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Transmission Electron Microscopic Study of Loose Bodies in Synovial Chondromatosis of the Temporomandibular Joint

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Abstract

Background: There are several reports of Synovial chondromatosis (SC) and loose bodies (LBs) analyzed with histological and immunohistochemical staining. However, the process of formation of LBs remains unclear. Furthermore, there are very few reports of electron microscopic analysis of the LBs of the human temporomandibular joint (TMJ). Recently, we reported findings of the LBs of the human TMJ with scanning electron microscopy (SEM). The LBs might develop in a multi-layer style, in which fibrous tissues were piled up loosely around the inside part. The proliferating activity of LBs grows from the inside to outside of SC in TMJ.

In this study, we investigated ultrastructural difference findings of inside and outside in human TMJ LBs with transmission electron microscopy (TEM).

Methods: Specimens were surgically removed from the TMJ of three female patients clinically staged in phase II. Small pieces of the specimens were soaked in a buffered mixture of 0.5% glutaraldehyde and 4% paraformaldehyde for one week. The specimens were observed with a TEM (JSM-5500, JEOL, Tokyo) at an accelerating voltage of 3 KV.

Results: Ultrastructurally, cartilagenous cells were located in the fibrillar matrix intermingled with collagen fibrils, and accompanied micropodia extending toward the myxoid matrix. The cartilaginous cells were rich in rough endoplasmic reticula and Golgi apparati. Glycogen particles and fat droplets were clustered in the cytoplasm. The matrix was occasionally associated with deposition of amorphous electron-dense material, probably deriving from secretory products or cellular debris of stromal fibroblastic cells. Near the surface of the LBs, fibroblast-like cells, rich in rough endoplasmic reticula and bundles of intermediate filaments, were laminated.

Conclusions: There are different morphological features inside and outside of the human TMJ LBs.

Keywords: Temporomandibular joint (TMJ), Synovial chondromatosis (SC), loose body (LB), Transmission electron microscope (TEM)

Introduction

Synovial chondromatosis (SC) is a rare joint disease characterized by formation of nodules of metaplastic cartilage under the surface of synovial membranes, joints, tendons and bursae. Haller first reported loose bodies in the temporomandibular joint (TMJ) in 1764 [1]. The first accurate scientific description of SC

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of the TMJ was given in 1933 by Axhausen, who described SC as metaplastic chondrogenesis in the synovial membrane [2]. Two forms of SC have been recognized: primary and secondary. Primary SC is uncommon, and the etiology is unknown. A response to repetitive, low-grade trauma has been proposed. Secondary SC is more common and may result from inflammatory or non-inflammatory arthropathy [3].

There are several reports of SC and loose bodies (LBs) analyzed with histological and immunohistochemical staining [4-8]. However, the process of formation of LBs remains unclear. Furthermore, there are few reports of electron microscopic analysis of the LBs of the human TMJ.

Recently, we reported findings of the LBs of the human TMJ with scanning electron microscopy (SEM) [9]. Collagen fibers were densely arranged as bundles inside the LBs. A porous pattern was seen on the surface of LBs. It is plausible that the LBs are supported by fibroblastic cells, and the LBs may develop in a multi-layered style: namely, fibrous tissues are piled up inside the LBs.

In this study, we investigated ultrastructural difference findings of inside and outside LBs in human TMJ with transmission electron microscopy (TEM).

Materials and Methods

Specimens were surgically removed from the TMJ of three female patients clinically staged in phase II [10].

The age of the patients was 30, 37 and 68 years old. We obtained approximately 70 LBs from case I and approximately 40 LBs from case II and III, respectively. The size of LBs ranged from 1 to 8 mm, with the mean of 2.4 mm. Six LBs were evaluated for TEM in each case.

