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Synovial neoformations and tumours

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An important group of soft tissue tumours and tumour-like lesions originates from the synovium of the joints, bursae and tendon sheaths. These include synovial chondromatosis, diffuse articular lipomatosis (lipoma arborescens), villonodular synovitis, synovial haemangioma, synovial chondroma and fibroma (intracapsular and peri-articular), primary chondrosarcoma originating from the synovium and synovial sarcoma. The main clinical symptoms of these tumours, such as pain, swelling, effusion and joint locking, are not specific, so the diagnosis can easily be missed in clinical practice. The most important clinical characteristics and the differential diagnostic clues for synovial tumours and tumour-like lesions are described in this chapter. In addition, the new results of genetic and histological studies are discussed, together with a summary of the available evidence-base for therapy.

Key words: benign and malignant synovial tumours; tumour-like lesions of the synovium.

The synovial tumours and tumour-like lesions represent a distinct entity within the family of soft tissue tumours. Joints, bursae and tendon sheaths have the same type of synovial membrane, so tumours can develop from all of these structures, although there are still some preferred sites. The common tissue origin is shown by the similar cellular and histological structure. Synovial epithelial cells and chondroid tissue, for example, are found in both villonodular synovitis and synovial chondromatosis.[1] Another peculiarity is that, in some cases, their 'tumorous' and 'tumour-like' nature can be contemporarily observed, as in the giant cell tumour of tendon sheaths and in pigmented villonodular synovitis.[2,3] Although both of these are rare, they still occur more frequently than true benign synovial tumours such as haemangiomas, lipomas, fibromas and synovial (intracapsular) chondromas.

The clinical symptoms of synovial tumours and tumour-like lesions are uniform. They usually appear as a visible and palpable masses within and/or around the joints. Synovial effusion, if any, is blood stained or xanthochromic.

The diagnosis can be made by a careful analysis of the history, examination, laboratory data and imaging methods, including computed tomography (CT) scanning and magnetic resonance imaging (MRI).[4,5] Conventional radiographs are informative in only a minority of cases, such as synovial chondromatosis or chondroma of the tendon

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sheaths. A definitive diagnosis can only be obtained after surgical intervention and histological examination of the removed tissue (see the practice points table).

This chapter explains a practical approach to management that can be used in everyday rheumatological practice. This is important because the great majority of synovial tumours present with non-specific joint symptoms, so the rheumatologist may be in a position to make the first diagnosis.

We will first discuss the clinical features, followed by the imaging methods and differential diagnostic clues. The possible aetiology, histological features and treatment will be only briefly mentioned.

TUMOUR-LIKE LESIONS OF THE SYNOVIUM

Synovial (osteo)chondromatosis

Primary synovial chondromatosis is a rare tumour-like lesion with cartilaginous metaplasia, originating from the synovium. However, cell proliferation studies[6] and immunohistochemical examination[7] for growth potential in the loose bodies suggest that the condition is not simple metaplasia but also has a proliferative component. Mertens et al[8] and Sciot et al[9] have observed specific cytogenetic features suggesting that primary synovial chondromatosis is a clonal proliferation.

Clinical features

Synovial osteochondromatosis is found equally in males and females, most frequently in those between 30 and 50 years of age. The condition usually occurs in one joint and is rarely polyarticular. It most commonly affects the knee and hip joints, followed by the shoulder, the elbows, the temporomandibular joints and the joints of the hands and feet.[10] The principal symptoms include swelling of the joint, sometimes in the form of a palpable, firm mass, with or without limitation of movement. Restriction of movement in the hip joint can be considerable in some cases of synovial osteochondromatosis as a result of the capsular restriction of the hip joint.[11]

The joints do not appear inflamed, and the cell count of the synovial fluid is low. Articular loose bodies may cause locking and pain in the joint. The condition progresses slowly, and it may take years before a patient presents to a physician.[12] Because of the prolonged pathological process, however, synovial osteochondromatosis can lead to secondary osteoarthritis.

In the early phase of the condition, when no calcified chondromas can be identified on plain radiographs, the diagnosis of synovial chondromatosis may easily be missed. It should still, however, be considered when an unexplainable osteoarthritis is diagnosed.

Imaging

At an early stage, radiographs show widening of the articular joint space as an indirect sign. At a later stage, loose bodies of various sizes become calcified and can be seen on radiographs (Figure 1); X-ray signs of secondary osteoarthritis can also be observed. MRI with gadolinium enhancement and/or CT scanning arthrography is suitable for the detection of chondromas at an early stage, prior to the characteristic calcification that is seen on plain X-ray.

Figure 1. Calcified spherical loose bodies of synovial (osteo)chondromatosis in the elbow joint (antero-posterior view).

Differential diagnosis

Calcified loose bodies within the joint, similar to those of synovial chondromatosis, can frequently be seen on the X-rays of patients after joint trauma, osteochondritis dissecans and severe forms of osteoarthritis. In advanced osteoarthritis, this feature usually occurs in older age and with fewer osteochondromas compared with primary synovial chondromatosis. Synovial deposits of calcium pyrophosphate dihydrate crystals can also produce radiological images similar to those seen in synovial osteochondromatosis. In some neurological conditions with joint destruction, such as syringomyelia, the calcification and new bone formation appear at both intra- and peri-articular sites.

All these calcifications and loose bodies can be considered to be *secondary* osteochondromatosis. In contrast, *primary* synovial chondromatosis is a histologically verified entity with subsynovial metaplastic chondroid islands.

