. The positive lateral of the right knee joint X-ray showed that there was a kind of circular low density area in the lower part of the right tibial plateau, and a thin high-density enhancement ring was seen at the margin. The internal density was slightly uneven, considered the possibility of bone cysts. Right knee joint computed tomography (CT) suggests: right tibia epiphysis, cystic lesion, right knee joint lesion, tuberculosis cannot be excluded. Because of the lack of typical clinical manifestations, the above physical examination findings cannot be confirmed as PVNS.

4. Timeline

Three milliliters of synovial bloody liquid was aspirated through joint puncture, and cytological examination showed more epithelioid cells, multinucleated giant cells and hemosiderin cells, suggesting that the giant cell tumor of synovium (Fig. 1). CT guided tissue puncture biopsy was further confirmed for PVNS. The patient underwent open synovectomy of the right knee joint. In operation, we can see a small amount of brown effusion, dark brown villous synovial, like the brown tumor lesions of suprapatellar bursa and hyperplasia of infrapatellar fat pad tissue and the lesions in the posterior articular capsule invaded the surrounding tissue. Postoperative pathology was further confirmed as diffuse PVNS (Fig. 2). Postoperative swelling and pain disappeared completely, without radiotherapy.

5. Diagnostic assessment

Two years after operation, the patient presented with knee pain again and progressive aggravation. Checking the right knee medial joint space tenderness was positive and the range of motion of the knee was limited. Magnetic resonance imaging (MRI) (Fig. 3) showed that the synovial membrane thickened obviously and irregular in shape, and mixed PD low signal; the right knee joint cavity and suprapatellar bursa had striped PD high signal; the right knee joint cartilage surface became thin in varying degrees. For PVNS, because of the lack of specificity of digital radiography (DR) and CT, identification of similar disease is very difficult. But MRI examination shows a specificity for signal changes caused by deposit of hemosiderosis, which shows low signals of long T1 and short T2. So it can be identified with some diseases, such as synovial sarcoma, rheumatoid arthritis, synovial joint tuberculosis, hemophilia arthropathy, and so on. Through the MRI performance, we considered that the recurrence of PVNS.

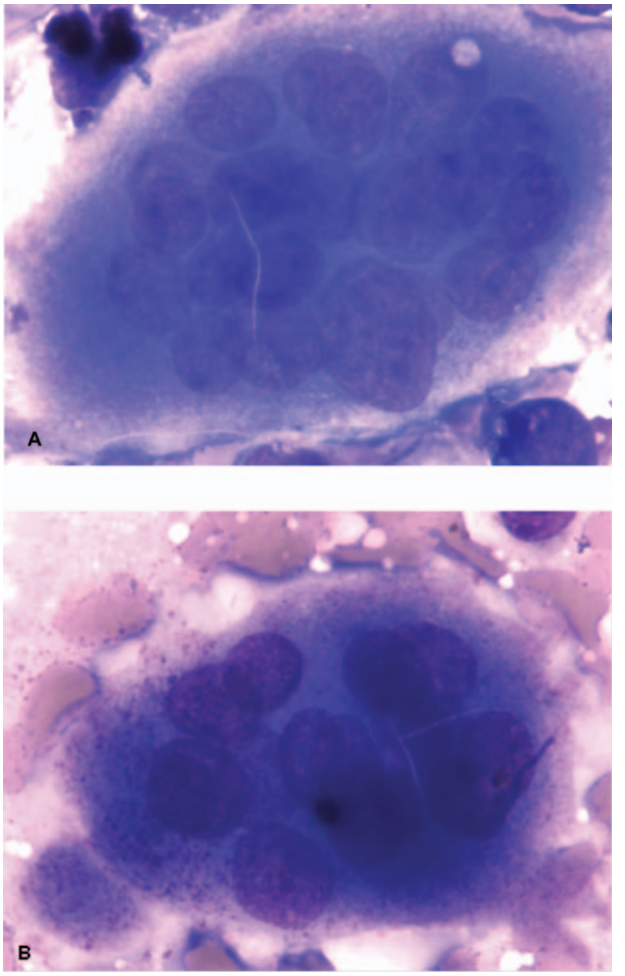

Figure 1. A and B indicated that epithelioid cells, multinucleated giant cells, and hemosiderin cells.

