Acta orthop. Scandinav. 40, 448–460, 1969

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PIGMENTED VILLONODULAR SYNOVITIS OF JOINTS

Histological and Clinical Problems in Diagnosis

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Received 29.iii.68

Pigmented villonodular synovitis is a benign lesion located in joints, tendon sheaths, or bursae. The characteristics of the lesion and its identity in relation to other pathological synovial states were described by Jaffe, Lichtenstein & Sutro in 1941. Previously, and even nowadays, however, several other diagnostic terms are encountered, many of them confusing, *e.g.* xanthoma, xanthogranuloma, giant-cell tumor, benign giant-cell synovioma, fibrohemosideric sarcoma, polymorpho-cellular tumor of the synovial membrane. All these names refer in various ways to the complex histological picture. Jaffe et al. combined the various components into a single entity, with the microscopical characteristics of pronounced hyperplasia and proliferation of synovial cells and undifferentiated connective-tissue cells in the synovial membrane. The cells contain varying amounts of hemosiderin pigment and/or lipid granules. Multinuclear giant cells are also encountered in varying numbers. Macroscopically, the lesion takes the form of nodular, tumorous, reddish-brown or yellowish-brown excrescenses of the synovial membrane, usually diffuse in a joint but more localized in a tendon sheath.

Lesions of this type are fairly common in tendon sheaths of the fingers and toes. Pigmented villonodular synovitis of joints, on the other hand, is a rare complaint. The lesion is always monoarticular, the knee joint being by far the most common location. In a review of the literature, Smith & Pugh (1962) found 202 published cases of pigmented villonodular synovitis (including seventeen of their own) with the following locations: knee joint 164, ankle joint 14, hip joint 12, tarsal joints 4, carpal joints 4, elbow joint 3, and shoulder joint 1 case. Most individual reports comprise only a few cases. Larger series have

been published, for instance, by Jaffe (1958) 25 cases; Smith & Pugh (1962) 17 cases; Nilsonne (1966) 16 cases; De Santo & Wilson (1939) 9 cases; Wright (1951) 8 cases; and McMaster (1960) 6 cases.

As the majority of authors have pointed out, it may be difficult to make a differential diagnosis between pigmented villonodular synovitis and other lesions, particularly synovial sarcoma. An incorrect diagnosis may result in the wrong treatment. The consequences will be particularly serious if a pigmented villonodular synovitis, which is a benign lesion, is treated as a malignant disease. The purpose of the present paper is therefore to analyze the histological and clinical criteria for the diagnosis pigmented villonodular synovitis.

MATERIAL

The material comprises 29 cases of pigmented villonodular synovitis of a joint. This was the primary diagnosis in 14 of the cases; the others have been reclassified. The primary diagnosis was thus synovial sarcoma in 10, nine of which come from a basic material of one hundred and sixty synovial tumors that was used by Moberger, Nilsonne & Friberg, Jr. (1968) for a study of ninety cases of synovial sarcoma. The primary diagnosis in 3 other cases was chronic unspecific synovitis and in 2 cases giant-cell xanthoma.

The distributions by sex, age, and location are shown in Figure 1. The female: male ratio was 20:9. All age groups are represented, though more than half of the cases concern individuals between 20 and 50 years of age. The knee joint was affected most often, 19 cases; whereas the hip joint was represented in 4 cases, the ankle joint in 3, the wrist joint in 2, and the metatarsophangeal joint in 1 case.

SURVEY OF CLINICAL CASES

Hip Joint, 4 Cases

Pain was the predominant symptom in pigmented villonodular synovitis located in the hip joint. The pain emanated from deep in the groin

