Transmission electron microscopy of ameloblastoma: A study on six cases

Rajeshwar Chawla, Karthikeyan Ramalingam1, Amitabha Sarkar1, Savita Muddiah2

Department of Oral and Maxillofacial Pathology and Microbiology, JCD Dental College, Sirsa, Haryana, 1Oral Pathology and Microbiology, 2Oral and Maxillofacial Surgery, Surendera Dental College and Research Institute, Sriganganagar, Rajasthan, India

Address for correspondence:
Dr. Ramalingam Karthikeyan, Department of Oral Pathology and Microbiology, Surendera Dental College and Research Institute, H. H. Gardens, Sriganganagar, Rajasthan, India. E-mail: drrkn79@gmail.com

Abstract
Background: Ameloblastoma is a rare, benign tumor of odontogenic epithelium, but with an aggressive clinical behavior. Aim: The present study aims to assess the ultramicroscopic features of the epithelial and connective tissue components of ameloblastoma. Materials and Methods: Six cases of ameloblastoma were subjected to electron microscopy. They included three cases of follicular type and three cases of plexiform type. Results: The study reveals that the ameloblastoma contains the full complement of cells normally found during odontogenesis. However, these cells resemble the enamel organ in an undifferentiated stage. Conclusion: Ultramicroscopy revealed the presence of different cell types among follicular type. The morphology of plexiform variants and correlation with odontogenesis could be elicited. The electron microscopic differences between follicular and plexiform types could help us in better understanding its pathogenesis.

Key words: Ameloblastoma, electron microscopy, follicular, plexiform

INTRODUCTION

The ameloblastoma is a relatively rare, odontogenic neoplasm generally considered to be related to tooth germ epithelium, but is of insufficient differentiation to allow for actual formation of calcified tissues.[1-3] This study reflects the ultrastructure of ameloblastoma as well as the electron microscopic differences between follicular and plexiform variants, which could be related to histological differences.[4] Electron microscopy can demonstrate decisive structural peculiarities to classify different variants of ameloblastoma, and in treatment planning.[5,6] There is only one report of ultramicroscopy regarding ameloblastoma in the last decade, along with a few other reports in English literature.

Aim of the study

The present study aims to assess the ultramicroscopic features of the epithelial and connective tissue components of ameloblastoma.

MATERIALS AND METHODS

This study is an ultrastructural examination of six cases of ameloblastoma, out of which three were of follicular type and the other three were of plexiform type. The biopsy specimens of previously diagnosed ameloblastomas received in the Department of Oral and Maxillofacial Pathology, Government Dental College and Hospital, Nagpur, were utilized for this study. They were cut longitudinally into two unequal halves without causing any distortion of the tissues. The larger part was processed for routine histopathology and the smaller part was sent for transmission electron microscopy to TEM section, Department of Anatomy, AIIMS, New Delhi.

The ultramicroscopic features were assessed for the epithelial component, the connective tissue component, and the epithelial–connective tissue interface.
RESULTS

Ultramicroscopic assessment revealed that the follicular ameloblastoma contained two groups of cells, the peripheral cells and central cells, whereas the plexiform variant revealed a single cell group.

The peripheral cells were generally tall columnar cells with similarly elongated nuclei. The nuclei revealed an irregular outline and contained prominent nucleoli. Cytoplasmic organelles were scattered throughout the cytoplasm and did not show any sign of segregation. Mitochondria were somewhat swollen and were found on both sides of the nucleus. Bundles of tonofilaments and clusters of ribosome were scattered throughout the cell. Rough endoplasmic reticulum (RER) was present without any orientation. Numerous dense-cored secretory granules, condensing secretory granules, and several coated vesicles associated with Golgi complex could be seen, indicating that the cells were in pre-ameloblast stage or early secretory ameloblast stage [Figures 1-3].

The central cells were spindle to stellate shaped, which were joined with adjacent cells by desmosomes. The cells contained proportionately large nuclei which were centrally located, irregularly contoured, and contained patches of chromatin and nucleoli. The cytoplasm contained RER, randomly distributed mitochondria, and tonofilaments without any polarization. Numerous dense-cored secretory granules, condensing secretory granules, and coated vesicles were also present [Figures 4 and 5].

Follicular and plexiform ameloblastomas demonstrated differences in ultramicroscopy. Epithelial cells from follicular ameloblastoma were more tightly packed than from plexiform type. The cells from follicular ameloblastoma contained many lysosomes, whereas cells
from plexiform type contained many vacuoles. Tumor cells of plexiform variants also contained numerous tonofilament bundles and were joined by desmosomes, resembling squamous epithelium [Figures 6 and 7].

