

Pigmented Villonodular Synovitis

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Pigmented villonodular synovitis

Monoclonality and metastasis – a case for neoplastic origin?

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We report a 48-year follow-up of a case of recurrent pigmented villonodular synovitis of the knee. Subcutaneous metastasis to the contralateral thigh was an unusual finding. Histology demonstrated fibroblastic and histiocytic proliferation, as well as increased mitotic activity in recurrent lesions. Cytogenetic analyses demonstrated monoclonality and chromosomal abnormalities. Our findings support a neoplastic origin of this lesion.

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Case report

A 35-year-old woman presented at another hospital in 1943 with minor symptoms and a swelling in her left popliteal fossa. At operation a multilobulated structure resembling a ganglion occupied the whole popliteal fossa. The mass was excised without subsequent histological examination. In 1945, she presented with discomfort in her left knee. A hard 1 cm mobile intraarticular mass was found on the medial aspect of her left knee. In addition, a larger mass was felt on the lateral aspect of the knee. At arthrotomy a 2 cm oblong, pedunculated growth was seen medially and excised from the synovium. A larger lateral mass, similar to the first, was also excised through a separate arthrotomy. No other abnormalities were noted. Both specimens were submitted for histological examination and a diagnosis of giant cell fibrosarcoma was made (Figure 1). Consequently, the patient received 10 treatments with radiotherapy. The dose, however was not mentioned in the medical records. In 1947, a new growth was excised from the left knee in the region of the patella. Histological examination revealed inflammatory and giant cells with no malignancy and the patient remained symptom-free for the next 34 years. In 1981, at the age of 74 years, the patient was referred to our institution with a lump in the popliteal fossa of her left knee. Fine needle biopsy suggested the presence of an osteoclastoma or giant cell tumor of the tendon sheath. Subsequently, a 2x 2 cm tumor was marginally excised from the posterior capsule of the knee (Figure 2).

In 1984, the patient again noticed swelling of her knee and examination revealed a 4 x 5 cm soft tissue mass with a diffuse border situated medially over the tibial tuberosity. Fine needle biopsy showed giant cells with no evidence of malignancy. Exploration of the knee revealed an extensive soft tissue tumor that was fixed to the back of the knee joint and femur with skin and intramuscular extensions. The popliteal vessels and nerves lay plastered to the tumor. The tumor was firm and lobulated, with an appearance of pigmented villonodular synovitis (PVNS). The intimate relationship between the tumor and vital structures precluded extirpation and therefore only a confirmatory biopsy was performed. The patient refused amputation for the control of her disease and agreed to radiotherapy instead. She received 20Gy in 2Gy fractions between April and May of 1984. This failed to control progression of her disease and in November of 1985, the patient received 185 Mbq of intraarticular Yttrium-90.

A subsequent knee arthroscopy showed fibrotic changes in the suprapatellar pouch as well as a reddish-brown and hypertrophic synovium lining the intercondylar notch. In addition, there were many osteoarticular erosions in the intercondylar notch. The tumor continued to enlarge and in 1987 the patient agreed to an above-knee amputation. Dissection of the amputated specimen revealed massive intra- and extraarticular tumor with intraosseous and soft tissue extension. There were several satellite lesions within the proximity of the tumor. 5 years (1992) after amputation, the patient returned with a recurrence on her amputation stump. This was marginally excised. Several months after this, the patient reported a 2 x 2 cm, firm, smooth, subcutaneous lump in the lateral aspect of her contralateral thigh. It was not fixed to underlying tissue or overlying skin. Aspiration cytology of the mass was consistent with PVNS. The lesion was marginally excised and the previous diagnosis of PVNS remained unchanged.

1 year later, the patient, now aged 83 years, noted a further subcutaneous lesion at the site of the previous surgery on her right thigh. The second lesion was firm, oval-shaped, measuring approximately 2 x 3 cm and was fixed neither to the skin nor to the underlying deep fascia. It was not tender and there was no overlying skin reaction or edema. No inguinal lymphadenopathy was noted. The lesion was again marginally excised and found to be composed of 3 distinct nodular masses (Figure 3).

Investigations and results:

Histology

8 biopsy specimens between 1945 and 1993 were available for diagnostic re-evaluation. 6 biopsies (1945-1992) were from the left knee region, including the amputation material (1987) and the recurrence in the amputation stump (1992). The last biopsies came from the right thigh (1992 and 1993). The histological sections were stained with hematoxylin eosin and van Gieson (Table 1). Electron microscopy from the latest tumor (1993) revealed numerous fibroblast-like cells with dilated rough endoplasmic reticulis. A great number of histiocytes containing lysosomes and vacuoles were also present. Both types had long slender filopodia. A few cells had single membrane-bound bodies containing hemosiderin. No cell contacts were observed.

Clonality studies

Frozen operative tissue samples from the amputated limb in 1987 and the contralateral soft tissue recurrence in 1993 were available for DNA extraction and X chromosome inactivation analysis (Vogelstein et al. 1987). DNA was subjected to digestion with the restriction enzymes PstI and BstXI revealing a polymorphism of the X chromosomal gene, PGK. Samples from the two recurrences were then divided into two aliquots, one of which was further digested with the methylation-sensitive enzyme HpaII. After agarose gel electrophoresis and Southern transfer, the filters were hybridized to a probe from the PGK gene. The findings indicate a monoclonal origin at both tumors (Figure 4: Table I)

Cytogenetic analysis

Cytogenetic studies were performed on fresh operative samples in 1987, 1992 and 1993. Short-term cultures (Mandahl et al. 1988) were initiated and chromosome preparations made after 3 – 10 days. G-banding was obtained with Wright's stain and any chromosomal aberrations were classified according to the ISCN (1991). A massively rearranged genome was found in the third sample (Figure 5; Table I).