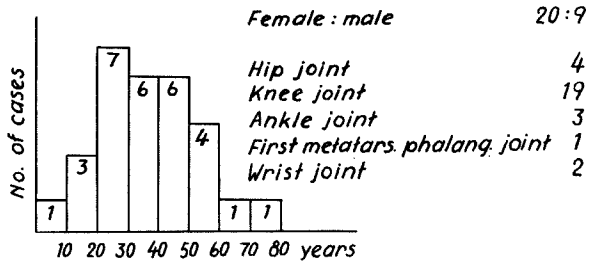
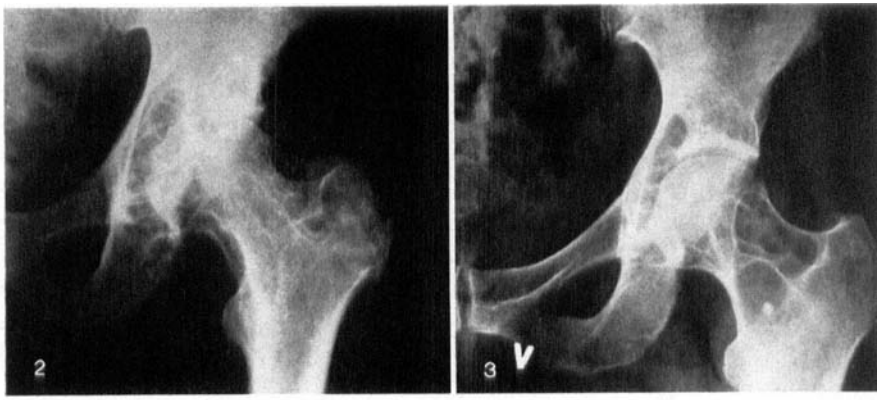


Figure 1. Distribution by sex, age, and localization of 29 cases of pigmented villonodular synovitis of joints.



Figures 2–4. Roentgenograms of pigmented villonodular synovitis in the hip joint showing cyst-like lesions of varying size in the femoral head and neck as well as in the acetabulum.

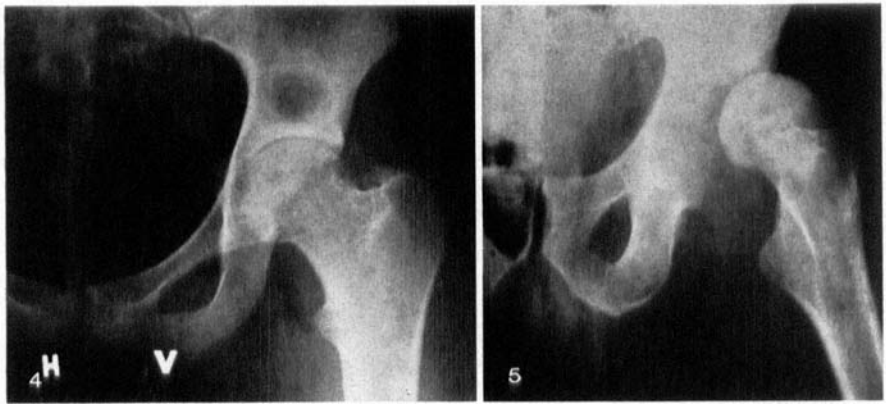


Figure 5. Pigmented villonodular synovitis in the hip joint with dislocation of the femoral head (see text).

and the proximal part of the thigh, occurring chiefly on movement and weight-bearing but not as a rule at rest. The pain also varied in intensity. The clinical examination showed slight to moderate impairment of hip-joint mobility. In one case the clinical picture was reminiscent of septic arthritis, with severe pain and pronounced swelling in the hip.

The X-ray examination (Figures 2–4) showed multiple well-defined cyst-like changes in the femoral head and neck as well as in the acetabulum, chiefly in its medial and distal parts. The articular cartilage was moderately reduced but the outline of the femoral head was unchanged. In the case with a clinical resemblance to septic arthritis, the

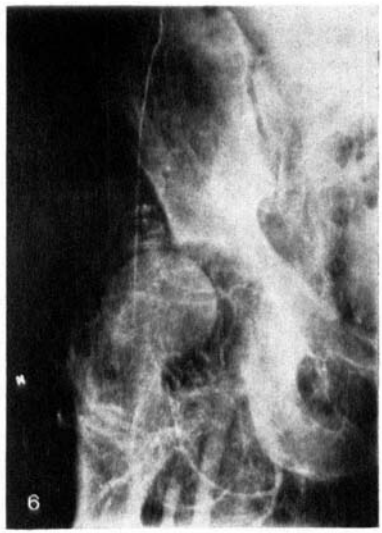


Figure 6. Arteriography of the case in Figure 5. Late arterial phase, marked hypervascularity. Tortous vessels of varying caliber are seen. Pathological arterio-venous shunt is noted.