The specimens for TEM were soaked in a mixture of 0.5% glutaraldehyde and 4% paraformaldehyde for one week. After cutting into half pieces, they were rinsed in 0.1 M phosphate buffer for one hour, alkali-treated with 4 N NaOH at 40°C for one hour, and neutralized with 0.1 M phosphate buffer for one hour. The specimens were then soaked in 1% tannic acid for two hours, washed with distilled water, and subsequently re-fixed in 1% osmium tetroxide for one hour. They were then dehydrated with ascending grades of ethanol, substituted with *t*-butyl alcohol, and freeze-dried using a lyophilizer (JFD-310, JEOL, Tokyo). The dried samples were adhered to a metal stage using a silver paste (Dotite, Fujikura Kasei Co., Tochigi, Japan), and coated with gold 4–5 nm in thickness using an ion sputtering coating instrument (JFC-1500, JEOL, Tokyo). The specimens were observed with a TEM (JSM-5500, JEOL, Tokyo) at an accelerating voltage of 3 KV.

The study protocols were approved by the Medical Ethics Committee of Osaka Dental University (Approval No. 1000917).

Results

The fine structures of LBs were fundamentally similar in the specimens sampled from all the three cases. Ultrastructurally, cartilagenous cells were located in the fibrillar matrix intermingled with collagen fibrils, and accompanied micropodia extending toward the myxoid matrix. The cartilaginous cells were rich in rough endoplasmic reticula, Golgi apparati and intermediate filament bundles. Glycogen particles and fat droplets were clustered in the cytoplasm (**Figure 1**).

The matrix was occasionally associated with deposition of amorphous electron-dense material, probably deriving from secretory products or cellular debris of stromal fibroblastic cells (**Figure 2**).

Near the surface of the LBs, fibroblast-like spindled cells, rich in rough endoplasmic reticula and bundles of intermediate filaments, were laminated (**Figure 3**).

Discussion

SC commonly affects large synovial joints such as the elbow, knee, wrist and hip. The TMJ has been involved in 3% of cases [11]. Clinical symptoms of SC in TMJ resemble those of other

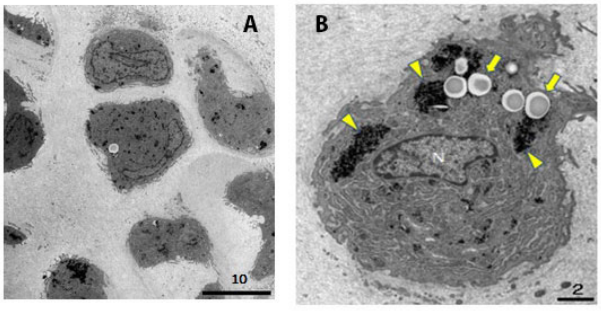

Figure 1. Cartilagenous cells embedded in the myxoid matrix of the loose body (**A**: lower-powered view, **B**: higher-powered view). Micropodia-forming cartilaginous cells are embedded in microfibrillar myxoid matrix. The cytoplasm is rich in rough endoplasmic reticula with clustered glycogen particles (arrowheads) and fat vacuoles (arrows). N=nucleus. Bars indicate 10 μm (**A**) and 2 μm (**B**).

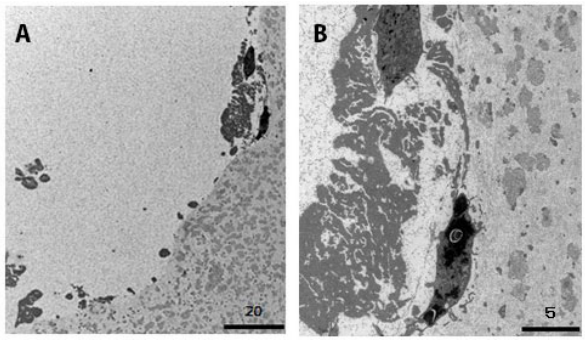

Figure 2. Deposition of amorphous, electron-dense material in the matrix of the loose body (**A**: lower-powered view, **B**: higher-powered view). Zonal clustering of the deposits is seen (**A**). It is likely that the deposits derive from secretory products or cellular debris of stromal fibroblast-like cells (**B**). Bars indicate 20 μm (**A**) and 5 μm (**B**).