Treatment and prognosis

Synovial chondromatosis is self-limiting in nature, which usually stops the further 'production' of chondromas. This unique feature should always be considered when a surgical procedure is planned, mostly in the case of primary chondromatosis of the hip joint, where total synovectomy is technically difficult to perform.

The aim of surgical procedures is two-fold: first, to remove loose chondromas when they cause locking episodes and pain; and second, to treat the condition by synovectomy. Several factors should be considered in the latter case, such as joint localization, the scale of synovial involvement and the stage of the disease. Partial synovectomy is usually appropriate because, in synovial chondromatosis, the whole synovium is not involved. Arthroscopic surgery is a useful tool for the procedure. The incidence of recurrence is estimated to be about 15–25%.[12,13]

Aetiology and staging

The aetiology of the process remains unknown, but the course of the disease can be divided into three main stages.

Initially, when the process is limited to the intrasynovial region, the microscopic chondroid islands can be demonstrated only by histological examination. Later on, when the chondroid islands are spreading, the macroscopic appearance of the synovium alters, the villi become swollen and dense, with a characteristic 'peduncular' appearance, and several chondroid loose bodies may be present within the articular cavity. At end-stage, the whole joint can be filled with several hundred chondroid loose bodies, ranging from 0.5 to 2.0 cm in diameter. At this stage, it is interesting to note that the synovium itself shows no signs of any further hypertrophy, and no more metaplastic chondroid islands are detectable on histological examination.

Prognosis

Synovial chondromatosis rarely becomes malignant. Wuisman et al[14] reported only 13 cases from the literature with secondary synovial chondrosarcoma. Bertoni et al[15] described two cases of primary chondrosarcoma developing *de novo* from the synovium and nine secondary cases, five patients dying from pulmonary metastases. A correct histological evaluation is sometimes difficult because of the lack of histological differentiation between synovial chondromatosis and chondrosarcoma of low malignancy.[13,16] Features of malignancy include a rapid increase in size of the tumour, a highly destructive process that also affects the bone and certain histological signs such as loss of the 'clustering' growth pattern, myxoid change of the cartilage matrix and necrotic areas in the synovium.[15,17]

Lipoma arborescens (diffuse articular lipomatosis)

Lipoma arborescens is not a true tumour but a diffuse, hyperplastic-type alteration of the subsynovial adipose tissue, producing a prominent villous transformation of the synovium. The designation 'villous lipomatous proliferation of the synovial membrane', suggested by Hallel[18], is quite correct.

Clinical features

This is a rare condition, only a few cases having been reported.[19–21] It is associated with diabetes, chronic inflammation and osteoarthritis. The primary location is the knee joint. The main clinical symptoms include diffuse joint swelling, repeated locking and joint effusions. The symptoms of accompanying osteoarthritis may modify the clinical presentation.

Macroscopically the entire synovium is thickened, and on histological examination the subsynovium contains typical mature fatty tissue. Bouraoui et al have described a case in which the removed synovium weighed 1.5 kg.[22]

Imaging

The diagnosis can be made on arthroscopy, and MRI can allow diagnosis at an early stage. In our own case, the massive tumour-like fatty alteration could be first visualized in the suprapatellar region, being easily distinguishable from the surrounding muscular tissue. The fatty, degenerated and thickened polypoid synovial villi are characteristic of the condition[23,24] (Figure 2).

Differential diagnosis

Lipoma arborescens should be differentiated from villonodular synovitis and synovial haemangioma; blood-stained effusion is more frequent in the latter. Haemophilia can be distinguished by the characteristic history and laboratory features.

Treatment

Synovectomy is usually an effective treatment, with excellent results and a low recurrence rate.

BENIGN TUMOURS OF THE SYNOVIUM

Apart from villonodular synovitis, the rare benign tumours of the synovium are histologically identical to other synovial tumours. The principal symptoms of benign synovial tumours include swelling, effusion, limitation of movement and occasionally locking of the joints. All these features can, however, also be caused by benign bone tumours, localized close to the joints, for example chondroblastoma, giant cell bone tumour or osteoid osteoma. More importantly, several common diseases, such as rheumatoid arthritis, osteoarthritis, osteochondritis dissecans, articular loose bodies and meniscal lesions, are all accompanied by similar symptoms; these should thus be considered in the differential diagnosis.

Villonodular synovitis

Villonodular synovitis is a group of benign proliferative lesions of the synovium and mesenchymal supporting elements. Jaffe, in 1941, reported that the disorder may involve the synovial lining of the joints (pigmented villonodular synovitis – PVNS), tendon sheaths (pigmented villonodular tenosynovitis, also called giant cell tumour of the tendon sheath) and bursae (pigmented villonodular bursitis). This was later confirmed by flow cytometric DNA analysis.[25] Depending on the extent of the synovial involvement, villonodular synovitis in the joints and bursae can be further subdivided to a 'diffuse' and a 'localized' form.

