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Research Article

Histopathologic Features as Strong Predictor of Syndromic Odontogenic Keratocysts

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Abstract

Background: Odontogenic Keratocysts (OKCs) represent approximately 11% of all odontogenic cysts and may be an early sign of Nevoid Basal Cell Carcinoma Syndrome (NBCCS). We aim to identify histologic nuances of syndromic OKCs in comparison to sporadic ones.

Materials and methods: With Institutional Review Board (IRB) approval, a retrospective search of the University of Florida, Oral Pathology biopsy service database between 1994 to 2020 was performed for cases with a diagnosis of OKC. Cases with insufficient diagnostic information or from extraosseous "peripheral" locations were excluded. Demographics, medical history, and histology of all cases were reviewed to confirm the diagnosis.

Results: A total of 33 OKCs from confirmed NBCCS cases were identified and evaluated as the study group. The control group included 521 sporadic OKCs. Syndromic OKCs demonstrate a variably thickened cystic lining with rete ridge formation, papillary projections, multilayer vacuolization within the lining, scant parakeratin with minimal corrugation, and full thickness hyperchromasia in comparison to the sporadic ones.

Conclusion: In this study, we report unique histological features that may aid in reliably discriminating syndromic OKC from sporadic ones. Our study may help provide a baseline for identification of syndromic OKC using simple microscopy.

Keywords: Odontogenic keratocyst; Nevoid basal cell carcinoma syndrome; Gorlin-Goltz syndrome; Syndromic odontogenic keratocyst; Histologic features

Introduction

Odontogenic Keratocysts (OKCs) represent approximately 11% of all odontogenic cysts that originate from the remnants of dental lamina [1-4]. They may appear either as sporadic or in association with Nevoid Basal Cell Carcinoma Syndrome (NBCCS) [1-3]. NBCCS also known as Gorlin-Goltz Syndrome, is an autosomal dominant disorder mainly characterized by cutaneous basal cell carcinomas, multiple odontogenic keratocysts, and skeletal anomalies [1-3]. Mutation of *patched homolog 1 (PTCH-1)* gene has been identified in NBCCS [1-3]. Loss of heterozygosity at the PTCH locus is also a pathogenic hallmark of OKCs seen with NBCCS [3]. The Patched protein is a tumor suppressor gene involved in the Hedgehog signaling pathway, an essential mechanism for cell differentiation and organ development during embryogenesis [5,6]. *PTCH-1* gene is located on the long arm of chromosome 9 (9q22.3) [5]. Mutation of *PTCH-1* gene has been identified in NBCCS and some related sporadic tumors including basal cell carcinoma, and medulloblastomas, supporting the tumor suppressor gene role of *PTCH-1* [1-3,5].

Several studies focused on various aspects of sporadic and syndromic OKCs including, clinical behavior, recurrence, and molecular differences. However, the histological differences between sporadic and syndromic OKCs are not well studied. We aim to identify histologic nuances of syndromic OKCs that may help discriminate syndromic from sporadic OKCs.

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Materials and Methods

An IRB approved retrospective search of the UF Oral Pathology biopsy service database between 1994-2020 was performed for cases with a diagnosis of OKC. Demographics and medical history of all cases were reviewed. All retrieved cases were microscopically examined independently by two Oral and Maxillofacial Pathologists and an Oral Pathology resident.

Study design

A total of 554 cases of OKC were identified, out of these, 33 OKCs were confirmed cases of NBCCS.

The cases were then divided into two groups:

A. Control group: included all diagnosed sporadic OKCs (n=521)

B. Study group: included all diagnosed OKCs in patients with a confirmed diagnosis of NBCCS (n=33)

Cases from extraosseous "peripheral" locations or with missing, insufficient tissue, and inconclusive biopsy diagnosis of OKC were excluded.

Results

Syndromic OKCs demonstrated unique microscopic features compared to sporadic ones.

The most prominent features include:

1. Full-thickness hyperchromasia that is histologically similar to carcinoma in situ-like' appearance (top to bottom changes) (Figure 1 A).