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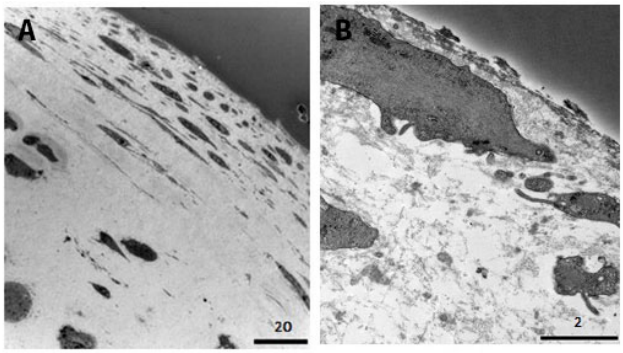

Figure 3. Lamellar distribution of fibroblast-like cells near the surface of the loose body (**A**: lower-powered view, **B**: higher-powered view). Fibroblastic cells are rich in rough endoplasmic reticula and bundles of intermediate filaments, and they form laminated structures near the surface. Bars indicate 20 μm (**A**) and 2 μm (**B**).

TMJ disorders: pain and swelling around the TMJ, mouth opening limitation and joint sounds. Malocclusion with cross bite and facial asymmetry are seen in severe cases [12].

In 1977, Milgram clearly categorized the disease process of SC into three distinct phases: phase I shows active intrasynovial disease with cartilaginous metaplasia but without forming LBs; phase II reveals transitional lesions with both active intrasynovial proliferation and free cartilaginous LBs; and in phase III, multiple free LBs often with calcification, ranging from a few to hundreds in number, are observed without demonstrable intrasynovial disease [10]. Histopathologically, cartilaginous nodules in phase I remain confined to the synovial membrane, being present as diffuse thickening with a cobblestone appearance. In phase II, the thickened synovial membrane breaks off and protrudes into the joint cavity as LBs. In phase III, LBs are often ossified.

Cartilagenous metaplasia of the mesenchymal cells plays an important role in the etiology of SC. The direct causes of SC have not been clarified: the candidates include embryological factors, degenerative joint changes continuously stimulating the articular disc, traumatic injuries and inflammations. SC caused by the embryological factors may be clinically aggressive, whereas SC caused by the traumatic injuries and inflammations may be chronic and less aggressive [13,14]. Traumatisms, parafunctions and infections are considered as causes of SC in a small percentage of patients [15-17]. There are several immunohistochemical analyses of SC in the TMJ, mainly focusing on cytokines and proteins in the synovium and LBs [4-8].

Yoshida reported that the expression of Ki-67 was hardly detected in any case of LBs, and mild labeling of Ki-67 was detected in the synovial membrane [5]. The results indicated that LBs released into the joint compartment do not have proliferative activity, whereas the synovial membrane may play an important role in the formation of LBs in SC. Yoshida *et al.* also reported scanning electron microscopic findings of LBs [9]. Collagen fibers were densely arranged as bundles inside the LBs. A porous pattern was seen on the surface of LBs. It is plausible that the LBs are supported by fibroblastic cells, and the LBs may develop in a multi-layered style: namely, fibrous tissues are piled up inside the LBs. The present TEM findings are consistent with such findings.

Conclusion

The LBs were ultrastructurally composed of cartilagenous cells embedded in the fibrillar and collagenous matrix. The matrix occasionally showed deposition of amorphous, electron dense material probably deriving from secretory products or cellular debris of stromal fibroblastic cells. Near the surface of the LBs, fibroblast-like spindled cells were laminated. These fine morphologic features support the previously reported structural characteristics.

List of abbreviations

SC: Synovial chondromatosis
TMJ: Temporomandibular joint
LB: Loose body
SEM: Scanning electron microscopy
TEM: Transmission electron microscope

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Authors' contributions	HY	HI	MY	NT	HI	MK	MT	RT	TI	YT
Research concept and design	√	--	--	--	--	--	--	--	--	--
Collection and/or assembly of data	√	--	--	--	--	--	--	--	--	--
Data analysis and interpretation	--	--	--	--	--	--	--	--	--	√
Writing the article	√	--	--	--	--	--	--	--	--	√
Critical revision of the article	√	--	--	--	--	--	--	--	--	--
Final approval of article	√	--	--	--	--	--	--	--	√	--
Statistical analysis	--	√	√	√	√	√	√	√	--	--

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