Synovia hyperplasia and calcification in the human TMJ disk

A clinical, surgical, and histologic study

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The aim of the study was to investigate the morphologic modifications occurring in the synovial tissue after severe derangement of the articular structures with dislocation or perforation of the disks. Light microscopic, ultrastructural, and immunocytochemical investigations were performed on 10 disks. Arthroscopic examinations had documented adhesions between the diskal surfaces and the glenoid eminence or the condylar head in all the selected cases. Histologic examination showed a remarkable hyperplasia of the synovial tissue with the formation of prominent protrusions. An evident increase of type B (fibroblast-like) cells and the presence of cells with the ultrastructural and immunocytochemical characteristics of myofibroblasts were observed. Foci of mineral precipitates and large deposits of calcified tissue were present in the synovial villi in three samples. Our observations suggest that functional failure and morphologic lesions of the synovia may be caused by arthropathy. **(Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1997;84:245-52)**

The synovial tissues play a fundamental role in maintaining the correct functioning of the articular components of a joint by the production and metabolic exchange of synovial fluids.

Interest has recently increased in the capacity of the synovia to accommodate and react to articular disorders and alterations in the relationships among joint components.[1-6]

The presence of cathepsins, particularly cathepsin L, was demonstrated in type A cells (macrophage-like cells) in the synovial lining in the normal temporomandibular joint (TMJ). This finding suggested that these cells digest components such as collagen and proteoglycan fragments present in the joint cavities.[7] Variations in the synovial fluid such as an increase in hydrostatic synovial fluid pressure have been observed in patients with altered mandibular positions.[8] Moreover, elevated tumor necrosis factor levels were found occurring in the TMJ disk displacement or in other degenerative joint diseases.[9] These observations suggested that synovial tissue and fluid may have a role also in the pathogenesis of some TMJ disorders through modifications of the intraarticular dynamics.

This research was supported by grants from the Italian Ministry of University and Scientific and Technological Research (MURST).

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Received for publication Dec. 4, 1996; returned for revision Jan. 23, 1997; accepted for publication Apr. 8, 1997.

1079-2104/97/$5.00 + 0 **7/12/82603**

In previous investigations of the morphologic modifications of the articular disk in patients with different articular pathologies, we frequently observed an involvement of the synovial layer as well.[10-12]

Therefore in the present study we investigated further the structural modifications that occur in the synovial tissue after articular arthropathy. The aim of this study was to find possible correlations between structural lesions and functional modifications.

MATERIAL AND METHODS

Investigation was performed on diskal and synovial tissues from 10 subjects belonging to a larger group of patients with TMJ arthropathy (Table I) and examined in the last 5 years at the Maxillo-Facial Surgery Division of the San Bortolo Hospital of Vicenza in Italy. The 10 patients were selected because of the hyperemic and hyperplastic aspect of the synovia observed during arthroscopy.

Diagnostic and therapeutic protocol consisted first of clinical examinations, tomography, and then of physical and bite therapy. The patients who did not respond to this conservative therapy were submitted to radiologic investigations (computed tomography [CT], magnetic resonance imaging [MRI] and Cine-MRI). The patients with a long period of articular pain and clinical signs and radiologic features of TMJ dysfunctions with internal derangement were submitted to arthroscopy. After this last examination those patients with pathologic features considered curable only by surgical therapy were submitted to TMJ arthrotomy.

At the clinical examination of the 10 patients with disks that were examined for this study, we observed many stigmata of TMJ dysfunction such as deviation

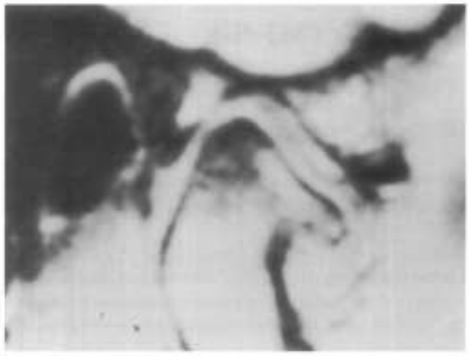

Fig. 1. NMR test of right TMJ of patient occlusion shows remodelling of condylar head.