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Discussion

Scant reports of PVNS do not help to resolve the etiology of this condition, though the majority of articles suggest an inflammatory patho- genesis. Jaffe and co-workers (1941) concluded that their observation of hyperplastic stromal cells in a milieu of hyalinized collagen was consistent with an inflammatory process. Electron microscopic evidence of hemosiderin-laden macrophages and fibroblasts synthesizing collagen and proteoglycan lend further support to this concept (Hirohata 1968). In contrast, Rao and Vigorita (1984) demonstrated the presence of a centrifugal growth pattern of the PVNS tissue as well as distinct differences between the lesional tissue and the adjacent hyperplastic synovial tissue. They concluded from these findings that PVNS was a true neoplastic process. There were histological similarities between this case and those reported by Rao and Vigorita (1984). We found both microscopic and ultrastructural evidence of proliferating synovial fibroblasts or primitive mesenchymal cells as well as histocyte-like cells (Figure 2). In addition, we saw greater mitotic activity in recurrent lesions (Figure 3). While many have classified PVNS as inflammatory. we concur with Rao and Vigorita that the peripheral nature of inflammatory changes, together with the nodular appearance, mitotic activity and propensity for recurrence after inadequate removal. contradicts this classification. The diagnosis of giant cell fibrosarcoma in 1945 was reassessed and a revised diagnosis of nodular synovitis was made (Figure 1). The multiple manifestations of PVNS and, in particular, abnormalities of the fibrous stroma and presence of giant cells are known to mimic sarcomatous tumors. Subsequent histological findings of soft tissue giant cell tumor, without evidence of malignancy in this case. support the overall diagnosis of PVNS. There was no histological evidence of malignant change during any stage of treatment. Therefore, it was particularly striking to find tissue consistent with PVNS in a distant nonsynovial site long after the initial diagnosis and subsequent amputation of the primary site. Metastasis has been noted in one previous report of PVNS, but only following malignant change to a malignant giant cell tumor of the tendon sheath on its second recurrence (Ushijima et al. 1985)

Clonality studies have suggested a monoclonal origin in most types of various human neoplasms (Fialkow 1971). Cytogenetic evidence of clonality in PVNS was first alluded to by Ray and co-workers (1990) who observed trisomy 7 in 35 percent of metaphases obtained from short-term in vitro cell cultures. In our study, evaluation of operative tissue from 1987 and 1993 showed an X-chromosome inactivation pattern consistent with monoclonality. Another case of PVNS studied by the same technique was reported to be of polyclonal origin (Sakkers et al. 1991). The authors concluded that PVNS is more likely to be a reactive process than a true neoplasrn because of their findings. They, however, did not comment on the possibility that polyclonality may be the result of a large number of cells contaminating the tissue analyzed. Our findings raise the possibility of monoclonality in this disease which, lends weight to the case for a neoplastic origin. The normal karyotype at the first cytogenetic analysis may be interpreted either as PVNS cells with submicroscopic mutations or as the karyotype of dividing stromal cells. We believe our findings are more in keeping with the latter explanation because overgrowth of fibroblasts is a common phenomenon in cultures of solid tumors. The massively rearranged genome detected by the third analysis is highly suggestive of aberrations from a monoclonal neoplastic cell population. In this regard. Fletcher and co-workers (1992) demonstrated non-random aberrations in uncultured cells of PVNS, while Mertens and co- workers (1993) demonstrated other clonal structural and numerical chromosomal aberrations in 3 of 5 tenosynovial giant cell tumor specimens. Thus, the only recurrent aberrations detected in tenosynovial giant tumors to date are +5 and +7. However, this information should be used with caution, as there have been reported cases of clearly non-neoplastic tumors presenting with chromosomal anomalies involving +7 (Gueneri et al. 1991, Johansson, et al. 1993). Nevertheless, it is interesting to speculate whether the trisomic alterations of the short arm of chromosome 5 and tetrasomy of the long arms of chromosome 5 and 7 that were found in our case also evolved from cells showing only +5 and +7 We could not demonstrate other cytogenetic denominators common to the present and previously reported cases.

Radiotherapy is a recognized tumorigenic agent. Our patient received 3 separate courses of radiation as part of her treatment. One may speculate that the 35 years between her first course of radiotherapy in 1946 and her presentation in 1981 might have given sufficient time for any malignant change to become evident. However, at no stage following this course did the tissue from the irradiated sites exhibit malignant change. Considering the limited dosages used in 1984 and 1985. it would be reasonable to assume that the time between these 2 radiation treatments (1984 and 1985) and her subsequent above-knee amputation (1987) was insufficient for any malignant change to occur.

Although the chromosomal changes observed in the sample from 1993 accord with the previously described cytogenetic patterns in PVNS. it is possible that the radiotherapy may have influenced the karyotype. Only one other report refers to a case of PVNS treated with radiotherapy where the patient was followed for 48 years (Kindblom and Gunterberg 1978). There was no evidence of histological evolution to a more malignant character in that case either. The lack of reports about these changes, specifically in PVNS, makes a more definite conclusion difficult, though it seems unlikely that radiation was an etiologic factor in the genetic aberrations noted.

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PIGMENTED VILLONODULAR SYNOVITIS

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Pigmented villonodular synovitis (PVNS) is a benign proliferative disorder of the synovium of uncertain cause. Although described by various names previously, the landmark 1941 article by Jaffe, Lichtenstein, and Sutro served to unite the forms of the disorder (those involving joints, tendon sheaths, and bursae) into a single entity termed *pigmented villonodular synovitis*, *pigmented villonodular tenosynovitis* (also called giant cell tumor of tendon sheath or localized nodular tenosynovitis), or *pigmented villonodular bursitis*, depending on the area involved. (12) Localized and diffuse forms of synovial involvement occur and subclassification has been indicated by adding the appropriate prefix L or D. (10) Imaging plays an important role in the diagnosis and the management of the various forms of this disorder and in follow-up. In this article, we review the clinical features of the disorder and the imaging features of this disease, concentrating on the findings and utility of MR imaging.