Villonodular synovitis as a group is a rare condition. The giant cell tumour of the tendon sheath is more common than villonodular synovitis involving the joints and the bursae. In a large epidemiological study conducted in 12 hospitals of Shelby County, including the Memphis area, the incidence of giant cell tumour of the tendon sheath

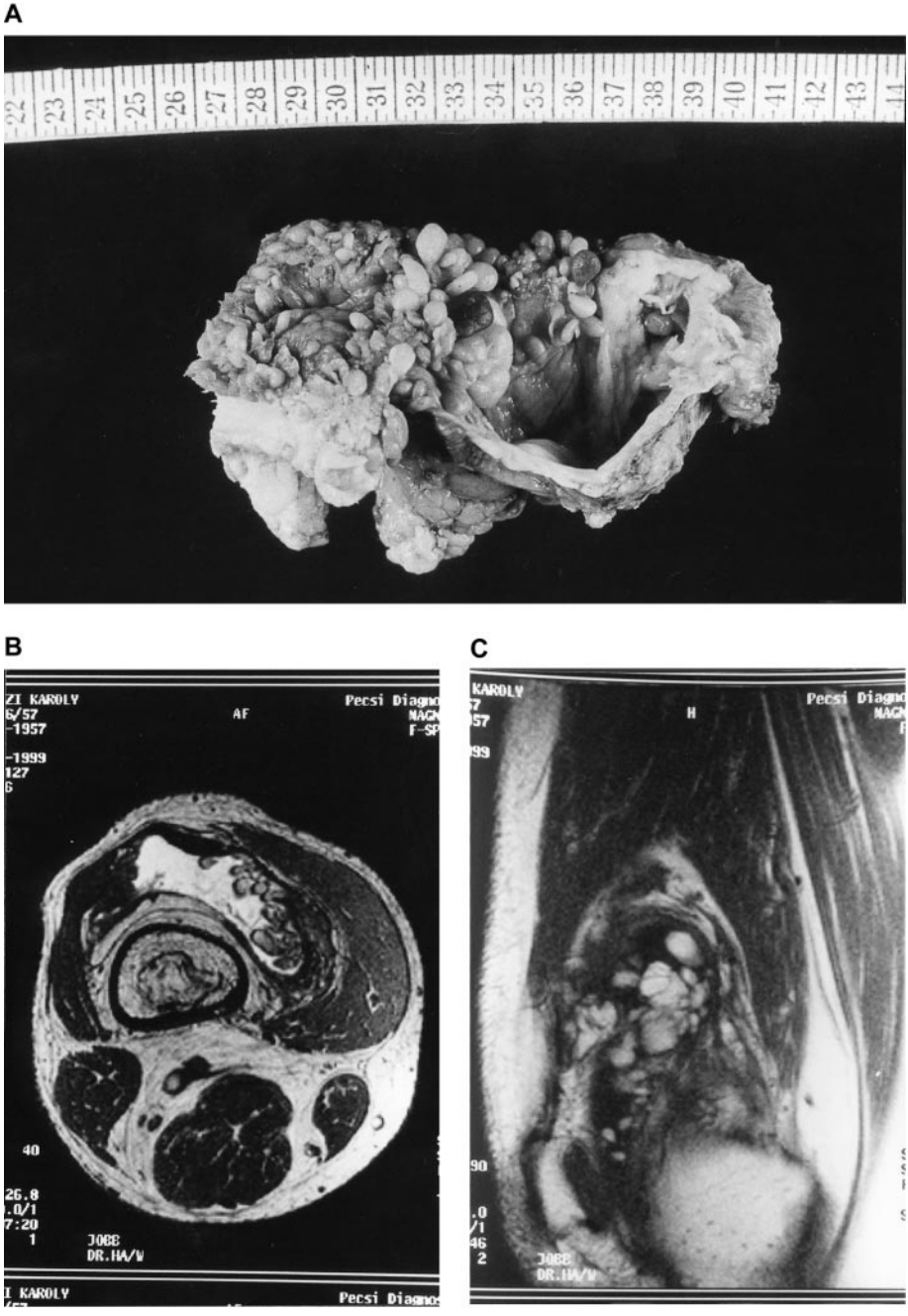


Figure 2. Lipoma arborescens, removed from the knee. (A) Note the finger-like thickened fatty synovial villi and thickened lipomatous subsynovial tissue (surgical specimen). Typical magnetic resonance imaging (MRI) appearance of the lipoma arborescens. On the axial (B) and saggittal (C) MRI pictures, a 15 × 9 × 6 cm large tumour is present. The fatty tumour-like alteration of the synovium appears as heterogeneous fluid-containing tissue, the thickened finger-like synovial villi being clearly presented.

was found to be 9.2 cases per million. In comparison, PVNS of the joints occurred in 1.8 cases per million per year, and there were no documented cases of pigmented villonodular bursitis over the 17-year study period.[26]

Clinical features

Villonodular synovitis can affect all age groups, and both a male and a female preponderance has been reported by different series.[26,27]

Villonodular synovitis can present in three ways. The most common presentation involves the tendon sheaths, known as a giant cell tumour, presenting with a mass on a finger. In a bursa or joint, the process may diffusely involve the synovium – the so-called diffuse form – which may present with pain, joint swelling and usually a blood-stained effusion. The condition may also appear as a pedunculated nodule within the joint – the localized form – with pain and joint locking. These three presentations are thought to be a continuous spectrum of the same pathological process.

Giant cell tumour of the tendon sheath is the most common soft tissue tumour of the hand.[28] The presenting symptom in this lesion is a painless mass on a finger. In a series by Myers et al[26], the right hand was twice as commonly involved as the left, and the volar aspect was affected twice as often as the dorsal. On radiographs, about 10–25% of the lesions cause erosion and atrophic pressure on the underlying cortical bone.