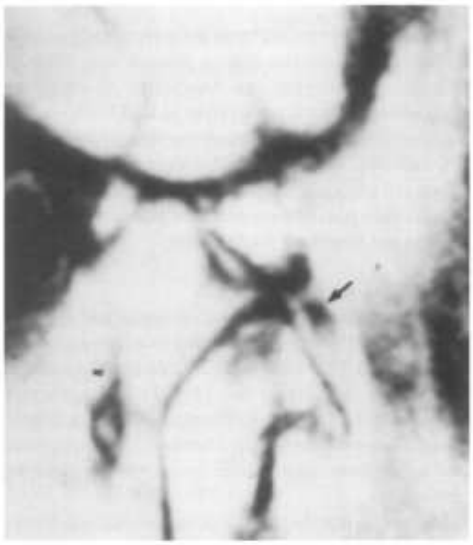

Fig. 2. NMR test of right TMJ; maximal opening demonstrates dislocation of articular disk *(arrow)*.

Fig. 3. Arthroscopic view shows perforation of articular disk *(asterisk)* and the condylar head *(arrow)* underneath it.

Fig. 4. Arthroscopic view shows anteromesial adhesion *(arrows)* between articular disk and glenoid eminence.

Table I.

Diagnostic and therapeutic protocol	*Number of patients*
Clinical examination*	227
Tomography	145
Physical therapy	145
Bite therapy	145
CT	42
MRI, Cine-MRI	83
Arthroscopy	71
Arthrotomy	22

*Age of the patients selected after clinical examination ranged from 19 to 58 years.
The ratio between female and male patients was 2.5:1.

during mandibular opening, articular clicking or roar, condylar hypomobility or hypermobility, all different types of occlusal pathoses. These clinical features were always accompanied by severe articular pain.

Radiologic and MRI tests (Figs. 1 and 2) documented a rearrangement of the endocapsular morphology with arthrotic features and flattening of the condylar head and glenoid articular surfaces. Dislocation of the articular disk was observed in all 10 cases; perforation of the disk was also present in 6 cases.

Arthroscopic examination (Figs. 3 and 4) always documented the presence of adhesions between the diskal surface and the glenoid eminence. Moreover, in two cases a large adhesion area connected the inferior diskal surface, covered by synovial tissue, and the condylar head.

Because of all these findings, removal of the articular

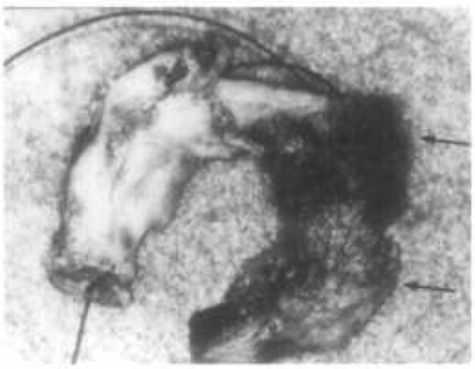

Fig. 5. Stereo-microscopic view of inferior surface of disk; extended synovial tissue hyperplasia *(arrows)* corresponding to the protrusions adhering to the condylar head is evident. (Original magnification ×2.)

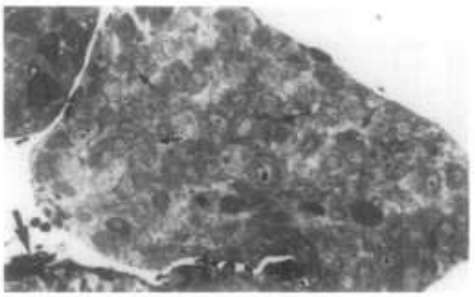

Fig. 6. Light microscopic view of large synovial protrusion with different cell types (clear and basophilic cells) and microcalcifications *(arrows)*. On the left, a cluster of basophilic material is present in a portion of the synovial surface *(broad arrow)*. Original magnification ×284.)

disks during arthrotomy was considered necessary in these 10 patients.

The arthrotomy demonstrated the anteromedial migration of the articular disks and their deviation in form.

Light and transmission electron microscopy

After removal the central part of the disks and the adhering synovia were washed in saline buffer solution and dissected into small pieces; most of them were immersed in a fixative solution of glutaraldehyde (2.5%) and paraformaldehyde (2%) in 0.1 M sodium cacodylate buffer (pH 7.4) for 5 hours at 4°C. They were postfixed in 0.1 M OsO_4 in 0.2 M collidine buffer (pH 7.4) for 2 hours at 4°C, dehydrated, and embedded in epon. Semithin sections (0.5 μm) were stained with toluidine blue, and ultrathin sections (80 nm) stained with uranyl acetate and lead citrate for transmission electron microscope observation.