6. Therapeutic intervention

The patient further underwent arthroscopic synovectomy of the knee. In the operation, we could see diffuse nodular hyperplasia of the yellow-brown synovial membrane in the whole joint and a

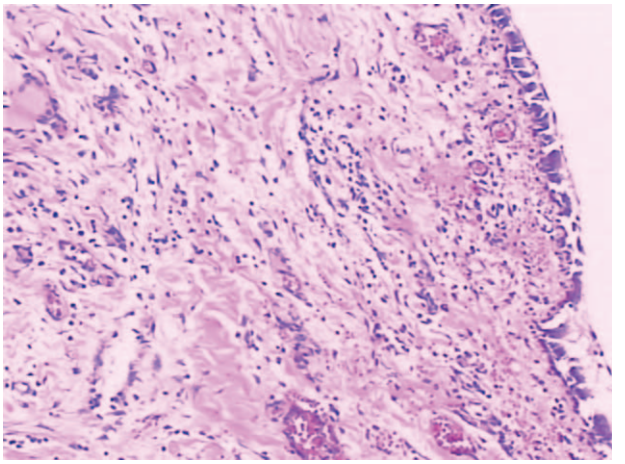

Figure 2. A large number of hyperplastic synovial cells are seen in the figure, which contain hemosiderin.

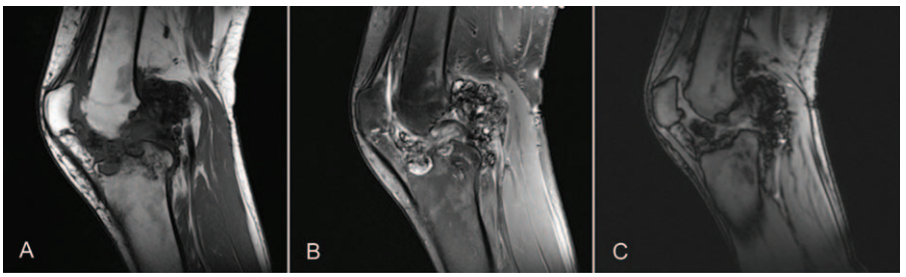

Figure 3. A–C were the same location of lesions, sagittal T1WI sequence, T2WI sequence, and proton weighted fat suppression sequence: the right knee joint peripheral synovial thickening widely, showed multiple nodular or lump low signal in varying size in T1WI and high and low mixed signal in T2WI, joint space narrowed obviously, and adjacent bone were absorbed and destroyed.

large number of nodules of phyllodes tumor tissue in anterior cruciate ligament, posterior articular capsule and fat pad, seriously invaded the surrounding tissue. Meantime, there was also extraarticular synovial lesion. To remove all synovial lesions and pathological examination showed that papillary projections of synovial cell coverage, seen large amounts of hemosiderin and phagocytic cells, confirmed recurrence of PVNS (Fig. 4). Twenty days after operation, the patient was treated with 3-dimensional conformal radiation therapy, linear accelerator 6 MV X-ray external irradiation. The total dose of 3000 cGy, each time for 200 cGy, 5 times a week.

7. Follow-up and outcomes

After radiotherapy, the patient was followed up for 3 years by MRI examination of the knee, there were no chronic toxic side effects such as joint activity limitation and no signs of recurrence.

8. Discussion

PVNS is a rare and relatively benign lesion, with progressive synovial hyperplasia and macrophages, multinucleated giant cells and hemosiderin deposition. The disease has 2 forms. The localized form is characterized by single, nodular or pedunculated masses and surrounded by normal synovial tissue, while the diffuse form affects most or entire synovium of the affected joint, leading to bone erosion and subchondral cysts. In clinic, diffuse PVNS is more common.