The diffuse form of PVNS usually involves the knee as a monoarthropathy and presents insidiously in the third or the fourth decade, although it can occur at any age. The youngest reported case was an 8-month-old infant[29], the oldest a man of 84 years.[26] Swelling, stiffness and pain are the presenting symptoms, although the boggy swelling is out of proportion to other symptoms. The knee is warm, and haemarthrosis can be found in up to 75% of patients.[26] However, in another series of 25 cases with diffuse PVNS, 56% had non-bloody effusions.[30] Haemarthrosis may therefore be an unreliable sign of PVNS.

The localized form of intra-articular PVNS, an even more rare manifestation of the disorder, can present with pain and 'locking' of the joint. The pedunculated nodules can undergo torsion and infarction, leading to acute pain.

Differential diagnosis

The giant cell tumour of the tendon sheath should be differentiated from several other lesions. The ganglion is firmer and is generally located above the radiocarpal or carpometacarpal joint, is more painful and may occasionally show changes in size. In the case of foreign body granulomas, the history is usually characteristic.

Haemarthrosis can also be seen in trauma, clotting disorders such as haemophilia, Charcot's joints, sickle cell anaemia and Ehlers–Danlos syndrome. Clinical examination and the appropriate laboratory investigations can rule out most of these conditions, and hence recurrent bloody effusions in the knee should raise the possibility of PVNS. Apart from the knee, this disorder has been described in the ankle, hip, wrist, spine, shoulder (Figure 3) and temporomandibular joint.[31–33] Multiple joint involvement is extremely rare, but has been described.[34] Heberden's nodes in the elderly may be multiple on the extensor side of the distal interphalangeal joint. Radiographs can be helpful in the diagnosis of soft tissue chondromas occurring above the proximal and distal interphalangeal joints.

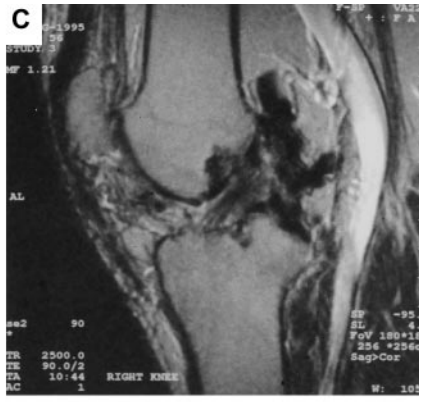
Figure 3. Pigmented villonodular synovitis of the shoulder. Note the massive swelling, the stretch marks on the skin and the absence of erythema.

Imaging

Plain radiographs in PVNS are non-specific, although the joint space can be intact and bone density may be normal until late in the disease, despite the presence of erosions[35] (Figure 4A). Erosions and cartilage destruction occur earlier in the hip and knee joints. Calcification is rare, and its presence should raise the possibility of synovial osteochondromatosis.

Arthrograms, bone scans and ultrasonography have limited value in the assessment of PVNS and hence are rarely used. On CT scanning, PVNS lesions show high attenuation because of the presence of haemosiderin pigment, a feature also seen in patients with chronic haemarthrosis resulting from haemophilia or trauma.[35,36] Villonodular synovitis lesions enhance on intravenous contrast because of increased vascularity. CT scanning is especially useful for delineating bony erosions and cyst formation.

MRI is the investigation of choice in PVNS and reflects the histological composition of the tumour (Figure 4B and C). The most consistent finding is that the lesion appears dark on all pulse sequences, secondary to the ferromagnetic properties of haemosiderin that cause a shortening of both the T1 and T2 relaxation time.[37] The signal intensity on T2-weighted images can be heterogeneous because of the varying haemosiderin content



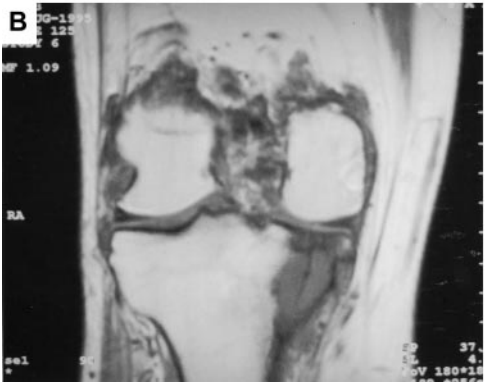


Figure 4. Pigmented villonodular synovitis of the knee. (A) Anteroposterior radiograph of the knee showing cystic changes in the medial femoral condyle and tibial plateau. The joint space is preserved and the bone density is otherwise normal. (B) A coronal T1-weighted magnetic resonance (MR) image shows low-signal hypertrophied synovium in the intercondylar notch and around the femoral condyles. The lesion in the medial tibial plateau has low signal on this image. On T2-weighted images, the signal in this lesion was high, compatible with a cyst. (C) On a sagittal T2-weighted MR image, hypertrophied synovium is low in signal posteriorly and has intermediate signal strength anteriorly. There is erosion and invasion of the adjacent femur and tibia.

between acute and chronic haemorrhage. MRI is especially useful for delineating the extent of the lesion to assist in surgical planning. However, the MRI appearance of PVNS is not pathognomic as similar regions of dark synovium can be observed in haemophilic and amyloid arthropathy, synovial osteochondromatosis and rarely rheumatoid arthritis.[35] Giant cell tumour of the tendon sheaths has very similar MRI findings. The lesion is iso-intense to muscles on T1-weighted imaging and on T2-weighted images it has varying intensity depending on the haemosiderin content.[32]