X-ray picture could also be interpreted in the same way (Figure 5). The joint was distended by a large exudate that had dislocated the femoral head, in which small cysts were noted. Diffuse, irregular destruction was observed in the acetabulum. Arteriography (Figure 6) showed hypervascularization, tortuous vessels, and pathological arterio-venous shunting, indicating the presence of a neoplastic condition.

The preoperative diagnosis was pigmented villonodular synovitis in the case illustrated in Figure 4, and tumor or osteoarthritis was suspected in the other cases.

At operation, the first three cases presented a diffuse intra-articular transformation of the joint capsule, which was greatly thickened, villous, and reddish brown. Erosion was found both in the acetabulum and the femoral neck. The intra-articular destruction was particularly pronounced in the fourth case, in which a yellowish-brown, villous tissue had caused marked erosion of the bone besides occurring unattached in the exudate.

A histo-pathological diagnosis of pigmented villonodular synovitis was made on resected tissue in all 4 cases.

Knee Joint, 19 Cases

Moderate pain and swelling of the knee joint were typical symptoms in these cases. In 5 of them, the symptoms first appeared in close connection with direct trauma (without fracture) to the knee. In the other

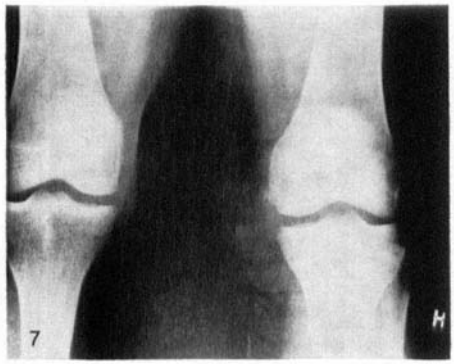


Figure 7. Pigmented villonodular synovitis in the knee joint. Marked medial soft-tissue swelling (the knee to the right in the picture).

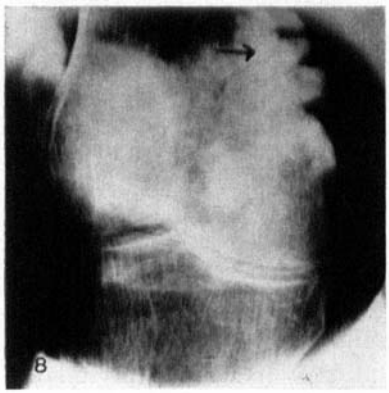


Figure 8. Arthrogram of pigmented villonodular synovitis in the knee joint. Filling defects in the form of villonodular protrusions from the synovial wall are demonstrated (arrow).

cases, there was no known trauma or else the patient described an insignificant trauma many years previously. Aspiration of the joint demonstrated hemarthrosis in nine cases. A palpable resistance, interpreted as a tumor, was found in the suprapatellar region in 4 cases, at the level of the joint cavity in 2 cases, and in the popliteal space in 4 cases. Intra-articular obstruction was indicated by locking of the knee in 5 cases.

The radiographic appearance varied widely. Nothing abnormal was seen in 8 cases, whereas 6 cases resembled an insignificant and nonspecific osteoarthritis of the joint. More pronounced swelling of soft tissues was registered in 2 cases (Figure 7); and cyst-like changes in the bone ends of the joint in 2 cases, one of which also presented a cystic destruction of the head of the fibula. No X-ray examination was performed in one case. Arthrography revealed villonodulous contrast defects in four of the five cases in which it was performed (Figure 8).

The preoperative diagnosis was pigmented villonodular synovitis in only one case. In the majority of cases, the operation was undertaken on a diagnosis of chronic unspecific synovitis or bursitis. In 5 cases it was thought that the meniscus had ruptured. A malignant tumor was suspected in 3 cases.