HISTOLOGIC FEATURES

The gross pathologic features of the diffuse form of PVNS are typified by the formation of a thick plush synovium consisting of matted masses of villi and synovial folds and sessile or pedunculated nodules (Fig. 1). (22) The villi usually are long and delicate but may be entangled and matted to form masses of tissue with a cut surface likened to a sponge. (6) In the diffuse form of the disorder, the synovial lining is characteristically colored orange-yellow to red-brown. (22) PVNS may invade the joint capsule and soft tissue and coat adjacent nerves and vessels. The tissue may accumulate near the chondro-osseous junction and

around vascular and ligamentous attachments to bone. (22) Bone invasion is thought to occur through these areas.

Microscopic examination is characterized by the presence of synovial cell hyperplasia and surface proliferation and subsynovial accumulation of cells with a histiocytic appearance. Multinucleated giant cells, hemosiderin-laden macrophages, and fibroblasts are present among these cells. Important to the imaging features described later is the presence of hemosiderin (both extracellular and intracellular within the synovial lining and subsynovial cells) and of aggregates of foamy macrophages filled with lipid. (22) Nodules formed by the fusion of villi may undergo massive fibrosis. The localized form of joint disease (localized nodular synovitis) is typified by the presence of a nodule that is usually pedunculated, has a firm consistency, and is yellow to yellow-brown in color. (6) The mass may be lobulated. The histologic features are identical to the nodules seen in the diffuse form of the disease. These masses are most often found in the anterior portion of the knee.

Localized nodular tenosynovitis also has the same cellular constituents as does diffuse villonodular synovitis. This form of tendon sheath involvement is seen most often in the hand or wrist or the foot or ankle. The lesion most commonly involves the flexor tendon sheaths of the fingers, most often the index finger. (22) In contrast to the diffuse form of the disease, localized nodular tenosynovitis is more often seen in women, usually in the third to the fifth decades of life. (22) The mass is usually painless. (22)

Hemochromatosis and hemosiderosis are histologically distinguishable from PVNS in that pigment is largely confined to the synovial lining cells and /or macrophages in cases of hemochromatosis and hemosiderosis, whereas the pigment is present more diffusely throughout the lesion in PVNS. Also, giant cells and accumulations of histiocytic cells, some containing lipid, are not features of hemosiderotic synovitis but are characteristic of PVNS. (1,26)

ETIOLOGY

The cause of PVNS is not known but several possibilities have been suggested including (1) a neoplastic process, (2) an inflammatory process (although no specific inflammatory agent has been isolated), (3) localized abnormal lipid metabolism with secondary inflammatory and traumatic changes, and (4) a reactive response to chronic trauma and repeated hemorrhage (although injection of blood or iron into the joint fails to create all of the pathologic findings of PVNS). Most authors believe that the disease is either a locally aggressive neoplasm or a reactive synovitis. Cytogenetic data have shown various results; one report demonstrating clonality of the cells in a case of PVNS suggesting neoplastic proliferation, whereas another report has failed to show this feature.

The neoplastic theory is, however, supported by a case report that has shown metastatic disease from articular PVNS.

INCIDENCE

Epidemiologic study of cases coming to surgery by Myers et al has shown the average annual incidence of PVNS to be 1.8 per million population and the incidence of the localized nodular tenosynovitis to be 9.2 cases per million. Of the 190 patients reviewed, 70% had PVNS of tendon sheath, 6% localized intraarticular PVNS, and 24% diffuse PVNS. In most series, the knee is by far the most frequent joint affected with the diffuse or localized forms, although any synovial joint or bursa may be involved. Localized nodular tenosynovitis is most frequent in the fingers and is the most common soft-tissue tumor of the hand.

CLINICAL FEATURES

The diffuse form of this disorder usually affects the knee and presents during the third or fourth decades with the insidious onset of discomfort. Typically, swelling is prominent and is out of proportion to the patient's symptoms. Stiffness and warmth may occur. Males and females most likely are equally affected (although some reports show a predominance of one sex or the other). Monarticular involvement is the rule, although rare cases of bilateral or multiple joint involvement have been reported. Hemarthrosis is a common finding in cases of PVNS with Myers et al noting 75% bloody and 25% yellow fluid aspirates of 16 cases of PVNS and their literature review documenting 69% bloody, 22% yellow, and 9% brown aspirates. Flandry et al however, noted characteristically bloody fluid on aspiration in only three of seven cases of diffuse disease of the knee and concluded that aspiration is unreliable in establishing this diagnosis. The localized intraarticular form of the disease also is most often seen in the knee and may produce signs suggesting internal derangement. Acute pain may occur if the nodule undergoes torsion and infarction. Localized nodular tenosynovitis usually presents in slightly older women as a slowly enlarging, pain-free mass. The fingers (particularly the flexor tendons), wrist, foot, or ankle are most often involved.