Aetiology

Until recently, there had been a considerable debate over the origin of villonodular synovitis, in particular over whether the synovial proliferation is inflammatory or neoplastic in nature. Synovial proliferation similar to that seen in PVNS has been produced in experimental canine models by repeated injections of autologous blood into the knee joints of adult dogs[38] but not puppies.[39] This model did not show all the histological features of the condition, giant cells, for example, being absent. Cytogenetic studies have since confirmed that PVNS lesions consist of clonally proliferated cells. Several chromosomal abnormalities, such as trisomy 7[40], aberrations of the short arm of chromosome 1[41] and X chromosome inactivation[42], have been reported in cultures of cells derived from PVNS tissue. Based on these and other histological findings, for example nodular growth and a propensity to recurrence after excision, villonodular synovitis is now considered to be a benign neoplasm of the synovium.

Interestingly, 'malignant' villonodular synovitis has also recently been reported. Bertoni et al[43] described eight cases of malignant villonodular synovitis showing several histological features of malignancy (see below). Four of these eight villonodular synovitis patients died with pulmonary metastasis.

Histological features

All three lesions of villonodular synovitis are characterized by an exuberant proliferation of synovial lining cells that spread along the joint surfaces, bursae or tendon sheaths. These cells have invasive properties as they produce finger-like extensions or villi that may fill the complete joint space with lobulated masses, invade deep into the subsynovial connective tissue and lead to bony erosions and destruction. Macroscopically, the tissue appears to be yellowish-brown or orange-red and has been described as 'a plush angora rug'.[28] The matted masses of villi and synovial folds have sessile and pendunculated nodules that differentiate these brownish-red lesions from haemachromatosis and haemosiderosis. The soft rubbery tumour tissue can invade the joint capsule and can spread over adjacent nerves, vessels and tendons, as well as accumulating near the chondro-osseous junctions.

Microscopic examination is characterized by synovial cell hyperplasia, the accumulation of histiocytes, and the presence of multinucleated giant cells and haemosiderin-laden macrophages (Figure 5). Haemosiderin, which gives the characteristic reddish-brown colour (and the name 'pigmented') to this lesion, is present in macrophages and fibroblasts as well as in the extracellular space. Collections of 'xanthoma cells' – macrophages with a characteristic foamy cytoplasm owing to lipid accumulation – are also seen. Haemorrhage is common, and inflammatory infiltrate is often seen near haemorrhagic foci.

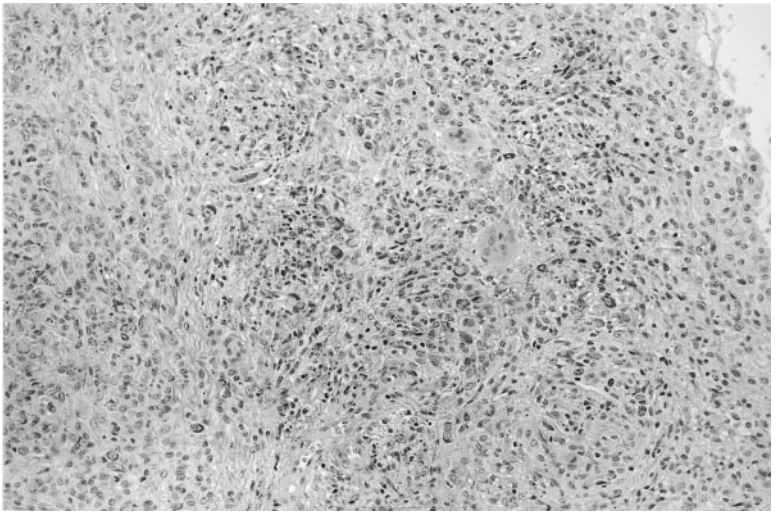


Figure 5. Histology of pigmented villonodular synovitis (PVNS) involving the knee of the patient in Figure 4 (low-power magnification; reproduced here ×6). The figure shows classical features of PVNS including multinucleated giant cells, spindle-shaped synoviocytes, foamy histiocytes and haemosiderin pigment within macrophages and the extracellular space.

PVNS can be locally invasive and cause bone destruction via osteolysis, erosions and bone cysts. Both the hyperplastic synovial cells and the osteoclast-type giant cells are responsible for the cartilage and bone loss.[44]

Giant cell tumour of the tendon sheath, the most common neoplasm of the hands, is histologically very similar to PVNS. Fine-needle aspiration biopsy and cytology of these lesions can be diagnostic, showing polygonal histiocytes with rounded, eccentrically located nuclei and multinucleated giant cells.[45] Many authors have described occasional mitosis in villonodular synovitis lesions, but the histological features of malignancy are usually absent.

Treatment and prognosis

Marginal surgical excision of the giant cell tumour of the tendon sheath is the treatment of choice. There is a low recurrence rate. In the knee joint, arthroscopic removal of the lesion has also been reported.[46]

Because of the rarity of PVNS, no randomized controlled trials have been reported. Most of the reported papers on management describe the collective experience at individual centres and that too mainly concerns PVNS involving the knees. No drug has been shown to be effective in controlling villonodular synovitis, the current treatment options being limited to surgery and/or radiation therapy. Flandry et al[30] reviewed their 25-year experience of treating diffuse PVNS of the knee with total synovectomy. Twenty-three patients (25 knee joints) treated with this procedure were followed on a long-term basis (an average follow-up of 58 months). The recurrence rate of 8% (two patients) was much lower than the previously reported rates of 30%[47] and 46%.[48] The authors concluded that the recurrence was

dependent on the degree of technical difficulty and that adequately excised lesions did not recur.