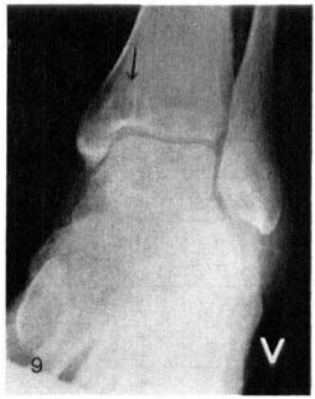


Figure 9. Pigmented villonodular synovitis in the ankle joint. Small cysts in the tibia (arrow). Slight soft tissue swelling distal to the lateral malleolus.

At operation, all the cases presented hyperplastic, reddish-brown, hemorrhagic synovialis. The changes were chiefly located to the supratellar bursa in 2 cases, and the semimembranosus bursa in another 2; whereas localized, pedicled intra-articular formations were found in 1 case. The other cases presented a diffuse intra-articular process.

A primary histopathological diagnosis of synovial sarcoma was made on resected tissue in 5 cases.

Ankle Joint, 3 Cases

In 2 of these cases, a palpable resistance anterior to the joint was interpreted as a ganglion or tumor. The third case had a swelling and tenderness on palpation just distal of the lateral malleolus. In view of an early trauma, this was thought to represent a ruptured ligament.

The X-ray examination showed normal conditions in 1 case and bony destruction of the articular ends as well as of the cuneiform bones in 1 case. In the latter case arteriography demonstrated pathological vessels with arterio-venous shunting. In the supposedly post-traumatic case the roentgenographic picture (Figure 9) demonstrated small cysts in the tibia and slight soft-tissue swelling of the lateral part of the joint.

A primary histopathological diagnosis of synovial sarcoma was made on resected tissue in 2 cases.

First Metatarsophalangeal Joint, 1 Case

The symptom in this case was a tender resistance on the dorsal side of the first metatarsophalangeal joint. Biopsy showed intra-articular proliferation of reddish-brown tissue. The primary histopathological diagnosis was synovial sarcoma.

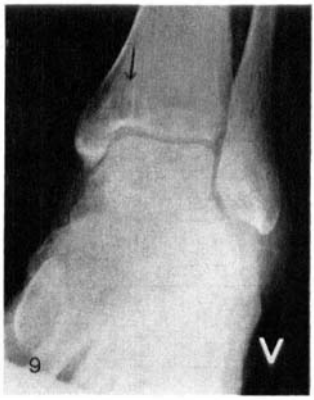


Figure 10. Pigmented villonodular synovitis in the wrist joint showing small cysts in the capitate bone.

Wrist Joint, 2 Cases

In both these cases, a resistance on the dorsal side of the wrist joint was interpreted as a ganglion. An X-ray examination showed small cyst-like changes in the capitate bone in one of these cases (Figure 10). The primary histopathological diagnosis was synovial sarcoma in both cases.

EFFECTS OF ERRONEOUS PRIMARY DIAGNOSIS

As indicated above, an erroneous primary diagnosis of synovial sarcoma was made in 10 cases altogether. This resulted in amputation in 5 of these cases: at the thigh in two, at the lower leg in three. Two of the amputated patients were subsequently found to have been registered as having died from metastases of synovial sarcoma, in both cases 7 years after the operation. On reclassification, however, it was found that the cause of death was primary lung cancer.

In another 2 cases, complications arose because irradiation therapy was given for the supposedly malignant process. In one of these cases, the patient incurred a pathological fracture of the distal femur. A biopsy undertaken in connection with open reduction of the fracture showed necrotic osseous tissue. Although the fracture ultimately healed, the patient was permanently disabled. In the other case, a severe local skin reaction resulted in many years of discomfort from recurrent dermatitis.

The remaining 3 cases also received local irradiation therapy but no complications materialized.

