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LOCAL AMYLOID FORMATION IN THE HIP JOINT CAPSULE IN OSTEOARTHRITIS

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In osteoarthritis there are joint-capsule changes without any specific characteristics corresponding to the findings in traumatic synovitis, due partially to detritus in the joint (Hultén & Gellerstedt 1940, Roy 1967). In advanced cases there is a fibrous thickening and villous hypertrophy, at times focal cartilaginous or osteochondromatous metaplasia (Sokoloff 1969).

In the course of total reconstruction of the hip done by the method of Charnley for osteoarthritis in October 1970, we found macroscopic suspicion of chondromatosis. The microscopic examination was performed by a pathologist with special experience of amyloidosis (H.E.C.), who found amyloid in the fibrous capsule.

We therefore initiated a study on the occurrence of amyloid by a systematic study of the hip-joint capsules from all patients undergoing total reconstruction of the hip joint by the method of Charnley.

MATERIAL AND METHODS

From November 1970 to May 1972 total reconstruction of the hip joint by the Charnley method was performed in 60 cases with systematic investigation of the joint capsule for myeloid.

During the operation we anteriorly removed a fairly large piece of the hip-joint capsule, which comprised the fibrous as well as synovial capsule. The specimen was immediately fixed in neutral formalin 10 per cent for 24 hours, thereafter cut into 10–20 blocks 2–3 mm thick, embedded in paraffin, and cut into 6 μ slices stained routinely with haematoxylin-eosin, alkaline Congo red, and picric acid-fuchsin (van Gieson). All sections were systematically examined. In the presence of amyloid the preparations stained with alkaline Congo red show a characteristic orange-red. As a criterion of the presence of amyloid we also demanded that microscopic examination of these areas in polarized light show double refraction and green dichroism. This test is specific and very sensitive. In some cases special studies were carried out (Christensen & Sørensen 1972).

Table 1. Diagnosis of hip joint disease in 32 males and 24 females.

	Males	Females	Total	Hip Joints
Osteoarthritis of the hip	29	18	47	51
Fracture of femoral neck with necrosis of head	1	2	3	3
Rheumatoid arthritis	–	2	2	2
Spondylarthritis (Bechterew)				
Gouty arthritis				
Seq.to Calve-Perthes' disease	2	2	4	4
Seq.to epiphysiolysis of fem. head				
Total	32	24	56	60

RESULTS

From Table 1 it is apparent that among the 60 cases studied, 2 had rheumatoid arthritis, 1 spondylarthritis, 2 sequelae to Calvé-Perthes' disease and epiphysiolysis respectively. None of these joint capsules contained amyloid. One patient with gouty arthitis had large amounts of amyloid in the joint capsule. Among 3 patients with necrosis of the femoral head after fracture of the neck, only one had moderate quantities of amyloid in the joint capsule.

Below, only the findings in the 47 patients with 51 hip joints operated upon for osteoarthritis will be described.

Table 2. Amyloid in the hip-joint capsule in osteoarthritis.

	Number of Hip Joints			
	Males		Females	
Amyloid	+	—	+	—
Symptoms for less than 10 years	5	9	3	8
Symptoms for more than 10 years	9	9	0	8
Total	14	18	3	16
	44%		16%	
Age, 45–59 years	5	7	0	5
Age, 60–69 years	8	9	0	8
Age, 70–78 years	1	2	3	3

It may be seen from Table 2 that in 17, or 33 per cent of the studied hip joints, deposition of amyloid was found in the fibrous capsule, almost three times as often in men as in women. No correlation was found between the duration of symptoms and the deposition of amyloid.

There was also no definite relationship between age and occurrence of amyloid. The mean age and age distribution were the same for the 14 men with and the 18 without amyloid deposits, viz. 62 years.

Clinically the severity of the osteoarthritis is stated, according to Merle d'Aubigné & Postel (1954) in the modification of Charnley, as three figures: for pain, walking ability, and mobility, graded from 1 to 6. The degree of severity was found to be exactly the same for the 14 men with and the 18 men without amyloid in the hip-joint capsule. All the figures averaged 2.1–2.8, and the difference between the three figures in the two groups did not exceed 0.3. Bilateral osteoarthritis of the hip occurred in 18 men, with 21 operated hips. Amyloid was found in 11 hips. Thus, there is no relationship between the severity of the osteoarthritis and the presence of amyloid in the joint capsule.

Table 3. Degree of amyloidosis, hyalinization and inflammation of the hip joint capsule.

Degree	—	+	++	+++
Amyloid	34	8	2	7
Hyalinization	14	7	10	20
Inflammation	11	18	11	11

Table 4. Incidence of hyalinization or inflammation in the presence of amyloid in the hip joint capsule.

	Amyloid	
	—	+
No hyalinization	9	5
Hyalinization	25	12
No inflammation	2	9
Inflammation	32	8

Histologically the quantity of amyloid as well as the degree of hyalinization and inflammation were assessed (Table 3). No relationship was found between duration of symptoms and age on the one hand and the quantity of amyloid on the other.

Hyalinization and inflammation are generally not combined with deposition of amyloid (Table 4), but if amyloid is present there is generally also hyalinization. When hyalinization is present, there is usually also inflammation (in a total of 28 cases). Deposition of amyloid is rare in inflammation.