Osmic acid or radiation synovectomy was proposed by Flipo et al[49], either as a first operation or as an alternative method when surgery could not be performed. The recurrence rate was 14%, and one-third of the 58 patients had later to undergo total hip arthroplasty. Oglivie-Harris et al[50] studied the role of arthroscopic procedures in the treatment of PVNS but concluded that total synovectomy is hard to accomplish. However, localized or focal forms of PVNS can be successfully treated with arthroscopic partial synovectomy.[50,51] In a Mayo Clinic series of 18 patients with PVNS of the knee who underwent synovectomy followed by total knee arthroplasty, 14 had a good outcome with a functioning prosthesis at an average of 9.9 years.[52] All of the four failures occurred in patients who had 'active' disease at the time of the surgery, although only one had recurrence and the three failures were caused by aseptic loosening.

Radiation treatment is generally reserved for 'high-risk' patients in whom the extent of the lesion makes it inoperable or in patients who have recurrent PVNS after surgery.[53] In a retrospective review of 14 cases who received radiation therapy for high-risk or recurrent PVNS, O'Sullivan et al[53] reported an 'excellent' response with no recurrence in 13 cases after a mean follow-up of 69 months. Six of these cases were 'inoperable' as a result of the involvement of extensive parts of skin, muscles, neurovascular bundles or bones, and the remaining eight had undergone a mean of 2.5 surgical procedures early on in their disease. The dose of radiotherapy was 35 Gy in 51 fractions.

Synovial haemangioma

This lesion appears in either a localized or a diffuse form. Devaney et al[54] reported 20 cases, 60% of them involving the knee joint. Nonetheless, there have also been cases described in articular bursae. The condition can appear at any age and affects both males and females. The synovial involvement may be a part of a heterogenous syndrome, involving haemangiomas of the skin, bone and muscles (Klippel–Trenaunay disease).

The clinical symptoms are mild, which may be why patients present late.[55] Painless swelling of the joint is rarely accompanied by symptoms of articular haemorrhage, joint locking or decreased range of motion. In the differential diagnostics, PVNS, haemarthrosis of traumatic origin[56], menisceal lesions and other causes of haemarthrosis should be considered. MRI usually reveals a localized lesion; T1-weighted images show a low or median intensity, while T2 weighting indicates high signal intensity with the presence of fatty connective tissue septa. Early views of angio-MRI with gadolinium enhancement are also useful.

Angiography in some cases reveals abnormal vascular glomeruli. During arthroscopy, the occasionally peduncular, purple-blue tumour is pathognomic. Histology shows haemangioma of a capillary or cavernous type.

Surgical excision is indicated, if possible, at an early stage before the slowly progressing lesion infiltrates the whole articular synovium.

Synovial (intracapsular, peri-articular) chondroma

This is a rare, chondroid tumour, 1–2 cm in size, originating from the connective tissue of the articular capsule and the tendon sheaths. One hundred and four cases were

reported by Chung and Enzinger in 1978.[57] The tumour, which was described by these authors as 'chondromas of the soft tissues', appeared around the small joints of the hands in 64%, and of the feet in 20%, of the cases.The lesions can develop at any age, although they are more frequent in the third and fourth decades. Synovial chondroma is a slow-growing tumour, so clinical symptoms are generally aspecific, for example swelling around the joints and limitation of movement.

Radiographs often show a lobular appearance on the volar or dorsal side of the small joints, with various calcifications and ossifications (Figure 6). Based on the clinical appearance, synovial chondroma needs to be distinguished from the giant cell tumour of the tendon sheath and, on the basis of radiographs, from the quite rare chondrosarcoma of the hand. The latter grows more rapidly and involves the surrounding bones. Steiner et al[58] reported 4 cases of synovial chondroma: 3 in the knee and 1 in the hip. These authors called attention to the importance of differentiation from synovial chondromatosis.

Figure 6. Synovial chondroma above the first proximal interphalangeal joint of the hand.

Histologically, the lesions are generally composed of mature hyaline cartilage, with the possible occurrence of calcification as well as metaplastic ossification. In some cases, a certain degree of cellular atypia or hyperchromasia may mimic malignancy.

Marginal surgical excision is the choice of treatment, this generally not being followed by any recurrence.[57,58]

Synovial lipoma and fibroma

Unlike in other visceral localizations, true lipomas and fibromas originating from the synovial tissues are extremely rare.[59] The former have been described in the knee joints, while the latter have been found in the small joints of the hands and feet, although they may also occur in connection with the tendon sheaths. The lesions show a regular appearance and have capsules. Restriction of motion, articular swelling,

synovitis and locking of the joint may be present. The correct diagnosis can be obtained by histological examination following surgical removal. The lipoma with a capsule should not be mistaken for hyperplasia of the Hoffa's fat pad, which generally accompanies secondary traumatic or inflammatory processes.