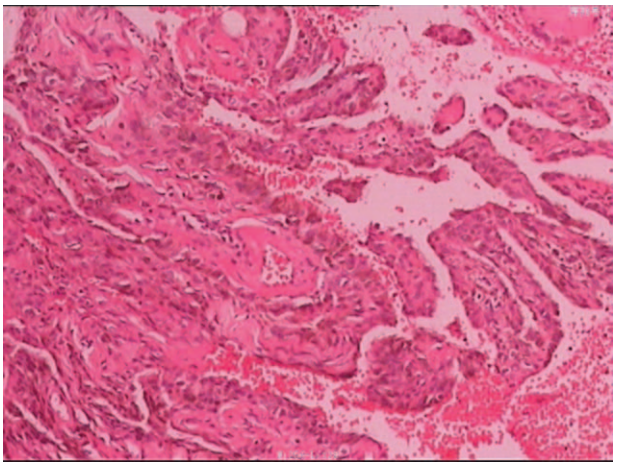

Figure 4. Papillary projections of synovial cell coverage, seen large amounts of hemosiderin and phagocytic cells.

PVNS is a rare and the incidence is estimated to be 1.8 per million for PVNS.[1] There is no consensus on the etiology and pathogenesis of the disease. Most scholars believe that it is associated with chronic inflammation, intraarticular repeated bleeding and trauma, tumor progression and lipid metabolism disorders. According to Oehler et al[8] research, chronic inflammation plays an important role in the process of PVNS. It increases the risk of intraarticular bleeding, disrupts the ability of local synovial macrophages to treat iron and leads to iron load. Furthermore, the transformation of macrophages to B cells and fibroblasts was induced by chronic inflammation. The permanent proliferation and activation of these cells may explain that why PVNS acts like a tumor process. However, Choong et al[9] considered that PVNS is a kind of the origin of the tumor disease. In recent years, some researchers have found that the chromosome morphology and number of PVNS are abnormal. The most distorted site was 1p11–13 on the short arm of the first chromosome,[10] trisomy aberration of the seventh and the fifth chromosomes.[11]

Because of nonspecific symptoms of PVNS, it is very difficult to diagnose the disease as early as possible. Performance of X-ray and CT imaging is lack of specificity, and MRI plays an important role in the initial diagnosis of PVNS. MRI scan shows characteristic findings that a low or equal single on the T1 weighted sequence, a low single on the T2 weighted sequence and significant low single on the gradient weighted echo sequence. Among that, the low signal of T2 weighted sequence is the typical characteristic of PVNS.[12] Therefore, for patients with repeated joint swelling, pain, joint mobility limitation, and joint effusion, it is recommended to perform MRI examination in order to avoid misdiagnosis and delayed diagnosis. Preoperative MRI examination is helpful to identify the extraarticular lesion and avoid incomplete excision of the tumor leading to disease recurrence.[13] Histopathological examination is recognized as the gold standard for the final diagnosis of PVNS. The major pathological features of the localized PVNS were localized nodules with clear boundary, which a single pedicle or no pedicle, yellow or brown. The diffuse type PVNS shows that the surface of the synovial membrane was villous, the color was reddish brown, yellow, and so on, a wide rage involving the adjacent vessels and nerves. Both of 2 forms are similar histologically: the proliferation of synovial cells, the presence of multinucleated giant cells, macrophages and fibroblasts, hemosiderosis in a variety of cells inside and outside, nodular lesions with multiple fibrotic villi.[14]

Complete excision of all lesions is the standard treatment for PVNS.[15] In the clinical, open, arthroscopic, or combination of the both surgeries have been applied. For localized PVNS, simple excision of the diseased synovial tissue is considered the golden

standard,[16] and can achieve a 0% recurrence rate which the longest follow-up of 7 years.[17]

