



## Synovial chondromatosis of the hip : A case report and clinicopathologic study

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Primary synovial chondromatosis (PSC) is a rare, usually monoarticular disorder of synovial joints. PSC is characterised by the formation of osteocartilaginous nodules in the synovial connective tissue. We report the case of a 32-year-old male with PSC of the left hip. At clinical examination abduction of the left hip was limited and rotation was painful. Ultrasound examination of the hip revealed joint effusion and multiple hyperechogenic foci due to distal acoustic shadowing. Plain radiographs showed a slight soft tissue swelling around the femoral neck and multiple round or ovoid calcifications of a uniform size. MRI revealed a large joint effusion with multiple small filling defects. Open total synovectomy was performed after dislocation of the femoral head. The diagnosis of PSC was confirmed by histological examination of the excised material. The majority of cells failed to exhibit any staining for c-erb B-2 and ki-67. None of the sections showed more than 5% labelling for DNA-fragmentation proven by terminal deoxytransferase-mediated dUTP nick-end labeling (TUNEL), and all were completely non-reactive for p53 as well. In conclusion, immunohistochemical analysis suggests that in this case PSC originated from metaplasia and not from a proliferative process. After two years, the patient was free of symptoms and radiological control did not show evidence of recurrence or femoral head necrosis. Physical findings, diagnosis, histological features and management of PSC are discussed.

### INTRODUCTION

PSC is characterised by the formation of osteocartilaginous nodules originating in the synovial connective tissue (21) and is believed to be caused

by synovial metaplasia (5). This theory was first published in 1900, when Reichel (27) described hyperplastic metaplasia of the synovium. In the initial stage of PSC, joint function is not significantly affected. Diagnosis is often delayed to a more advanced stage of the disease, when symptoms like pain, swelling and loss of joint movement occur. The disease may recur and malignant transformation has rarely been reported (6, 18). If left untreated, synovial chondromatosis may lead to secondary osteoarthritis due to cartilage wear. Therefore early diagnosis and treatment are mandatory to prevent disabling disease. Besides standard histological staining, immuno-labeling can be added to the diagnostic investigation.

In this paper we present a case of synovial chondromatosis of the hip joint and analyse the principles of diagnosis, histopathological findings and treatment.

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**Fig. 1.** — Ultrasound examination of the left hip showing joint effusion and a well-defined mass, containing multiple hyperechogenic foci, due mostly to mineralisation and distal acoustic shadowing.



**Fig. 2.** — Anteroposterior radiographic view of the left hip of a 30-year-old patient showing calcifications around the femoral head and neck.

## Case report

A 32-year-old man presented with a progressive inguinal swelling since approximately one month. He complained of pain around the hip and proximal thigh with weight-bearing and sitting. He denied any previous injury. Function of the left hip became increasingly impaired. Clinical examination showed limitation of abduction of the left hip and pain was elicited with internal and external rotation. Ultrasound examination of the left hip revealed joint effusion and demonstrated multiple hyperechogenic foci, mostly due to distal acoustic shadowing in areas of mineralisation (fig 1). Plain films showed slight soft tissue swelling around the femoral neck and multiple round or ovoid calcifications of a uniform size (fig 2). MRI revealed a large joint effusion with multiple small filling defects, suggestive of synovial chondromatosis (fig 3). Open total synovectomy, requiring dislocation of the femoral head, was performed. Macroscopically, innumerable glistening blue-grey nodules presented throughout the synovial surface. Nodules ranged from 2.0 mm to 1.0 cm in diameter and were firm on cut sections (fig 4 a, b). Histologically the lesions had a typical nodular architecture. Each nodule was composed of hyaline cartilage showing increased cellularity (fig 5 a, b). Chondrocytes were clustered and most had pycnotic dark-stained nuclei. Some cells had atypical features including large nuclei, dispersed chromatin and nucleoli. Mitotic figures were not identified in any of the sections. The histological appearance was compatible with synovial chondromatosis. The majority of cells failed to exhibit staining for c-erb B-2 and ki-67. None of the sections showed more than 5% labelling for DNA-fragmentation proven by terminal deoxytransferase-mediated dUTD nick-end labeling (TUNEL), and all of them were completely non-reactive for p53 as well.

Two years after surgery, the left hip is fully mobile ; radiological control shows no evidence of recurrence or femoral head necrosis.