Light microscopy immunocytochemistry

Some pieces were fixed with 4% paraformaldehyde in 0.1 M sodium cacodylate buffer (pH 7.4) for 6 hours at 4°C, dehydrated, and paraffin-embedded for immunocytochemical reaction. Deparaffinized sections were exposed at room temperature to 0.15 M TBS for 10 minutes, TBS containing 0.3% H_2O_2 for 25 minutes, TBS for 10 minutes, and TBS containing 1:20 normal goat serum for 30 minutes. They were then incubated overnight with 1:100 primary monoclonal antibody to smooth muscle actin (ORTHO code C 34931) in TBS containing 1% bovine serum albumin, washed in TBS for 10 minutes, and treated with 1:100 sheep antimouse biotinylated IgG (AMERSHAM code RPN 1001) for 1 hour, TBS for 10 minutes, 1:100 Streptavidin-biotinylated peroxidase complex (AMERSHAM code RPN 1051) for 30 minutes, TBS for 10 minutes, 0.05 M TBS for 10 minutes, diaminobenzidine tetrachloride in 0.05 M TBS for 5 minutes, counterstained with Harris hematoxylin, and mounted with coverslips.

These pathologic samples were compared with three control samples removed at autopsy from subjects without a clinical history of TMJ disturbances.

RESULTS

Stereo and light microscopy

At stereo microscope examination, all the pathologic disks showed markedly modified structure with irregular hyperemic protrusions corresponding to the synovial adhesions to the functional surfaces of the condylar head and glenoid eminence. Moreover, six disks were perforated, and one of them (Fig. 5) assumed a bent shape with the hollow edge corresponding to the perforation area.

Under a light microscope (Fig. 6), the synovial tissue showed an evident hyperplasia in all the samples. It consisted in the thickening of the tissue with numerous irregular layers of packed cells. Variously shaped and evident clusters of cells protruded from the irregular surfaces of the tissue. The surface of the synovia was occasionally covered by some layers of dense basophilic material.

In three disks some tissue protrusions (Fig. 7) had central cores consisting of mineralized tissue that sometimes had a bone-like feature enclosing cell bodies. Microcalcifications (Figs. 6, 8, and 9) were also present in the matrix surrounding the cells. They were strongly

Fig. 7. Light microscope appearance of extensive calcified portion of synovial projection. Some cells had been enclosed in the mineralized area. (Original magnification ×284.)

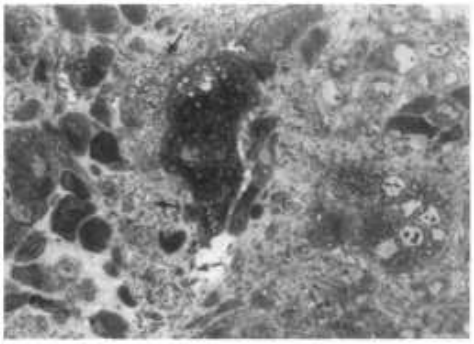

Fig. 8. Light microscopic view of multinucleated giant cells with vacuolar cytoplasm. Deposits of granular material are present among the cells *(arrow)*. (Original magnification ×363.)

positive to basophilic stain and had sometimes a metachromatic reaction with toluidine blue stain.

The synovial cell population (Figs. 6, 8, and 9) consisted of numerous basophilic cells and less numerous pale cells and multinucleated cells with a vacuolized cytoplasm. The articular disks were composed of undulated bundles of collagen fibers with fibrocytes and fibroblasts. The limits between the synovial lining and the diskal tissue (Fig. 9) were easily identifiable because of the different cellular types and the presence of fibers in the disks.

Light microscopy immunocytochemistry

The immunocytochemical reaction (Fig. 10) showed a positive staining to the treatment with antibody to actin in numerous cells of the synovial villi in seven cases.

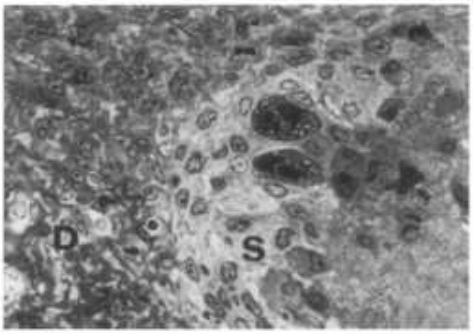

Fig. 9. Microphotography of limit between diskal and synovial tissues. The disk *(D)* is predominantly formed by bundles of collagen fibers whereas the synovia *(S)* consists of different cellular types. (Original magnification ×363.)