IMAGING

Radiography

Although PVNS is infrequent, it is of importance to the radiologist because of the help that imaging studies can provide in the diagnosis and treatment. The classically described findings are (1) monarticular involvement (2) synovial swelling especially if lobulated or nodular, (3) absence of calcification within the swelling, (4) normal bony mineralization of the affected joint, and (5) preservation of the cartilage space. Corticated erosions and cysts on both sides of the joint may especially in those articulations with relatively tight capsules such as the hip Smith and Pugh noted cysts or erosion in one third of patients with diffuse disease. In the knee, osteophytes and osteopenia as well as cystic changes have been noted to the patellofemoral rather than the femorotibial articulation preferentially; however, some of these changes may be related to patellar tracking as a consequence of chronic suprapatellar soft-tissue swelling. Although not specific, the radiographic features of PVNS should suggest the condition. The preservation of cartilage spaces density until late in the disease may help differentiate PVNS from an inflammatory synovitis. Calcification is rare in PVNS so that usually the presence of calcification should suggest an alternative diagnosis such as synovial osteochondromatosis. Despite the absence of calcification in PVNS, high iron content may be present within the synovium, producing a higher radiodensity than adjacent joint effusion or soft tissue. Concentric cartilage space narrowing in the hip has been noted to occur in PVNS as well as in other causes of "hemosiderotic synovitis". Thus, chronic bleeding into a joint due to bleeding diatheses, synovial hemangioma, and chronic trauma may produce radiographic findings similar to those of PVNS. The localized intraarticular form of PVNS most often occurs in the anterior portion of the knee where it may produce a soft-tissue mass visible on radiographs because of its contrast with Hoffa's fat pad. The nodular form of PVNS involving tendon sheaths produces localized swelling most often along the volar aspect of a finger. As in diffuse PVNS, well-corticated cysts or erosions of adjacent bone may be seen and the cartilage space usually remains normal. No calcifications are present. In the series of Myers et al, 25% of cases of PVNS of tendon sheath showed adjacent erosions or cysts, whereas 54% of diffuse PVNS cases and 20% of localized intraarticular PVNS had these findings. The usual differential possibilities are a ganglion (which may be evaluated by ultrasound if necessary) or a gouty tophus. Although helpful in diagnosis, evaluation of radiographs of patients with PVNS of the knee by Flandry et al found no predictive value of the radiograph in determining the likelihood of recurrence or the histologic grade of the disease.

Arthrography

Cases of diffuse PVNS may show multiple filling defects projecting into the distended joint. The lesions appear irregular and fixed to the joint lining. Differential diagnosis includes rheumatoid arthritis, in which multiple joints are usually involved, and synovial osteochondromatosis, in which the cartilaginous nodules are smooth and may be calcified or ossified. Localized PVNS in the knee may be visible at arthrography as an infrapatellar mass. Differential considerations include uncalcified loose bodies, fibroma, hemangioma, intraarticular ganglia, and fat pad hypertrophy.

Bone Scanning

Bone scanning usually is not performed for evaluation of PVNS. In the few cases reported, areas of erosion produce increased uptake on bone scan. Increased blood flow

and blood pool uptake has been noted corresponding to the location of the soft-tissue masses.

CT

Masses of PVNS tissue may demonstrate high attenuation due to the presence of hemosiderin. When high attenuation tissue is identified within the joint, the differential diagnosis includes tissue with iron deposition (due to PVNS, hemophilia, or chronic bleeding, for example) and calcification. Abnormal tissue also may show attenuation less than that of muscle. Enhancement after intravenous contrast administration appears to be the rule. CT is of greatest utility in the delineation of bone erosion and cyst formation. This can assist in surgical planning; some defects requiring bone grafting prior to total joint prosthesis or curettage during synovectomy may be identified MR imaging may show the bony lesions as well as does CT.

Arteriography

Arteriography is rarely used for evaluation of patients with PVNS. Previous reports have identified these masses to be vascular, with arteriovenous shunts and irregular vessels. (23). The appearances may mimic malignancy. (13) More fibrotic (and, therefore, presumably more mature) cases may be avascular. (23)

Ultrasonography if effusion is present, ultrasonography may show the nodular synovial masses of PVNS. (13,23).

MR Imaging

Appearance: The findings on MR imaging should reflect the histologic composition of the tissue including components containing hemosiderin, lipid, inflammation, and fibrosis. The presence of hemosiderin results in the most characteristic findings. In particular, the ferromagnetic properties of hemosiderin within PVNS tissue cause shortening of both the T1 and T2 relaxation times. This effect is likely to be concentration dependent, and when PVNS tissue contains enough hemosiderin, it appears characteristically dark on all pulse sequences (Fig. 10). This is the most consistent finding in cases of PVNS reported in the literature. (13,14,20,30) Because of differences in magnetic susceptibility between hemosiderin laden tissue and surrounding tissue, the size of the region of abnormal tissue may appear slightly larger on T2-weighted images ("blooming" effect) as well as on gradient echo images (Fig. 11). Although most cases display a region of characteristically dark synovium on all pulse sequences, (13) commonly, areas of PVNS tissue show areas of intermediate signal intensity on T1-weighted and proton density weighted images with very dark synovium on T2-weighted images (Fig. 12). The synovial masses may be extensive in the diffuse form of the disease or limited to a single nodule in the localized form. Areas of bright signal on T2-weighted images may be present within the abnormal synovium and are believed to represent loculated areas of joint fluid within the synovium. Areas of signal intensity consistent with fat have been described by some authors and are thought to correspond to accumulations of foamy macrophages; however, this appears to be an uncommon finding. (14) Erosion into bone and extraarticular extension are also well demonstrated on MR imaging (Fig. 13). The MR appearance of PVNS is not pathognomonic of the disease, and regions of dark synovium may be observed in rheumatoid arthritis (Fig. 14), hemophilic arthropathy, amyloid arthropathy, synovial osteochondromatosis, and fibroma of tendon sheath as well as in osteoarthritis (Fig. 15), sclerosing hemangioma, and desmoid tumors. Clinical information can assist in reaching the proper diagnosis but biopsy is usually necessary. The extent of PVNS within and outside the joint is best evaluated with MR imaging. Extraarticular extension should be evaluated and described carefully to assist in surgical planning. In the knee there is commonly involvement of the semimembranosus, semitendinosus, gastrocnemius bursa (Baker's cyst) (Fig. 16). PVNS tissue may accumulate beneath a meniscus or erode bone in areas difficult to see at surgery or arthroscopy (Fig. 17). The localized form of PVNS usually demonstrates a single mass either within the tendon sheath or within a large synovial joint. The signal

characteristics may be similar to those of diffuse PVNS. A peripheral rim of low signal hemosiderin has been noted (see Fig. 4).