MALIGNANT TUMOURS OF THE SYNOVIUM

Primary chondrosarcoma originating from the synovium

Chondrosarcomas may develop in the soft tissues or in the bones, either centrally or peripherally, as primary or secondary lesions. It is questionable, however, whether a chondrosarcoma can develop primarily from the synovium.[2]

Differential diagnosis is difficult because there are currently no histological or molecular biological methods available by which low-grade chondrosarcomas can, with complete reliability, be distinguished from benign cartilaginous lesions.[16,60] According to certain authors[15], chondrosarcomas may appear as *de novo* primary lesions in the joint, although this manifestation is quite rare. Differentiation should be made between cases of primary chondromatosis, secondary chondrosarcomas arising from these, and the rare primary synovial chondrosarcomas.

Synovial sarcoma

Synovial sarcoma is the third most frequent malignant soft tissue tumour, accounting for 5–10% of all soft tissue tumours.[1] This tumour has been designated as a synovial sarcoma because of its anatomical location (most of them originating from the capsules of the joints, bursae and tendon sheaths) and its histological similarity to normal synovial tissue. There is no convincing evidence that the tumour really originates from the cells of the synovium, as synovial sarcoma has also been described in very different locations, such as the lung[61], the parapharyngeal space[62], the oesophagus[63], the prostate[64], the pericardium[65] and bone.[66]

Clinical features

From the reports of Brodsky et al[67], Oda et al[68] and Singer et al[69], synovial sarcoma usually presents between the third and the fifth decades, although it may occur at any age. It is usually located in the extremities (90%) and lower limbs (60%). The main sign is a large, deep-seated and rapidly growing mass in association with a tendon, tendon sheath or joint capsule. These masses are rarely observed *within* the joints. The involved joint sites include the knee, feet, thighs, hips, elbows, hands, shoulders and trunk.

Synovial sarcoma is also the most common malignant soft tissue tumour of the hands and feet (Figure 7). Most of them grow rapidly, but in some cases a synovial sarcoma may persist for years as a small, superficial, indolent lump in the hands or feet. It can be mistaken for synovitis or a ganglion and excised marginally, only histological examination of the lesion making the diagnosis.[70] Deep, radiating pain is present in about 50% of cases.

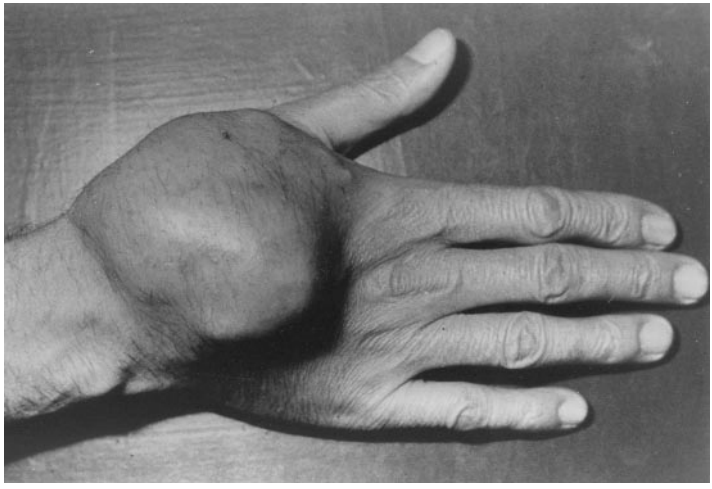


Figure 7. Synovial sarcoma: macroscopic view of the tumour on the dorsal side of the hand.

Imaging methods

The tumour may be recognized on conventional plain X-ray films because tissue calcification occurs in about 20–40% of cases, MRI is the best tool for the detection of the lesion's lobular structure and extent. Ultrasound may also be helpful in distinguishing the tumour, mainly from Baker cysts in the popliteal region, although in many cases the synovial sarcoma may also contain large multicompartmental cysts filled with mucoid substance similar to synovial fluid.

Histological features

In the early stages, the tumour is localized and has a pseudocapsule. Later on, it starts to spread into the viscera and muscles, infiltrating the surrounding joints and bones.

Histologically, biphasic and monophasic forms can be differentiated. The former comprises characteristic epithelial cell components arranged in solid cords, whorls or nests, surrounded by irregular cyst-like spaces. The spindle cell sarcomatous tissue components are the most prominent, forming solid areas or dividing the epithelial cell nests. Histologically, it can be difficult to differentiate these monophasic, round or spindle cell tumours from other malignant soft tissue tumours, such as fibrosarcomas, leiomyosarcomas, malignant peripheral nerve sheath tumours or poorly differentiated sarcomas.

In recent decades, there has been great progress in the diagnostic accuracy of different soft tissue sarcomas by cytogenetic examination. Many of the soft tissue tumours can be characterized by different specific chromosomal translocations; for example the reciprocal translocation t(X;18) (p11.2;q11.2) is thought to be the primary cytogenetic abnormality and specific to synovial sarcoma.[66,71] Cloning of the breakpoints reveals that these translocations result in the production of tumour-specific chimaeric transcripts such as SYT–SSX1, SYT–SSX2 in the synovial sarcoma. The sensitive reverse transcriptase polymerase chain reaction SYT–SSX1/2 can be used as a marker for synovial sarcoma in frozen materials and also in fine-needle aspirations or paraffin-embedded histological specimens.[72–74] The genetic features of the tumour

may relate to morphology and outcome. Nilsson et al[75] found that the SYT–SSX1 variant of synovial sarcoma was associated with a high rate of tumour cell proliferation and a poor clinical outcome.