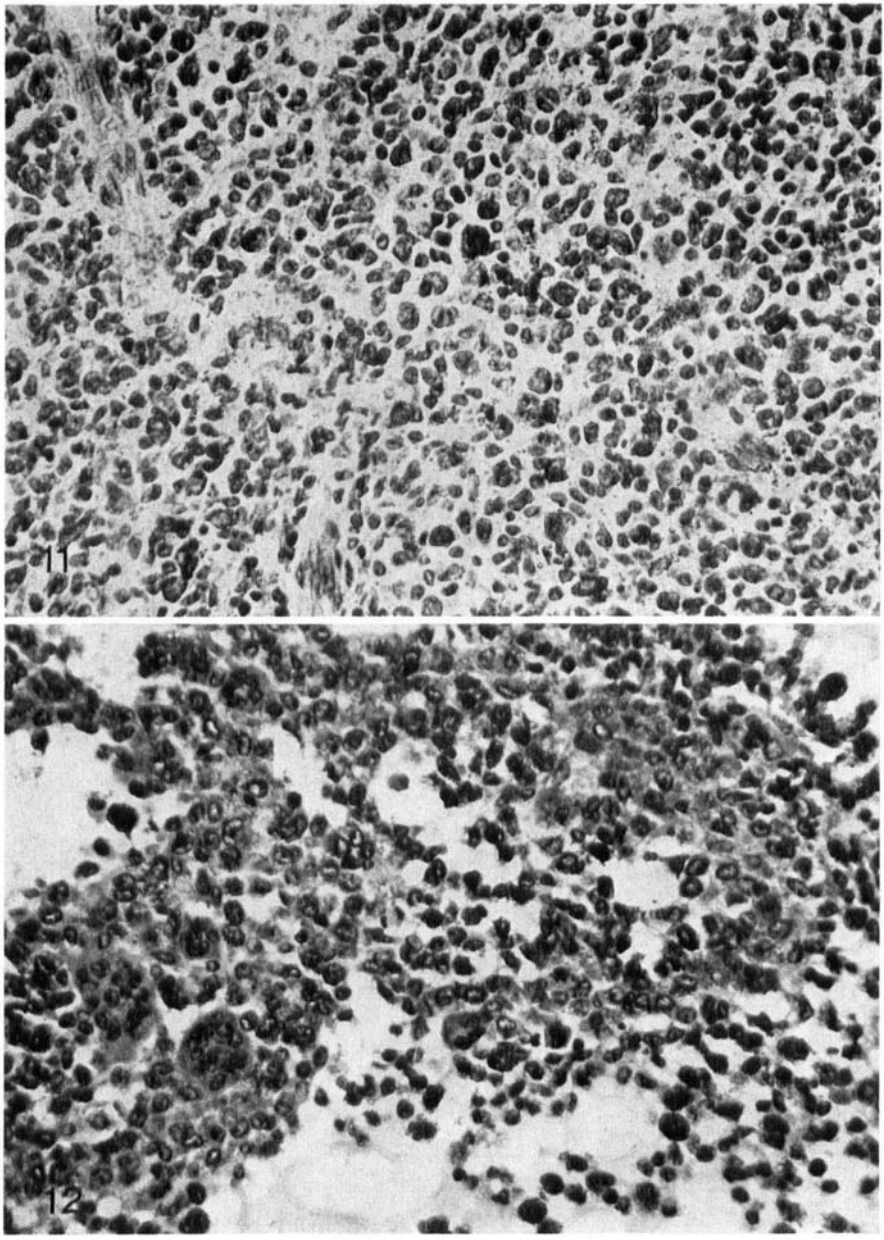


Figure 11. Pigmented villonodular synovitis. Photomicrograph × 150. Granulomatous, highly cellular proliferations with scattered multinucleated giant cells.

Figure 12. Pigmented villonodular synovitis. Photomicrograph × 400. Tendency to increased dissociation of individual cells and numerous multinucleated giant cells.