Imaging Technique: The standard imaging technique used at the Brigham and Women's Hospital for evaluation of PVNS emphasizes standard spin echo imaging. Imaging is performed in all three planes and dual echo T2-weighted images are used as the basis for

judging the amount and location of abnormal synovium. The T2-weighted images are obtained in the plane with the least potential for partial volume artifact (axial for the knee) and usually in one plane perpendicular to this (sagittal in the knee to demonstrate abnormal tissue posterior to the cruciate ligaments). Although gradient echo sequences are helpful for detecting small amounts of hemosiderin, they are subject to overestimation of the amount of tissue and artifacts after surgery. In particular, susceptibility artifact from sutures may produce findings indistinguishable from recurrent PVNS on gradient echo images, whereas typical susceptibility artifact on spin echo images allows proper diagnosis. On spin echo images, sutures and postoperative findings usually show a bright area immediately adjacent to a dark region (severe susceptibility effect), whereas PVNS tissue rarely produces such a severe amount of susceptibility artifact (Fig. 18). The entire joint should be included on the MR study because isolated regions of synovial hypertrophy may be overlooked otherwise. A common error is to exclude the most superior portion of the suprapatellar pouch or the most inferior portion of the popliteus tendon sheath. This incomplete imaging may lead to incomplete surgical debridement or inappropriate treatment choices.

TREATMENT (5,9-11,17,19,24)

Although the forms of this disorder may be pathologically related, their biologic behavior may vary. The three types of clinical presentation, disease isolated to tendon sheath localized PVNS occurring intraarticularly usually in the knee, or diffuse PVNS should be distinguished for treatment planning. Schwartz et al (24) suggest that the tenosynovial form of the disease may differ from the disorder affecting large joints and, therefore, separates these patients for analysis of treatment results. The diffuse form of the disease is characterized by recurrence, thought actually to be due to incomplete excision of the abnormal synovium. Localization of the abnormal tissue by MR imaging prior to treatment may prevent such incomplete resection. Although some authors indicate treatment of the intraarticular nodular form to be usually successful after surgical excision, (10,17) others indicate a similar prognosis to the diffuse form of the disease. (24)

Treatment Planning

Proposed treatments have included arthroscopic synovectomy, open surgical synovectomy, radiation synovectomy, or combination therapy. Arthroscopic synovectomy may be performed through anterior arthroscopic portals or a combined approach. Similarly, surgical synovectomy may be performed through an anterior approach or a combined anterior and posterior approach. Radiation synovectomy consists of the intraarticular injection of a radioisotope, usually a beta emitter, for local radiation therapy of the synovium. (27) The choice of treatment may depend on the distribution and thickness of tissue seen on the MR examination. Arthroscopic surgery anteriorly, for example, allows the suprapatellar pouch, lateral recesses of the joint, and the anterior joint to the synovial reflection over the anterior cruciate ligament to be reached. Resection may be performed to the level of the joint line inferiorly. Arthroscopic surgery posteriorly allows resection of tissue posterior to the femoral condyles and the region within the posterior joint to the level of the tibial joint line and as far anteriorly as the synovial reflection over the posterior cruciate ligament. This leaves several regions inaccessible to removal of PVNS tissue by arthroscopy. These include the region between the posterior cruciate ligament and its synovial reflection, the popliteus tendon sheath, a popliteal cyst, the extracapsular soft tissue, and the area beneath the meniscal insertions (see Fig. 17). Radiation synovectomy is only appropriate when the thickness of the residual PVNS masses is less than 5 mm. This tissue thickness can be evaluated on MR imaging. At the Brigham and Women's Hospital, surgical debulking is followed by radiation synovectomy. MR imaging is performed before surgical debulking to localize the areas of PVNS for resection. A repeat MR examination is performed 6 weeks after surgery and before radiation synovectomy to confirm the adequacy of resection.

Longitudinal Evaluation

The sensitivity of MR imaging in identifying the abnormal synovium of PVNS coupled with the noninvasive nature of the test make it an excellent method for following patients after treatment (Figs. 19 and 20). MR imaging can detect recurrent disease prior to clinical symptoms. (Bringham and Women's Hospital, 1991, personal experience, unpublished data). As noted, the spin echo images are relied upon on follow-up examination so that confusion with suture artifact is avoided. Tissue that continues to enlarge after treatment is considered likely to be due to recurrence, whereas tissue that regresses is likely due to postoperative inflammation.

CONCLUSION

Although PVNS is an unusual entity, recent imaging techniques, particularly MR imaging, have changed the evaluation, treatment planning, and follow-up of the disorder. It is hoped that the clearer delineation of soft-tissue involvement provided by MR imaging will lead to more complete removal of abnormal tissue and an improved prognosis.

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Arthroscopic Synovectomy of the Knee: Is It Helpful?

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Summary: We performed 211 arthroscopic synovectomies over a 10-year period.

The results were assessed at follow-up of at least 2 years using the criteria of pain,

Synovitis, and effusion, range of motion and function. In rheumatoid knees (112

Cases) , we had good or excellent results in 80 %. However in seronegative arthriti-

Des (32 cases) , only 60% were successful. Pigmented villonodular synovitis was

successfully treated with an 11% recurrence rate (19 cases total). Synovial chondro-

matosis (17 cases) had no recurrences. In patients with nonspecific synovitis or

posttraumatic synovitis, the synovitis was improved in 60% but only half the

patients had pain relief and good function. Looking specifically at the posterior

portals, there were five complications, all related to the posteromedial portal involv-

ing the saphenous nerve and vein. Overall excellent results can be achieved with

due care and attention to detail. **Key words:** Synovitis - Knee arthroscopy -Rheumatoid - Synovectomy

Arthroscopic synovectomy of the knee has become a technically feasible operation. The techniques have been well developed along with special instrumentation for it to be carried out safely. However little has been written on the overall results of arthroscopic synovectomy despite its potential application for a wide variety of conditions including rheumatoid arthritis, seronegative arthritis, pigmented villonodular synovitis, and synovial chondromatosis.