Treatment and prognosis

The 5-year survival rate for synovial sarcoma depends on the stage of the tumour and has been estimated to be between 25% and 60%.[67–69,76] The results of limb-sparing surgery are no worse than amputation if wide excision can be performed in the normal tissues. Tumour size is one of the most important prognostic factors influencing survival. Brodsky et al[67] found the 5-year survival to be 86% for tumours smaller than 5 cm in diameter but only 22% for those larger than 10 cm. Bergh et al[76] reported the outcome for 121 patients with synovial sarcomas. They found that risk factors for local recurrence included large tumour size (more than 5 cm) and an inadequate surgical margin, whereas the risk factors for tumour-related death were poor histological differentiation, large tumour size, age above 25 years and the development of local recurrence. The observable mitosis count and the presence of poorly differentiated areas are also of importance[77], as is the presence of distant metastases. The localization or histological (mono- or biphasic) type of the tumour is not considered to be a significant prognostic factor. There are no differences between the outcome with adjuvant pre- or post-operative chemotherapy and radiotherapy.[69,76]

SUMMARY AND CONCLUSIONS

The most frequent benign tumour of the synovium is the giant cell tumour of the tendon sheath, mainly developing on the fingers. PVNS is less common, the typical sites of appearance being the knee and hip joints, with possible involvement of the bones accompanied by repeated blood-stained joint effusions in the late stages. Other benign tumours, such as lipomas, haemangiomas, fibromas and chondromas, rarely occur in the synovium, in contrast to other soft tissue locations. They are usually recognized during the course of surgery or histological examination performed for another diagnosis (e.g. menisceal lesion, osteoarthritis, etc.).

In typical cases, recognition of synovial chondromatosis by radiography is not difficult. Unknown mechanisms may sometimes lead to secondary chondrosarcoma, usually developing from monoarticular synovial chondromatosis. Another pseudo-tumour is the diffuse fatty hyperplasia of the synovium ('lipoma arborescens'), which should be distinguished from real lipomas and hyperplasia of Hoffa's fat pad.

Synovial sarcoma is the third most frequent malignant visceral tumour. The synovial epithelial origin has not yet been proved. Synovial sarcoma is generally highly malignant, growing in close association with the joints, bursae and tendon sheaths. The 5-year survival rate is around 25–50%. Correct diagnosis is possible using modern molecular biological methods including cytogenetic analysis of the tumour cells and the demonstration of chromosomal abnormalities. The proliferation index and size of the tumour, the presence of distant metastases and tumour-free surgical margins are all important prognostic factors. Limb-sparing surgery is preferable to amputation if the tumour can be removed adequately. Studies on a larger number of cases are needed in order to verify the positive effects of pre- and post-operative chemotherapy and radiotherapy.

Practice points

Table I. Clinical characteristics of synovial tumours and tumour-like lesions.

Diagnosis	age (decades)	localization–clinical findings	symptoms and signs	differential diagnostics	imaging	treatment
• **Tumour-like lesions**						
synovial chondromatosis	3–5	knee, hip, shoulder	pain, swelling, limitation of movement	menisceal lesion, PVNS, osteoarthritis, neurological diseases	numerous calcified, loose round bodies	(partial) synovectomy
diffuse lipomatosis (lipoma arborescens)	3–6	knee	tumefaction, joint effusion	PVNS, haemangioma, haemophilia	MRI: inhomogenous fatty tumour	synovectomy
• **Benign tumours**						
giant cell tumour of the tendon sheaths	3–5	hand and foot interphalangeal joints	0.5 to 3–4 cm lobulated nodules	ganglion, fibroma, foreign body granuloma	erosion of the underlying bone	marginal excision
pigmented villonodular synovitis (PVNS)	2–5	knee, hip, shoulder, elbow	swelling,bloody effusion	haemophilia, trauma, Charcot's joint	erosions, cysts, MRI (haemosiderin-containing lesion)	excision (radiotherapy)
synovial haemangioma	1–5	knee	pain, swelling, bloody effusion	PVNS	phleboliths, occasionally bone erosion	excision, synovectomy
lipoma	2–3	knee	swelling, locking	Hoffa's disease, meniscal lesion	MRI: well-encapsulated lipomatous tumour	excision
fibroma	2–4	hand, foot	firm nodule (1–2 cm)	nodular tenosynovitis	bony erosion	excision
synovial chondroma (chondroma of the soft tissues)	3–4	hand, foot	slowly growing nodule, limitation of motion	nodular tenosynovitis, chondrosarcoma, synovial chondromatosis	lobulated, calcified nodule around the joint	excision, marginal
• **Malignant tumours**						
synovial sarcoma	2–5	lower extremity (knee, foot, thigh), hand, forearm	slowly growing nodule, pain	ganglia, cysts, other soft tissue tumours	lobulated juxta-articular tumour (amorphous calcification in 20–30%)	wide excision, myectomy (amputation)

MRI = magnetic resonance imaging.

Research agenda

- histological markers for the differentiation of benign and low-grade malignant chondroid tumours need to be investigated
- the role of surgery and radiotherapy in the management of PVNS should be elucidated
- the long-term remission rates of various surgical and radiotherapy treatment regimens need to be compared
- an analysis must take place of the role of combination chemotherapy in the management of PVNS
- chromosomal abnormalities in synovial sarcoma need to be investigated
- factors that influence prognosis and outcome in synovial sarcoma remain to be analysed
- the effectiveness of radiotherapy and chemotherapy protocols should be estimated using randomized controlled trials in synovial sarcoma patients

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