## Immunohistochemical study

Representative specimens of PSC containing both the synovial lining and intrasynovial cartilage



**Fig. 3.** — Magnetic resonance imaging of the left hip shows a large effusion with multiple filling defects, suggestive of synovial chondromatosis ; (a,b) frontal and (c) transverse view.

were fixed in 4% paraformaldehyde at 4°C overnight and then embedded in paraffin. Sections (4 mm) were mounted onto poly-L-lysine-coated glass slides. They were dehydrated through a graded ethanol series and stained with Mayer's hematoxylin-eosin. The immunohistochemical analysis for c-erb B2- and ki67- protein expression was carried out as previously described (7). We used the technique of Terminal-transferase dUTP Nick End Labelling (ApopTag™-Kit, Oncor Appligen, Germany) to investigate for DNA fragmentation (10). Immunolabeling for p53 protein was used to detect mutations in the corresponding gene as reported previously (13). Positive and negative controls were carried out on slides from the same block (fig 6). Incubation without primary antibody served as negative control.

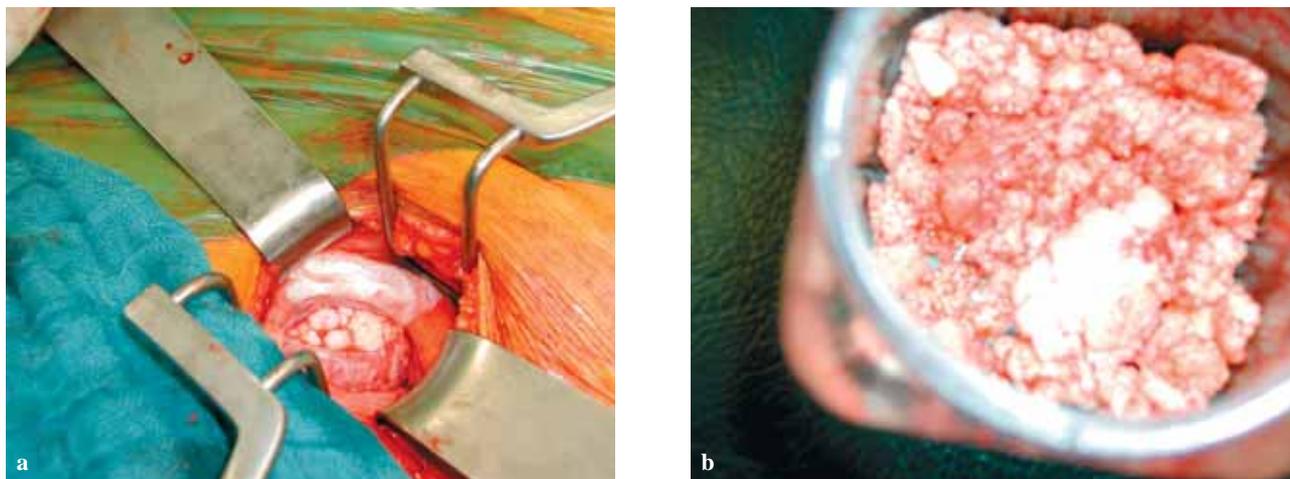
## DISCUSSION

Synovial chondromatosis is a rare benign condition characterised by cartilage formation within the synovium. Any synovial joint may be affected (25). The disease most often involves only one joint, but simultaneous appearance in several joints has been reported. Joints most often affected are the knee, hip, ankle and elbow (19). It occurs nearly always within the joints, but extra-articular disease has been described (31). There is a predilection in males, with a male-to-female ratio of 1.8:1 (6) and a peak incidence in the fifth decade (32). At physi-