Our study was designed to review the cases of arthroscopic synovectomy carried out over the past 10 years to determine the outcome and to try to determine the role of arthroscopic synovectomy in the management of persistent synovitis.

Materials and methods

Overall, there were 232 patients who had undergone arthroscopic synovectomy over the past 10 years with a minimum follow-up of 2 years. These patients had all undergone arthroscopic synovectomy. Adequate data were available on 211 of them for follow-up.

These patients were scored preoperatively and on each postoperative visit using the criteria of pain, synovitis and effusion, range of movement, and functional activity (Table 1). This assessment system was derived from one originally proposed by Laurin et al. Changes to the criteria for assessment were in the categorial headings (e.g. excellent, good) and including all four criteria in one table. As the patients had been assessed on each postoperative visit, this study was carried out by reviewing the preoperative data and the most recent assessment data available on them. The assessments were performed by different physicians using standard forms (Table 1)

The indications for arthroscopic synovectomy were persistent synovitis in the joint for at least 6 months despite adequate medical management. Medical management had consisted of the use of anti-inflammatories, often steroid injections into the joint, of physiotherapy and rehabilitation, and in some cases, other suitable drugs, such as gold methotexate in the rheumatoid patients. Therefore, all the patients in the study had persistent synovitis and an effusion. The vast majority also had pain and loss of functional capacity although the range of movement was reasonably well maintained. Specific data on the drug therapy and sys-

TABLE 1. Criteria For Assessment of the Results of Arthroscopic Synovectomy

Poor Fair Good Excellent
Pain Severe Moderate Slight None
Synovitis/Effusion Severe Moderate Slight None
Range of motion >20%loss 10% to 20% loss 0% to 10% loss No loss
Functional capacity minimum activity Some activity Most activities All activit

temic control of disease were not included in this study because of the great variability and lack of control of the medication. All patients had had basic investigations including blood analysis tests for the various rheumatic conditions. And radiography of the involved knee. A few of the patients had had magnetic resonance scans that showed the synovitis . but this was not considered essential or necessary. Therefore, the indications were based on the clinical findings. A standardized technique for arthroscopic synovectomy was carried out. This was performed using the six-portal technique. In all cases, a tourniquet was used. as was pressure irrigation throughout. At the end of the procedure , a drain was left in the knee joint for a period of approximately 2 hours. The drain was then removed and the patient was usually discharged the same day. The only indication for keeping the patient in hospital overnight was if there were concurrent medical problems such as diabetes or long-term steroid usage.

Postoperatively, the patients were placed on an active rehabilitation program. They were not placed on anti-inflammatory medications initially because of concern about extra bleeding. The patients were started on physiotherapy, particularly active quadriceps and range-of-movement exercises.

RESULTS

Altogether, there were 211 patients who underwent arthroscopic synovectomy who received adequate follow-up. The minimum duration of synovitis was 6 months, the maximum 3 years, and the average 1,6 years. No patients had advanced degenerative changes seen on radiographs. Overall, the mean follow-up was just over 3 years with a minimum being 2 and a maximum being 7 (Table 2). There were 12 patients who had rheumatoid arthritis, nineteen had pigmented villonodular synovitis and 17 had synovial chondromatosis . In 12 cases there was nonspecific arthritis- monoarthritis in which no specific pathology had been found. This was established postoperatively with synovial biopsies showing nonspecific synovitis. Thirty-two patients had seronegative spondyloarthropathy – psoriatic, ankylosing spondylitis, and Reiter’s disease. In 9 cases there was a posttraumatic synovitis. These were patients who had trauma to the knee and in which there had been persistent synovitis. In these cases, it was necessary to rule out significant chondral damage, ligamentous injury, or meniscal disruption. When there was no other obvious source of intra-articular pathology, we designated it as posttraumatic synovitis. Of particular note is that patients with osteoarthritis are not included in this review. This is because these patients do not qualify for an arthroscopic synovectomy of the type outlined above. In the osteoarthritic patients, the synovitis is clearly attributable to secondary phenomena and is not a primary disease of the synovium.

The overall results are summarized in Table 3. In all groups, there was improvement from the preoperative condition to the postoperative condition. In the patients with rheumatoid arthritis, pigmented villonodular synovitis, and synovial chondromatosis our results are particularly good. Approximately 90 % of the patients in these groups showed that they had elimination of the synovitis, significantly reduced pain, and improved function. In the patients with nonspecific synovitis, seronegative arthritis, and posttraumatic arthritis, our

Table 2. Number of patients in each group undergoing arthroscopic synovectomy

No	Mean (mo)	Min (yr)	Max (yr)
Rheumatoid	112	49	27
PVNS	19	38	26

Chondromatosis 17 45 2 7
 Nonspecific 12 34 2 5
 Seronegative 32 39 2 7
 Posttraumatic 19 31 2 6
 Total number 211

NOTE: The mean follow-up is given in months and the minimum and maximum follow-up in years.

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TABLE 3: Number of patients scoring good or excellent in each category of the assessment.