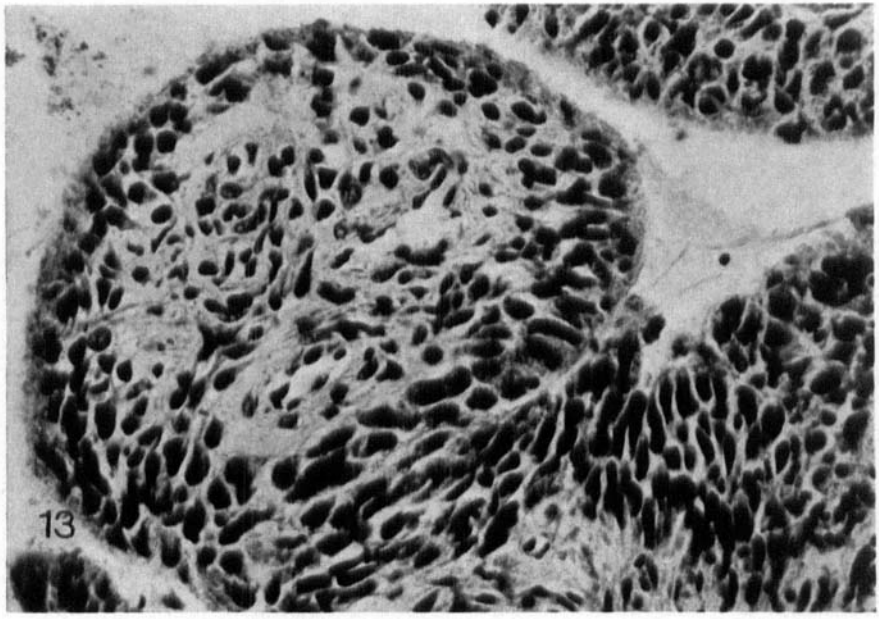


Figure 13. Pigmented villonodular synovitis. Photomicrograph × 400. Marked proliferation of the synovial cells lining the surface of the synovial membrane.

DIAGNOSTIC COMMENTS

Histology

Histologically, the synovial tissue in pigmented villonodular synovitis is characterized by enlarged, plump synovial excresences bulging into the joint cavity. Both these excresences and the tissue of the joint capsule that encloses them present a process with an abundance of cells which in principle resembles the tissue of a hyperplastic granuloma. The cell structure is reminiscent of that in so-called giant-cell tumors in tendon sheaths, though the cells are usually considerably more numerous (Figure 11). This great cellularity means that the process is readily mistaken for a tumor. The cell proliferation, however, is characterized by the presence of phagocytic elements, many of them containing lipid granules and hemosiderin pigment. The presence of numerous phagocytes of this type, often in clusters, is such a common phenomenon that the finding is of diagnostic importance. There are also multinuclear giant cells (Lichtenstein 1955) of the so-called foreign-body type. Another characteristic is the marked tendency to dissociation of the individual cells in the highly cellular process (Fig-

ure 12), which distinguishes this from synovial sarcoma. The number of lymphocytes varies, but usually they account for only a small proportion of the cells.

The highly variegated pattern of the abundantly cellular proliferation may make this deceptively like a pronounced cellular polymorphism. The synovial lining cells frequently display a marked tendency to proliferation (Figure 13) and the zone of transition to the granulomatous process may be indefinite. This may further strengthen the suspicion of a neoplastic process, particularly as some degree of cell atypia may be displayed in the proliferations of synovial cells (Wright 1952, Geiler 1961). On the other hand, the presence of giant cells, hemosiderin pigment, and dissociation tendencies are indicative criteria for the histological diagnosis. There may be necrosis against the surfaces of the joint but the picture does not include specific, inflammatory granulomatous tissue.

CLINICAL ASPECTS

Pigmented villonodular synovitis can hardly be diagnosed from the clinical or the radiographic examination alone. As indicated in the clinical survey above, the first clinical diagnosis proposed is usually unspecific synovitis, osteoarthritis, or tumor.

It used to be thought that the radiographic examination of these cases could simply show swelling of soft tissues as a sign of an excessive synovitis. Bony involvement was held to point to a synovial sarcoma (Lewis 1947). As the number of published cases increased (Breimer & Freiberger 1958, McMaster 1960), it was found that skeletal changes may occur in pigmented villonodular synovitis as well. Smith & Pugh (1962), for instance, report that osseous changes are present in about half of the cases. As demonstrated in the clinical survey of our cases, the lesions often appear as well-defined single or multiple cystic cavities in the bone ends of the joint. There may even be skeletal erosion suggestive of a malignant process, especially in the hip joint.