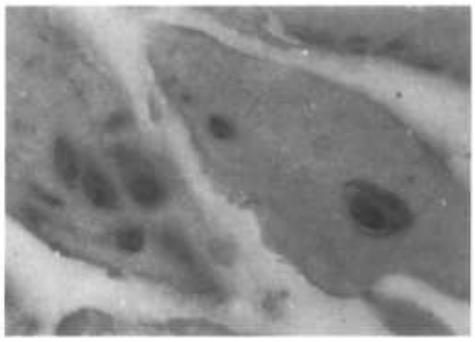

Fig. 10. Immunocytochemical reaction to detect the presence of α–actin. Some cells of the synovial villi are positive. (Original magnification ×200.)

Transmission electron microscopy

At the ultrastructural level (Fig. 11) basophilic material partially apposed to the synovial surface consisted of layers of unstructured electron-dense material covering synovial cells and floccular moderately dense intercellular matrix.

Cells with abundant cytoplasm characterized by an extended rough endoplasmic reticulum (RER) with sometimes dilated cisternae containing granular material were the most representative cellular type (Fig. 12). These cells had irregular profiles with microvilli. Other cells had a cytoplasm rich in rough endoplasmic reticulum cisternae and also in packed thin filaments.

A third type of cell (Fig. 13) consisted of elements with numerous vesicles, vacuoles, and lysosomes. They

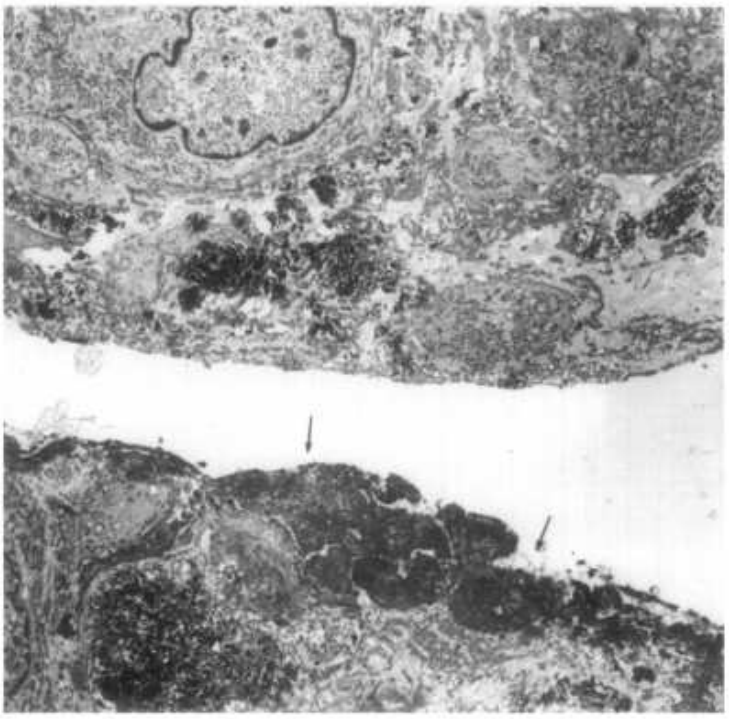

Fig. 11. Ultrastructural view of opposite surfaces of synovial villi with dense amorphous superficial material *(arrows)*. Foci of mineral precipitates of different sizes are present among the cells. (Original magnification ×3800.)

also had irregular contours with thin protrusions of the cell membrane. Vacuoles and lysosomes were the predominant organelles also in the multinuclear giant cells (Fig. 14).

These three different cell types were variously mixed. They were sometimes densely arranged (Fig. 13) with interlocking cellular protrusions but no specialized intercellular junctions were observed.

In some areas of the three samples with calcifications under light microscopy, the synovial cells were separated by an intercellular matrix consisting of variously dense amorphous material, collagen fibers, and deposits of calcified tissue. These deposits (Figs. 11 and 14) were represented by groups of crystals frequently associated with the dense component of the matrix or by large aggregates of mineral tissue.

DISCUSSION

Like other authors,[1,13] we think that the endocapsular tissue system may undergo modifications as a result of changes in functional needs. In other words, we think that modifications of the endocapsular dynamics can produce morphologic changes in the endocapsular tissues.