The connective tissue stroma consisted mostly of stellate cells and fibers. These cells were mostly fibroblasts. The cytoplasm was filled with RER, Golgi apparatus, and swollen mitochondria [Figure 8]. Many collagen fibers (cut in transverse and longitudinal sections) were also seen [Figure 9].

The epithelial–connective tissue interface was relatively smooth. The epithelial cells adjacent to junction contained many mitochondria. There were no changes in the basal lamina. There was no evidence of secretion of dentinal or enamel matrix, further supporting our findings that the tumor cells were in very early stage of development [Figures 10 and 11].

DISCUSSION

The ameloblastoma is a relatively rare, odontogenic neoplasm composed of enamel organ like tissue which does not differentiate to the level of enamel production.[7,8] Ultramicroscopy of the follicular type revealed two types of tumor cells, whereas in plexiform type, the tumor cells did not show any variation but resembled squamous epithelium.[4,6]

The Golgi complex of these columnar cells contained large number of vacuoles as seen in secretory ameloblast. However, the vacuoles in the columnar cells of the tumor were electron lucent.[1]
The stellate cells of the tumor epithelium were similar to stellate reticulum of the normal enamel organ. These cells were joined by desmosomes and the nucleus occupied the central position within the cell. The cytoplasm contained usual organelles without any polarization. 

Figure 9: Electron micrograph showing connective tissue cell (C) and collagen fibers cut in longitudinal section (Ls) and transverse section (Ts) (×4800)

Figure 10: Electron micrograph showing junction of epithelium and connective tissue. Basal lamina (bl) is relatively smooth (×12,000)

Figure 11: Ultramicrograph showing epithelium–connective tissue interface (Jx). Tonofilament bundles (Tf), mitochondria (M), and ribosomes (R) seen in epithelial cells near the junction (×12,000)

Figure 12: Photomicrograph showing follicles of ameloblastoma in the stroma (H and E, ×4)

Figure 13: Photomicrograph showing peripheral columnar cells and central stellate reticulum-like cells within the follicles (H and E, ×10)

Figure 14: Photomicrograph showing sheet-like patterns of anastomosing strands in plexiform ameloblastoma (H and E, ×4)
The tumors cells of plexiform variants contained numerous tonofilament bundles and were joined by desmosomes, resembling squamous epithelium.\cite{4} We consider that histological differences between follicular and plexiform variants represent the differentiation tendency of the remnant of dental lamina at the time of neoplastic transformation.

The connective tissue stroma did not reveal any signs of calcification. The connective tissue cells were stellate shaped and resembled fibroblasts. These cells contained well-developed RER and Golgi apparatus, indicating that they were active in collagen synthesis.\cite{1,7}

The epithelial–connective tissue junction was relatively smooth, and epithelial cells adjacent to junction contained many mitochondria. There were no changes noted in the morphology of basal lamina or the surrounding extracellular matrix. Despite the morphology favored the initial level of differentiation, there was no evidence of secretion enamel or dentin matrix.\cite{5,6}

The columnar cells and stellate cells in the epithelial islands of the follicular variant mimicked the inner enamel epithelium and stellate reticulum cells, respectively. Hence, the tumor islands of follicular type could be compared to the enamel organ during odontogenesis.\cite{1,3} The secretory ameloblasts are tall, columnar cells, but with segregation of organelles.\cite{10}

The cytoplasmic organelles were scattered throughout the cytoplasm and no segregation of organelles was seen in the columnar cells of the ameloblastoma. Furthermore, these cells contained free ribosomes instead of RER. In this respect, the columnar cells resembled the cells of inner enamel epithelium at an early stage of differentiation.\cite{2,4,6}

The presence of highly active fibroblast-like cells of connective tissue, in addition to the epithelial component resembling the enamel organ, suggested that the ameloblastoma contained the complement of cells normally found during odontogenesis. However, when viewing the epithelial and connective tissue components as a whole, the ameloblastoma resembled the dental organ at a very early stage of development.\cite{11}

There is only one report of ultramicroscopy of ameloblastoma\cite{12} in the last decade, along with very few reports in English literature.\cite{13-19} Our report would be a valuable addition to the limited literature available in this topic.

**CONCLUSION**

The present study describes the ultrastructural appearances of various cells which are found in the epithelium and connective tissue components of ameloblastoma. The study reveals that the ameloblastoma contains the full complement of cells normally found during odontogenesis. However, these cells resemble the enamel organ in an undifferentiated stage. This study also reveals the ultrastructural difference between follicular and plexiform types that are seen histologically, thus helping us to diagnose and understand the complex pathogenesis.

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