In the case of the knee joint, a chronic or recurrent swelling *with* hemarthrosis but *without* trauma should suggest the possibility of a pigmented villonodular synovitis. At exploration, a good macroscopic sign is the reddish-brown, thickened, and bearded appearance of the synovial membrane in an entirely intra-articular lesion. Synovial sarcomas, on the other hand, are almost always extra-articular, only 3

exceptions being found in a series of 90 by Moberger, Nilsonne & Friberg, Jr. (1968). Hemarthrosis and villous, intra-articular synovial excrescences with a brown pigmentation are thus very strong indications of a pigmented villonodular synovitis. Conversely, a histopathological diagnosis of synovial sarcoma should be regarded with suspicion if the change is intra-articular. The preoperative assessment of the lesion in relation to the joint cavity may be facilitated by the use of arthrography, cf. Rein et al. (1964) and some of the present cases. The nodular synovitis may then appear as defects in the contrast picture of the joint, whereas this would not be the case with an extra-articular process.

The radiographic picture in pigmented villonodular synovitis in the hip joint is characterized by multiple cysts in the acetabulum and the femoral head and neck. The appearance may resemble osteoarthritis of the hip and there may also be similarities in the clinical symptoms. In pigmented villonodular synovitis, the cysts in the acetabulum are chiefly located in the medial and distal parts of the joint, whereas in osteoarthritis they are usually located to the cranio-lateral part. Osteoarthritis involves deformation of the femoral head, whereas the outline of this is generally unchanged in cases of pigmented villonodular synovitis. These observations are in accordance with a report by Chung & Janes (1965).

The case illustrated in Fig. 5 had the clinical and radiographic appearance of a septic arthritis and should be regarded as an unusual manifestation. In some respects, however, it resembles a case published by Carr et al. (1954), in which a large retroperitoneal, synovial cyst originated from and was in open communication with the hip joint. Arthrotomy revealed considerable villonodular distruction of all the articular components. This description is identical with the findings at operation in our case, except that here the joint capsule was enormously distended. This may represent an alternative outcome of an increased intra-articular pressure, which in Carr's case resulted in herniation of the joint capsule.

Arteriography was performed in two cases in the present series, showing marked hypervascularity and pathological vessels in the lesional region. Similar findings were reported by Rein et al. in 1 case of pigmented villonodular synovitis of the knee joint. The presence of pathological vessels, however, is an unreliable indication of malignancy which should not be allowed to influence the pathologist's assessment of tissue specimens.

As far as pigmented villonodular synovitis in other joints than the knee and hip are concerned, the number of cases is still too small to indicate the principles for clinical diagnosis. The presence of the typical, intra-articular tissue described above and the appearance of cyst-like bony changes in roentgenograms should, however, guard the diagnosis.

DIAGNOSTIC CONCLUSIONS

Intra-articular lesions, particularly in the knee joint, that present the macroscopic appearance of a hyperplastic, villous synovial membrane with brown pigmentation should be suspected of representing pigmented villonodular synovitis. The diagnosis can be confirmed on the following microscopic criteria: cell-rich, granulomatous process with variegated cells and the presence of multinuclear giant cells as well as (clusters of) phagocytes containing hemosiderin pigment. The tendency towards differentiation of the individual cells in the cell proliferation may be a particularly important criterion in the differential diagnosis with synovial sarcoma. The great cellularity of the process may deceive the less-experienced pathologist into interpreting the picture as that of a malignant tumor, primarily a synovial sarcoma. A histological study of 160 cases with the primary diagnosis of synovial tumor (Moberger, Nilsonne & Friberg, Jr.) has shown that pigmented villonodular synovitis presents a characteristic cell picture. In particular, it may be noted that multinuclear giant cells do not occur in the malignant synovial tumors and that hemosiderin pigmented phagocytes only occur in extremely rare cases.

SUMMARY

The histological and clinical criteria are presented for the diagnosis of pigmented villonodular synovitis of joints in a study of 29 cases of the lesion. Special reference is made to the differential diagnosis with synovial sarcoma. Emphasis must be placed on the necessity of close cooperation between the orthopedic surgeon, the roentgenologist, and the pathologist in the diagnostic evaluation of these cases.

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