Some intra-articular components no longer need to move because of changes of condylar dynamics and modify their histologic characteristics in adapting to new functional requirements. These morphologic changes produce a good endocapsular remodeling when they happen in functional equilibrium. Instead, an excessive functional requirement produces the anatomic and histologic modifications found in TMJ arthropathy. Individual functional and morphologic characteristics can influence these events.

These considerations are necessary to explain some progressive articular pathoses in which the joint, starting from an initial condition with correct morphologic characteristics and function, gradually loses its morphologic and metabolic properties. The modified condylar dynamics, over the years, cause anatomic remodeling.

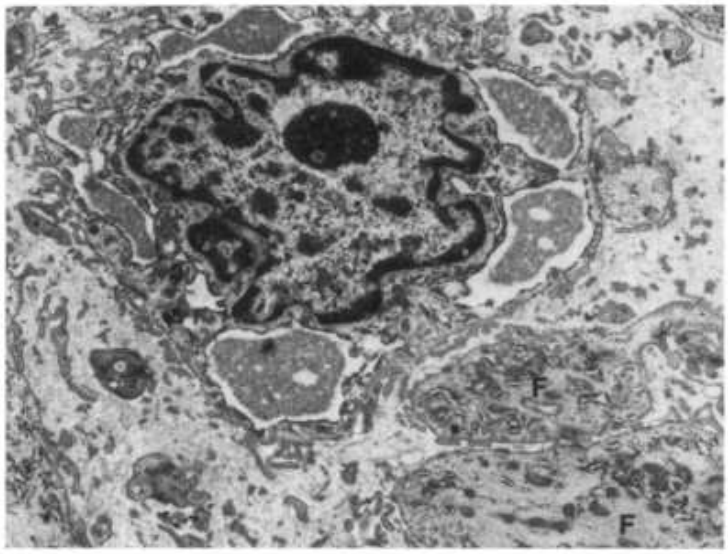

Fig. 12. One large cell with extended RER with dilated cysternae and microvillar protrusions and other cells with large number of filaments *(F)*. (Original magnification ×7500.)

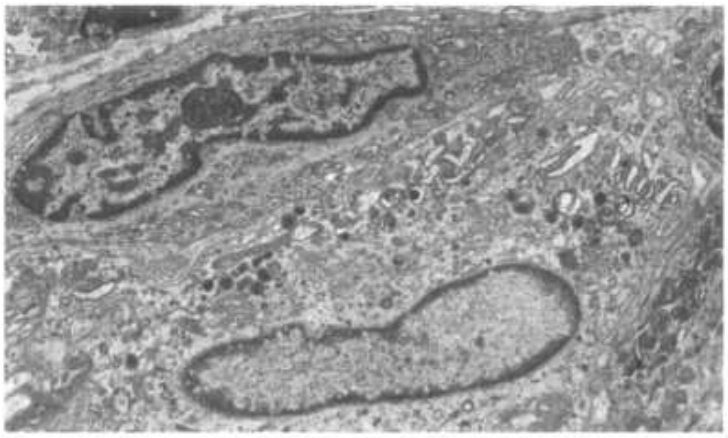

Fig. 13. Ultrastructural feature of one synovial cell characterized by the presence of vacuoles and lysosomes and another cell with RER and filaments. (Original magnification ×6100.)

In consequence of excessive tissue stresses and functional demands, the fibrocartilage and the cortical bone of the articular surfaces and the articular disk are modified.[14,15]

Through its secretory activity the synovia permits the maintenance of the morphologic aspects proper to the condylar and glenoid fibrocartilage and to the articular disk. This function is necessary because of the loading produced during the condylar dynamics in the articular space.