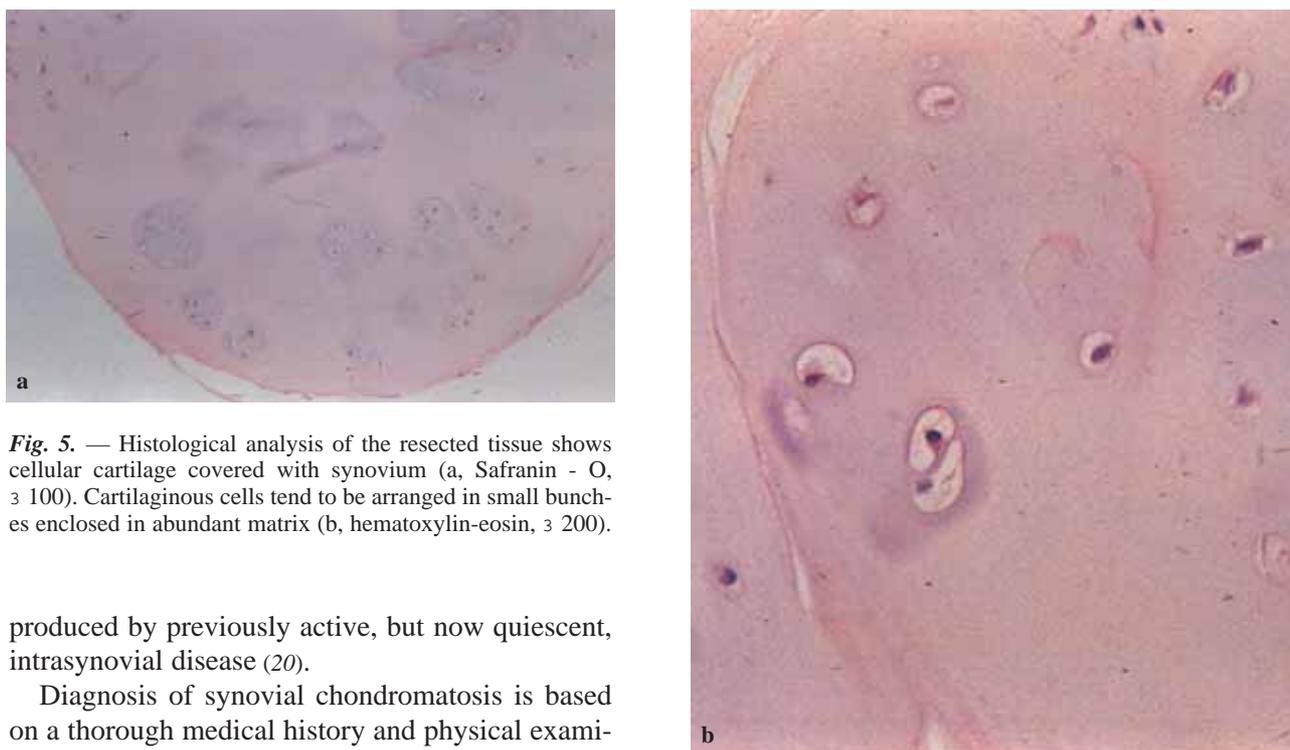
cal examination, the joint is usually swollen and the range of motion is decreased. It may be painful or painless. Intermittent giving way and locking sensation are present (5).

The aetiology of the disease is still unknown. Many theories have been formulated to explain the origin, but it has so far not been possible to pinpoint an aetiological *primum movens* (21). There is no family history and usually no convincing history of previous trauma (22).

The pathogenesis of synovial chondromatosis has been assumed to be a reactive, metaplastic process, but the prevalence of well-documented cases of chondrosarcoma originating in synovial chondromatosis gives indirect evidence for a possible neoplastic origin (11). Furthermore, the finding of fairly complex clonal structural chromosome aberrations indicate that clonal proliferation may be based on somatic mutations (19). This may lead to the conclusion that synovial chondromatosis is neoplastic rather than reactive in nature (30). The relative risk of malignant transformation (5%) is quite low at first view, but is much higher than the risk quoted for other well-organised bone diseases predisposing to malignant change (e.g. Paget's disease) (6). Chondromatosis presents three different pathological phases : (1) active intrasynovial disease with no free loose bodies ; (2) osteochondral nodules in the synovial membrane and osteochondral bodies lying free within the joint cavity ; and (3) multiple free osteochondral bodies, apparently



**Fig. 4.** — Clinical pictures during arthrotomy and synovectomy of the hip showing multiple loose bodies *in situ* under the inguinal ligament (a) and after removal (b).