Type Pain Post pain Syn Post Syn Func Post Func No

Rheumatoid 13(12%) 97(87%) 0 92(82%) 32(29%) 101(90%) 112
 PVNS 3(16%) 16(84%) 0 16(84%) 10(53%) 15(79%) 19
 Chondromatosis 2(12%) 16(94%) 0 16(94%) 7(41%) 16(94%) 17
 Nonspecific 2(16%) 7(58%) 0 8(66%) 3(25%) 9(75%) 12
 Seronegative 3(09%) 17(53%) 0 19(59%) 5(16%) 21(66%) 32
 Posttraumatic 0 7(37%) 0 13(68%) 1(05%) 12(63%) 19

results were not so good ,although there still was a substantial improvement.

Rheumatoid Arthritis.

Overall, there were 112 patients with rheumatoid arthritis. Preoperatively, all the patients had significant synovitis because this was the selection criterion. Post - operatively, at an average follow -up of just over 4 years, over 80% of the patients still had either no synovitis or very slight synovitis. Ninety percent of them had either no or minimal pain, and over 90% had improved function with minimal interference of function by the involved joint.

Pigmented Villonodular Synovitis

Patients who underwent an arthroscopic synovectomy were those who had the diffuse form of pigmented villonodular synovitis. Out of the 19 patients who underwent arthroscopic synovectomy, there were 2 recurrences of the pigmented villonodular synovitis. This is similar to our experience reported in an earlier series with an approximately 10 % recurrence rate. (3) In those in whom there was no recurrence, very good results were obtained Approximately 90 % of the patients were excellent or good in each of the categories of pain, synovitis, and function.

Synovial chondromatosis

In the diffuse form of synovial chondromatosis, we found that removal of loose bodies and arthroscopic synovectomy was particularly effective in these 16 patients. We achieved over 90 % good results in function , control of the synovitis , and pain .

Seronegative arthritis

There were 32 patients with seronegative arthritis . These patients were generally psoriatic but there were also some cases of Reiter's disease and ankylosing spondylitis. In general these patients had synovitis for much longer than the other groups (over 2 years v. 1 year for other groups)

Our results were not as good in control of the synovitis and pain and improved function as it had been in the rheumatoid patients. Overall, only 10% of the patients were good or excellent on pain preoperatively and this increased to 50%. We were able to control the synovitis in almost 60 % of the patients. At follow- up, there was no functional limitation from the knee in approximately two thirds of the patients, despite the fact that half the patients still had persistent pain.

Nonspecific Synovitis

There were 12 patients who had a monoarthropathy with persistent synovitis of the knee alone. Arthroscopy was partially diagnostic in that we were uncertain as to the cause of the monoarthropathy. We had effectively ruled out other causes of monoarthritis by appropriate investigations. When the biopsy indicated non-specific synovitis, this category was established. Follow-up showed that. In approximately two thirds of the patients, the synovitis was controlled. However, it recurred in one third of the patients. There was minimal pain in over half the patients, and function was improved in approximately three-quarters of the patients.

Posttraumatic synovitis

These patients had persistent synovitis after an episode of trauma to the knee. Other significant mechanical factors were ruled out by appropriate investigations and arthroscopy . These patients did not respond as well to arthroscopic synovectomy. Preoperatively, the main indication for the synovectomy was, in fact, pain: all the patients had significant pain preoperatively. Postoperatively, two third of the patients still had significant pain. However, the synovitis was eliminated in approximately two thirds of the patients. The knee was not a significant impairment of function in approximately two-thirds of the patients.

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DISCUSSION

Arthroscopic synovectomy has been developed as an effective tool for the ablation of the synovium in the knee joint. Effective and save methods of access to the different compartments of the knee have been developed (1-5). Providing that proper precautions are taken, the procedure can be carried out safely and with minimal morbidity; in a separate anatomical study, we have shown that the neurovascular stuctures in the posteromedial and posterolateral side of the joint can be safely avoided by flexing the knee

and by proper portal placement. A careful review of the portals shows that five patients did have complications in particular in relation to the posteromedial portal with residual pain or numbness secondary to neuroma formation. (7). In our series hemarthrosis was not a significant problem probably due to the use of drains postoperatively (see methods)

In this particular series, there was no significant difference between the range of movement preoperatively and

postoperatively (statistical analysis. P=96). This would be in contrast to open surgical synovectomy where there is often a significant loss of movement.

The efficacy of arthroscopic synovectomy in rheumatoid arthritis has been shown in the short term and also now based on a longer term follow-up. This concurs with the long-term results reported following open synovectomy.

However, over a 3 to 5 year time frame, the Arthritis and Rheumatism Council and the British Orthopaedic Association Committee of the evaluation of synovectomy found no significant benefits to synovectomy at 3 to 5

year follow-up. Both of these studies were following open synovectomy, which is probably less thorough than the arthroscopic synovectomy.

Pigmented villonodular synovitis is still a significant problem and certainly the results of arthroscopic synovectomy are encouraging but do have a substantial recurrence rate. The results of recurrence are significantly less in patients who have a total arthroscopic synovectomy compared with those who have a partial

arthroscopic synovectomy.

Following open synovectomy in pigmented villonodular synovitis there is significant stiffness and, even following a wide open excision, there was a substantial rate of recurrence. We feel that, at the current time, arthroscopic synovectomy both anterior and posterior offers the best chance for eliminating the disease, although careful follow-up is necessary over many years to determine if there is a recurrence. In this series, we have treated the recurrences by a second arthroscopic synovectomy followed by yttrium radiosynovectomy. These patients are also now followed by repeated magnetic resonance scans rather than just clinical examination alone to determine a rate of recurrence.