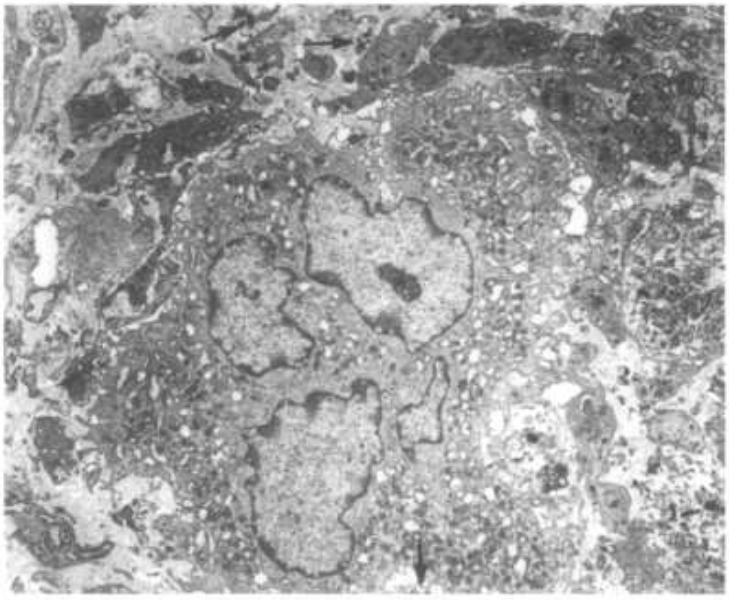

Fig. 14. Multinuclear cell: large number of vacuoles, lysosomes, and mitochondria in cytoplasm surrounded by protrusions of cells of other types and small aggregates of calcified material in the matrix. (Original magnification ×3150.)

The other synovial function is to remove the tissue metabolic products from the articular space. Overloading can render the synovia unable to perform this function. The disk perforation after a different distribution of the compression forces may modify the distribution of synovial fluid and compromise the lubrication of the joint.

In the clinical history and the radiologic tests of the patients, we detected a gradual and progressive remodeling of the TMJ components caused by articular overloading. Our radiologic investigations (Cine-MRI) demonstrated the effects of the flattening condylar heads under the anterior articular tubercle during performance of the function. In these anatomic conditions the functional demands can lead to the metabolic inability of the endocapsular tissues to respond to the overload of functional stresses.[16] In these patients the arthrotomy always demonstrated the intra-articular migration of the articular disks. The joint surgery also demonstrated the anatomic deformity that the intra-articular overloading has gradually produced on the articular disk. The anatomic remodeling and the histologic changes presented in these cases indicate that the endocapsular tissues always have the possibility of modification, also in case of an articular pathosis.

The first important finding of the morphologic investigation is the remarkable hyperplasia of the synovial tissue observed in all the samples. Moreover, we found a marked increase of type B cells (fibroblast-like cells). Synovial hyperplasia with increased vascularity and migration of synovial cells on the surfaces of the disk have been classified as regenerative phenomena after diskal perforation.[3] This hypothesis agrees with our observations, and it may also explain the presence of numerous myofibroblasts in some samples. In fact, this cell-type appearance has been described during reparative processes after tissue damage.[17-20] In addition, we have already observed the presence of myofibroblasts also in the diskal tissue where the altered functional conditions have modified the overload on the articular surfaces and the morphologic characteristics of the disks.[10]

The mononuclear and the multinuclear giant cells with many lysosomes and vesicles can be classified as different forms of synovial type A cells (macrophage-like cells).

Another remarkable finding is the presence of clusters of small crystals or large deposits of calcified material in the extracellular matrix of three disks.

In our opinion the features we observed in the syn-

ovial tissue not only correspond to reparative processes but seem also to be the result of different and more complex events. Particularly, synovial modifications consist not only of hyperplasia of the tissue with increase in the cellular amount, but also of cellular metaplasia with alterations in the balance among the different cell types and the subsequent prevalence of cells that produce the extracellular matrix components, such as fibroblasts and myofibroblasts. So we think that cellular hyperplasia may be the first response of the tissue to modified functional conditions, whereas metaplasia of the synovial cells perhaps results from the persistence of tissue stresses after increased modified condylar dynamics and endocapsular content. The altered ratio between type A and type B synovial cells may cause an increased production of extracellular matrix and decreased phagocytic and lubricating activity of the tissue.

The matrix changes could be the cause of the diffuse crystal deposition with calcification of the extracellular matrix. This hypothesis that modifications in the quantity and type of glycosaminoglycans explain the presence of crystals in osteoarthritic joints with similar matrix changes was formulated some years ago.[21,22] A deficient vascularity or an accumulation of shearing stresses may also be concomitant events involved in the mineral deposition that we observed, as has been suggested for aging diskal tissue.[23,24] In addition, modifications in the synovial fluid dynamic may have interfered with the synovial tissue metabolism and the following deposition of calcified matrix.

We thank Dr. E. Padula from the Maxillo-Facial Surgery Division, "S. Bortolo Hospital" of Vicenza for his vital collaboration.

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