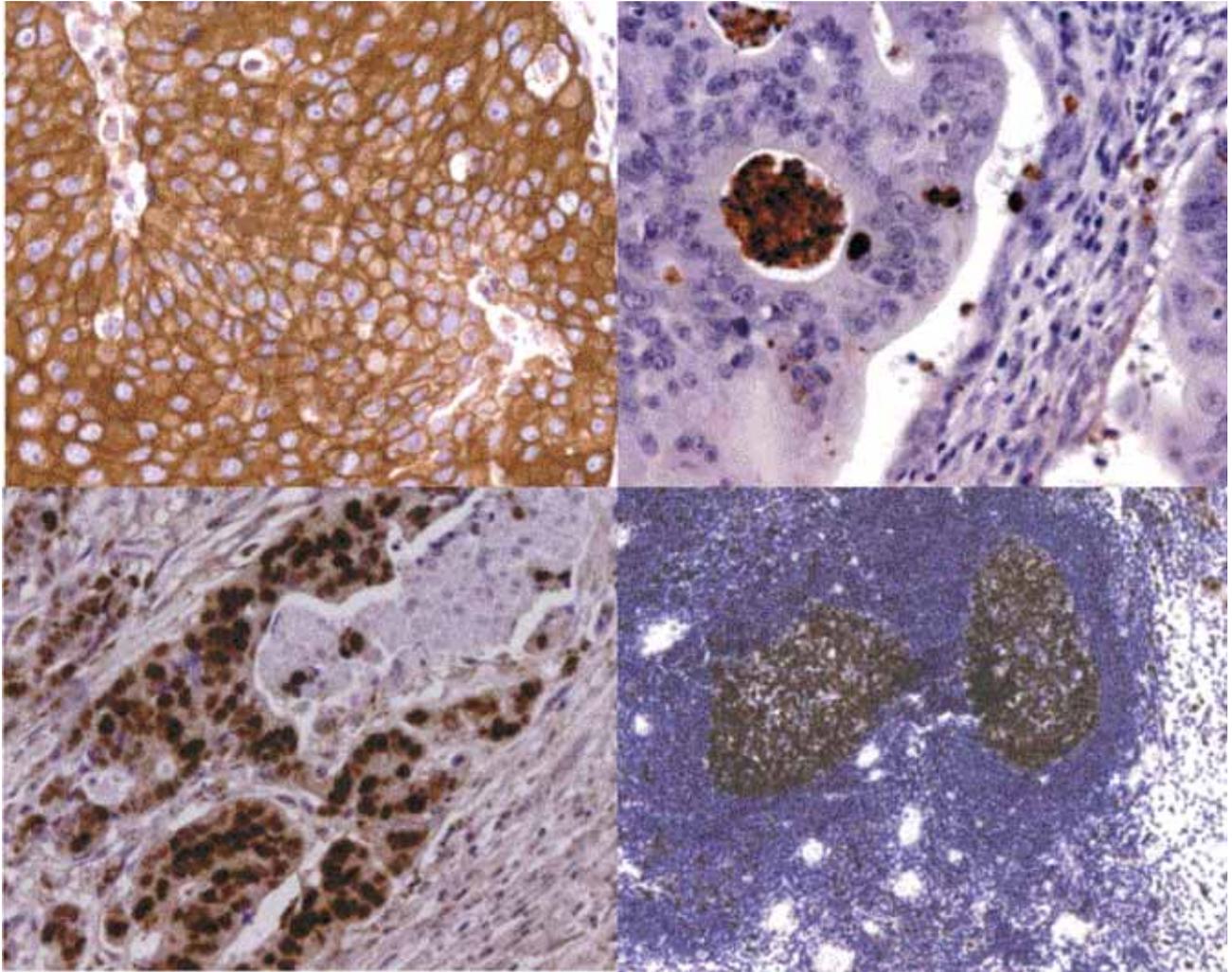


**Fig. 5.** — Histological analysis of the resected tissue shows cellular cartilage covered with synovium (a, Safranin - O,  $\times 300$ ). Cartilaginous cells tend to be arranged in small bunches enclosed in abundant matrix (b, hematoxylin-eosin,  $\times 200$ ).

produced by previously active, but now quiescent, intrasynovial disease (20).

Diagnosis of synovial chondromatosis is based on a thorough medical history and physical examination (5). Plain radiographs succeed to confirm the clinical suspicion in most cases of synovial chondromatosis of the hip joint. In the initial stages, however, the radiolucence of the metaplastic areas and loose bodies, require additional diagnostic procedures (21). Ultrasound features are typical in PSC and include a well-circumscribed peri-articular or intra-articular hypoechoic mass containing multi-

ple echogenic foci, synovial membrane thickening, widening of the joint space and secondary erosive and arthritic changes (4). Bone scintigraphy shows a non specific increased uptake of pentavalent technetium-99m dimercaptosuccinic acid (Tc-99m(V)), depending on the activity of the process (15).



**Fig. 6.** — Histologic analysis of positive controls : a, Neoplastic cells of a ductal breast carcinoma are labeled by c-erb B2 ( $\times 300$ ). b, Colon carcinoma showing p53 immunoreactivity ; chromogenic development was obtained by immersion of the sections in nickel chloride-complexed 3,3'diaminobenzidine solution ( $\times 200$ ). c, Detection of in situ DNA fragmentation by TUNEL-method in colon carcinoma. Stained cells were color-developed with diaminobenzidine and counterstained with hematoxylin ( $\times 200$ ). d, Ki-67 immunostaining; cells with sharp staining of nuclei and clear cytoplasm were designated as ki-67 positive (MIB1-antibody; lymphoid follicle;  $\times 160$ ).