In the patients with synovial chondromatosis, we performed removal of loose bodies and an arthroscopic synovectomy. In previous study we had shown that removal of loose bodies alone was not effective and did lead to recurrence. Since then, we have performed arthroscopic synovectomy on patients with generalized synovial chondromatosis as well as removal of loose bodies and we have no further recurrence. Coolican reported that arthroscopic removal of loose bodies and the abnormal synovium was the treatment of choice and our series would certainly support this. However, others have argued loose body removal alone is sufficient. In patients who have had a previous removal of loose bodies and a recurrence of the synovial chondromatosis, arthroscopic synovectomy is effective in ablating the abnormal synovium and preventing further recurrence. Patients with non-specific synovitis present with a monarticular condition.

Investigations need to be carried out to make sure that there is no other underlying pathology. In addition, this particular group has to be distinguished from those who clearly have mechanical derangement. Often, this can only be determined at arthroscopy, but the MRI scan may be particularly helpful in this group. Overall, the patients with nonspecific synovitis were improved, but not nearly as great a degree of success was obtained as with the rheumatoid group, pigmented villonodular synovitis, or chondromatosis. Therefore, we would only recommend arthroscopic synovectomy be carried out in this group when it has clearly been established there is no other pathology causing the problem and when the synovitis has persisted for at least 6 months and is causing considerable functional impairment.

The seronegative group of spondyloarthropathies has had little written about them in the literature from the point of view of synovectomy. Unfortunately, our results of synovectomy in this group are not nearly as effective as those who are seropositive (rheumatoid arthritis). After follow-up of approximately 3 1/2 years, just under 60% of the patients had control of the synovitis and just over 60% did in fact have a functional improvement. Half the patients still had significant pain. Therefore, although the synovitis can be controlled to some extent function improved, it really is not effective in relieving the pain in many of the patients. However, it is pertinent to point out that, in many of these patients, there was articular cartilage

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damage that was quite extensive at the time of the synovectomy and this may have been an adverse factor. Therefore, patients who are seronegative arthritis should be treated very selectively with arthroscopic synovectomy and it should be clearly explained that the procedure can decrease the swelling or synovitis of the knee and improve function, but that the pain will probably remain.

The patients with posttraumatic synovitis had a clear episode of trauma to the involved joint. The knee became swollen and the swelling persisted. Other traumatic injuries to the joint were ruled out either by preoperative investigations such as a magnetic resonance scan or at the time of arthroscopy. Therefore, the diagnosis of posttraumatic synovitis was only established after the

diagnostic portion of the arthroscopy was carried out. These patients did have persistent synovitis for more than 6 months and no other cause for their arthritis could be determined. Clearly some of these patients could belong to the nonspecific synovitis group or the seronegative synovitis group and just be in the early stages of development of the disease. It is probably for this reason that the results of the synovectomy were not particularly effective. All the patients had pain to a significant degree preoperatively and only about one third of them were relieved of this pain postoperatively. Once again therefore, the synovectomy was not effective as a method of relieving pain. This was despite the fact that two thirds of the patients had no synovitis or effusion and approximately the same number had improved function. As in the seronegative group, the indication for arthroscopic synovectomy in the posttraumatic group is persistent synovitis with significant functional impairment: the procedure should not be offered to try and decrease or eliminate the patient's pain.

Overall, arthroscopic synovectomy can be carried out in an efficacious and safe manner. Arthroscopic synovectomy is certainly beneficial for treating pigmented villonodular synovitis and synovial chondromatosis. For rheumatoid arthritis, we seem to be able to control the disease effectively for many years, although it cannot be determined whether the overall prognosis for the disease has been altered. In the seronegative arthritis, nonspecific and posttraumatic varieties, the procedure should not be offered for pain relief but can control synovitis and improve function in many patients.

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SOFT TISSUE TUMORS AND NONNEOPLASTIC CONDITIONS SIMULATING BONE TUMORS

Pigmented villonodular synovitis may occur in a localized or diffuse form. The localized form is apparently identical histologically to giant cell tumor of tendon sheath. The diffuse form also appears to be identical histologically to the localized form, but it involves the entire synovium. The diffuse form most commonly affects the knee, but the hip, ankle, shoulder, wrist, and other joints have been involved. The patient usually presents with monoarticular pain and swelling. A mass may be palpable. Aspiration of the joint characteristically reveals blood-tinged fluid. Routine roentgenograms may show bony erosion from without, especially if the hip is involved. Computed tomography is best to demonstrate bone involvement, and magnetic resonance imaging best shows the soft tissue masses associated with this lesion. Recommended treatment of the localized form is marginal excision and of the diffuse form is total synovectomy. Radiotherapy in the diffuse lesion may be justified if surgery fails to control the process. If significant bony erosion has occurred (usually in hip and shoulder lesions), joint reconstruction may be necessary.

Synovial Lesions

Pigmented Villonodular Synovitis:

Pigmented Villonodular Synovitis is an inflammatory synovial process of unknown etiology that causes monoarticular arthritis in children and young adults. Patients present with pain and intermittent, often chronic swelling. Examination shows swelling and synovial thickening, and aspiration of the joint reveals bloody or brownish hemosiderin-stained fluid. Cytologic examination of the fluid may reveal the presence of hemosiderin-containing macrophages. Early in the course of the disease, the radiographs are normal except for soft tissue swelling or effusion. Later, periarticular erosions and cyst formation occur and ultimately degenerative change of the articular with the radiographic features of osteoarthritis supervene.

Histopathologic inspection of the synovium reveals nodules, and villous projections, brownish in colour, containing fibrous tissue, giant cells, and monocytic cells with hemosiderin granules and hyperplasia of the synovial layer. Both nodular and diffuse forms have been described, with the diffuse form having a higher recurrence rate (approximately 50 percent) than the nodular form (25 percent) after synovectomy.

Treatment of the lesion involves synovectomy. Radiation synovectomy using dysprosium-165 has been reported to give satisfactory results, as has arthroscopic synovectomy of the knee. In joints such as the hip, or in the presence of large masses of the synovial tissue, open surgical synovectomy is usually preferable.