As in other types of amyloidosis, a PAS positive reaction (PAS = periodic acid-Schiff: oxygenation of the tissue with periodic acid followed by staining with Schiff's reagent) was found histochemically, indicating the presence of glucoproteins. Toluidine blue staining showed metachromasia at two different pH's. Alcian blue-van Gieson staining showed a greater variation in the reaction, the already localized amyloid areas giving a negative as well as a highly positive reaction, most often negative centrally and positive peripherally.

DISCUSSION

Amyloid is an eosinophilic hyaline, foreign material characterized by certain staining properties. It is a protein-carbohydrate compound with little lipid content. The protein makes up about 85 per cent and is of globulin nature, two-thirds being glucoprotein and the remainder acid mucopolysaccharide as connective tissue ground substance. Amyloid is difficult to analyse chemically and almost insoluble, not dissolving until reaching a pH of 11.5 (Christensen 1963).

Teilum (1969) has advanced the so-called biphasic cellular theory concerning the pathogenesis of amyloid deposition. In histochemical studies on caseinate-induced amyloidosis in mice, amyloidosis is present as a product of PAS-positive reticuloendothelial cells *in situ*. A primary, pyroninophilic phase, with proliferation of pyroninophilic cells and plasma cells and an increase in serum globulin, is followed by a secondary amyloid phase with successive inhibition of the pyroninophilia and the occurrence of PAS-positive reticuloendothelial cells in rapid succession in the marginal zone of the amyloid aggregates which rapidly develop in acceleration experiments. The PAS-positive cells perish immediately after local amyloid synthesis has taken place. Amyloid is deposited intracellularly. Nitrogen mustard and cortisone exert a highly accelerating effect upon the amyloid formation if administered after some weeks' stimulation by sodium caseinate.

Amyloid is encountered in primary and secondary, systematized amyloidosis, myelomatosis, familially, and locally, especially in the larynx, heart, and skin, and as amyloidosis of old age. In rheumatoid

arthritis amyloidosis is common when the disease has lasted for more than five years. In such cases amyoid occurs most often in the kidneys, liver, and spleen (Cohen 1968).

So far amyloid deposits in joint capsules have been reported only in myelomatosis (Lichtenstein & Jaffe, 1947). However, Laine et al. (1955) have demonstrated amyloid in joint capsules of patients with rheumatoid arthritis. With our technique we have not yet succeeded in confirming their findings.

To exclude myelomatosis and rheumatoid arthritis, systematic studies were carried out on 29 patients with 33 operated hips. These studies comprised sternal puncture, rectal biopsy, serological tests for rheumatoid arthritis, electrophoretic studies of serum proteins including immunoelectrophoresis, investigation for Bence Jones' protein, and clinical examination of all limb joints. In all cases myelomatosis and rheumatoid arthritis were excluded, and no amyloid was found in the bone marrow or rectum with our technique. In our series 9 of the 18 men and 2 of the 11 women had amyloid in the hip-joint capsule, 5 of the males large quantities. From 43 operated hips we studied bone marrow from the femoral neck. No amyloid was found. None of the 47 patients of the total material had rheumatoid arthritis.

Owing to the experimentally demonstrated accelerating effect of cortisone medication upon amyloid formation, we investigated whether previous injections of hydrocortisone into the hip had influenced the amyloid deposition. Six men and 5 women had received such injections. The joint capsules of the 5 women did not contain amyloid, but this was found in the joint capsules of 3 of the 6 men. These 3 men had received 2, 13, and 15 injections respectively. The patient who had received 13 injections had small amounts of amyloid in the subsynovial tissue. This localization was also found in a patient who had not received injections of hydrocortisone. A few of the patients had received many injections of hydrocortisone, but did not have amyloid in the hip-joint capsule. Thus, the amyloid deposition cannot have been by injection of hydrocortisone, as only 3 out of 17 patients with amyloid in the joint capsule had a history of such injections.

Amyloidosis may be induced in mice by injection of chondroitin sulphuric acid (Schmitz-Moorman 1968). In osteoarthritis of the hip, it may be imagined that chondroitin sulphuric acid may be liberated from the cartilaginous substance by the severe cartilaginous degeneration in which the cartilage is literally scrubbed off. Deposition of amyloid is closely bound up with tissue degeneration.

SUMMARY

At the Department of Orthopaedic Surgery and the Institute of Pathology of the Odense Hospital, Denmark, biopsies from 60 hip-joint capsules, removed in the course of total hip-joint reconstruction by the Charnley method, were studied from November 1970 to May 1972. Among 51 cases of hip-joint osteoarthritis, 17 exhibited histological signs of amyloid deposition in the fibrous capsule after staining with alkaline Congo red and demonstration of green dichroism in polarized light. Amyloid was found to be 3 times more common in males than in females. There was no correlation between age, duration or severity of the osteoarthritis, and the occurrence of amyloid or its quantity, and there was no correlation between amyloid and the possible coexistence of hyalinization or inflammation. Only 3 of the 17 patients had a history of hydrocortisone injection into the joint. By rectal biopsy, bone marrow study, serological tests for rheumatoid arthritis, and serum protein study as well as clinical examination, rheumatoid arthritis and myelomatosis were excluded by systematic investigation of 29 patients with 33 operated hips. There were no clinical signs of rheumatoid arthritis in any case. Thus, the deposition of amyloid must be a purely local phenomenon, perhaps induced by chondroitin sulphuric acid liberated from the cartilaginous substance in the degenerated articular cartilage. Local amyloid deposits have not previously been demonstrated in the joint capsule in osteoarthritis.

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