Sectional imaging by computed tomography (CT) or magnetic resonance imaging (MRI) has greatly improved radiological diagnosis. CT scans reveal ossified loose bodies not visualised on plain radiographs and may show associated erosions of the hip joint. MRI, thanks to its superior contrast resolution, is useful in demonstrating the extent and boundaries of the lesion (34). On MRI the cartilaginous bodies may appear as signal voids on all

sequences and may be surrounded by bright signal intensity on T2-weighted images (33).

If left untreated, synovial chondromatosis of the hip joint may lead to secondary arthritis due to cartilage wear, resulting from both mechanical disturbance caused by the loose bodies and disturbance of the nutrition mechanism of the articular cartilage (21). Therefore early diagnosis and treatment is mandatory. The treatment of synovial

chondromatosis is surgical, but opinions differ as to its modalities. Some clinicians advocate arthroscopy and removal of loose bodies with or without synovectomy, while others recommend an arthroscopic approach (5). Simple removal of loose bodies, as proposed by McIvor and King (17), does not arrest the progression of the disease. Synovectomy is controversial, and has been considered either useless (20), harmful (12) or essential (22). Most authors recommend partial synovectomy by either the Smith-Petersen (16) or Watson-Jones approach (2) or Marino Zucchi's modified approach, less traumatic for the periarticular vascular structures (8). For complete joint clearance, especially the acetabular fossa, dislocation of the hip is necessary. The long term clinical outcome of complete synovectomy with dislocation of the hip and removal of all loose bodies is excellent; it may prevent secondary arthrosis (26). The reported incidence of osteonecrosis of the femoral head after traumatic anterior dislocation is 8% (28). But only 2 out of 43 patients with traumatic anterior hip dislocation reduced by closed methods within 3 hours, developed radiologic signs of osteonecrosis after an average follow-up of 8 years (9). It is also suggested that operative dislocation of the hip is less traumatic for the vascular structures and limits the possible ischaemic damage to the femoral head.

Arthroscopic synovectomy has been shown to be a safe and effective method of synovial ablation, and when feasible, allows faster rehabilitation (5). Kim *et al* (14) report excellent results with arthroscopic removal of loose bodies and partial synovectomy in 4 patients with synovial chondromatosis. We preferred an open procedure in this case because of the extent of synovial chondromatosis.

The recurrence rate after surgery is reported to be as high as 15%, possibly due to inadequate removal of loose bodies and synovium at the time of initial surgery (6). After two years the left hip in our case is fully mobile and presents no clinical or radiographic evidence of recurrence.

The histological features of synovial chondromatosis are nodules of hypercellular hyaline cartilage that are embedded in synovial connective tissue (31). Nodules are circumscribed and round

and demonstrate greater cellularity than articular cartilage (24). Chondrocytes typically are clustered rather than evenly distributed throughout the matrix (31). Chondrocytes with an enlarged pleomorphic nucleus are present in areas of increased cellularity. Multiple binucleate chondrocytes without mitotic figures can be identified. The degree of cellularity and nuclear atypia found in synovial chondromatosis in most cases equals or exceeds that seen in low and intermediate grade chondrosarcomas. Hence, care must be taken to avoid an erroneous diagnosis of malignant neoplasm (24).

Ki-67 antigen is a nuclear protein that is expressed in proliferating cells and has been established a reliable marker for cell proliferation. Our results of ki-67 antigen staining are in accordance with the published data (7). It is shown that the ki-67 antigen is not expressed in synovial chondromatosis. Since no proliferating cells are detected, cartilage nodules most likely derive from metaplasia (1). Staining for C-erb B-2 was negative in the present case. This finding contradicts published and unexplained positive C-erb B-2 staining in PSC (6). Members of the caspase family appear to be key proteins that mediate highly specific proteolytic cleavage patterns in cells undergoing apoptosis. Evidence also suggests a direct role of caspase-3-activated DNase in DNA fragmentation (23). The presence of DNA fragmentation, typical of apoptosis, was determined using a terminal deoxynucleotidyl transferase-mediated dUTP nick-end labeling (TUNEL) assay. None of the sections showed more than 5% labelling for DNA-fragmentation, and all of them were completely non-reactive for p53. In conclusion, the reported immunostaining results (ki67, c-erb B-2, p53, TUNEL) are in accordance with the clinical features of PSC, inasmuch as a high turnover of cells (proliferation vs. apoptosis) is mainly present in malignant tumours. But one should be careful since chondromatosis runs in several phases and immunostaining results might be different in different phases. Therefore continued experimental and clinical research on PSC is expected to elucidate if immunolabeling data can be integrated with the presently available morphological and clinical information and used as an interpretative supplement.

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