Arthroscopically assisted mini open synovectomy for the treatment of localized PVNS is also a safe alternative treatment style. However, Richter et al[18] reported that arthroscopic, open, and arthroscopically assisted mini open synovectomy had a high recurrence rate of 58% (69/118), 36% (35/97), and 50% (5/10), respectively. It is important surgical approach for the treatment of diffuse PVNS with adequate synovectomy resection.[4] Chin and Brick[13] reported that the use of arthroscopic synovectomy in patients with extraarticular lesions of diffuse PVNS, and 38 patients had a poor prognosis with an average follow-up of 3.63 years. The cause of the high recurrence rate of arthroscopic treatment may be extensive joint involvement and extraarticular spread, and it is recommended that patients with diffuse PVNS should be treated with open synovectomy. Bruns et al[19] reported that a lower rate of recurrence of arthrotomy compared with arthroscopic surgery (25% vs 69%). Therefore, some scholars believe that open arthrotomy and complete synovectomy is the standard surgical treatment for diffuse PVNS of the knee.[4,20] Auregan et al[21] compared the efficacy of arthroscopic synovectomy, open synovectomy, and the 2 combinations for diffuse PVNS, and found that there was no difference in recurrence rate with an average follow-up of 4.47 years. In this case, the patient underwent open synovectomy for the first time, postoperative pathology confirmed diffuse PVNS. If before the operation, MRI examination could be done, the extent and depth of tumor invasion were clearly defined, which is more conducive to the extent of surgical resection and further therapy.

Because of the anatomical limitation of the lesion, radical resection of diffuse PVNS is very difficult. There is a high recurrence rate after operation (29%,[17] 33%,[22] 46%[23]). In order to reduce the recurrence rate, postoperative adjuvant radiotherapy is very necessary. Lee et al[24] analyzed that a total of 7 patients who were diagnosed as diffuse PVNS of the foot and ankle were treated with open synovectomy and adjuvant postoperative external radiotherapy, with a local control rate of up to 100% after followed up for 24 months. Wu et al[25] covered that 9 patients with diffuse PVNS of the knee were treated by the same method, followed up for a period of 67 months, with only 1 patient had local recurrence. de Carvalho et al[26] reported that 8 patients with diffuse PVNS of the knee underwent arthroscopic synovectomy combined with postoperative external radiotherapy, with a recurrence rate of only 12.5% after a follow-up of 96 months. Griffin et al[27] treated 50 patients with a mean follow-up of 94 months, with no recurrence of the disease in the 94% of the patients, and had better joint function in the 41 patients. The patient did not receive adjuvant radiotherapy after operation for the first time, and recurrence occurred 2 years after surgery. Further, she underwent arthroscopic total synovectomy of the right knee, followed by adjuvant external beam radiotherapy with moderate dose of 30 Gy and no recurrence after followed up for 3 years. A large number of reports have confirmed that adjuvant postoperative external beam radiotherapy can further reduce the recurrence rate.[26,28–31] Meantime, adjuvant postoperative external beam radiotherapy is still an important treatment for recurrent patient with diffuse PVNS. External beam radiation therapy was performed in 140 cases of high-risk patients, and after a maximum follow-up of 250 months, the local control rate was 84.5%.[32] Bruns et al[19] reported that patients with at least one history of recurrence were performed with adjuvant radiotherapy, with a local control rate of 86%.

Currently, it is well known that the treatment of diffuse PVNS adopts the way of postoperative external radiotherapy, but there is no consensus on the total dose of radiotherapy. Park et al[30] covered that the effect of low-dose radiation therapy on 20 Gy was similar to that of moderate dose (about 35 Gy). Berger et al[6] reported that 7 patients were treated with total dose of 30 to 50 Gy postoperative radiotherapy, followed up for 29 months without recurrence and late radiation reactions. Horoschak et al[7] believed that using 34 to 36 Gy radiation dose can achieve a better local control rate. Therefore, he suggested that 36 Gy be used as a conventional fractionated dose. Therefore, it is considered that for the relatively benign lesions, such as PVNS, low and moderate dose of postoperative radiotherapy can achieve a satisfactory local control rate, and the limb function after radiotherapy is not affected.[7,26,30] In this case, after the second operative the patient was performed with radiotherapy with moderate dose of 30 Gy. Up to now, there is no recurrence and late complications of radiotherapy such as limitation of motion of the knee. Therefore, it has been confirmed that moderate dose of postoperative external beam radiotherapy is feasible to reduce the recurrence rate.

In conclusion, adjuvant postoperative external beam radiotherapy is a safe and effective treatment modality for patients who incomplete resection or suspicious lesions.

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