2. Numerous rete ridge formations (Figure 1B).
3. Scant parakeratin with minimal corrugation (Figure 1B).
4. Variably thickened cystic lining (Figure 1C).
5. Proliferative lining presenting as 'intra-mural' papillary projections (Figure 1C).
6. Cellular vacuolization extending from the basal cell layer to the luminal surface of the cystic lining (Figure 1D).

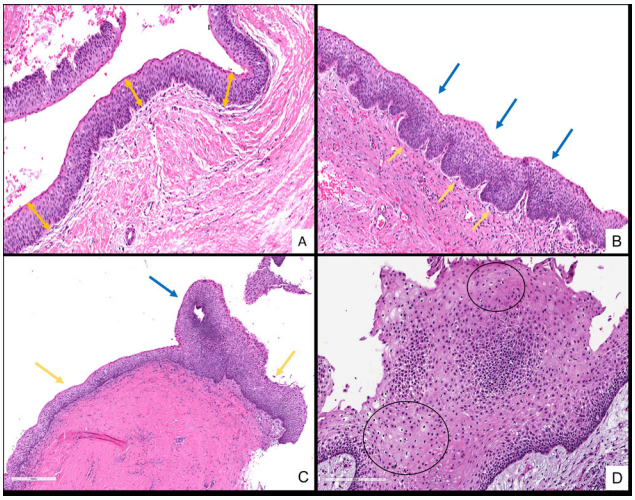

Figure 1: The proposed histologic criteria for syndromic odontogenic keratocysts. A) Full thickness hyperchromasia, magnification X200 (H&E*). B) Numerous rete ridge formation (yellow arrow) and scant parakeratin with minimal corrugation (blue arrow), magnification X200 (H&E*). C) Variably thickened cystic lining with papillary proliferation, magnification X100 (H&E*). D) Multilayer vacuolization (circle) within the lining, magnification X200 (H&E*). *Hematoxylin-eosin staining.

Discussion

To our knowledge, this is the first study to report histological differences between sporadic and syndromic odontogenic keratocysts (OKCs). Our study identified distinctive histological characteristics of syndromic OKCs which may aid in identifying syndromic cases with simple microscopy.

In addition to the typical diagnostic features of OKC described in the World Health Organization (WHO) classification of head and neck tumors [4], syndromic OKCs may exhibit full thickness hyperchromasia that can mimic a pseudo 'carcinoma in situ-like' histomorphologic appearance. In contrast, the sporadic OKCs, histologically exhibit hyperchromasia confined to the basal cell layer only. Additionally, increased rete ridge formation is another finding noted with syndromic OKCs, while this is lacking in the sporadic ones. Furthermore, the lining epithelium in sporadic OKCs is usually uniform in thickness and composed of 6 to 8 layers of squamous cells, while syndromic OKCs are characterized by variably/significantly thickened lining. Other histologic features that were noted in syndromic OKCs included scant luminal surface parakeratin with minimal corrugation, proliferative tendency of the lining resulting in the formation of 'intra-mural' papillary projections, and numerous foci exhibiting vacuolization of the cells within the cyst lining extending from the basal cell layer on the mural edge to the cells on the luminal surface.

Conclusion

In this study, we report unique histological features that may aid in reliably discriminating syndromic OKC from sporadic ones. The most prominent features include a variably thickened cystic lining with rete ridge formation, papillary projections, and multilayer vacuolization within the lining, scant parakeratin with minimal corrugation, and full thickness hyperchromasia. Our study may help provide a baseline for identification of syndromic OKC using simple microscopy.

Declarations

No financial support was provided for this work and the authors do not have conflicts of interest.

Authors' Contributions

All authors contributed to the study conception and design. Conceptualization by Mohammed N Islam, material preparation, data collection, and analysis were performed by Saja A Alramadhan and Mohammed N Islam. The first draft of the manuscript was written by Saja A Alramadhan, the final review and editing were performed by Mohammed N. Islam, Indraneel Bhattacharyya, and Donald M Cohen and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics Approval

This retrospective chart review study was performed with the approval of The Human Investigation Committee (IRB) of the University of Florida and complies with required ethical standards. Given the retrospective nature of the study, patients were never contacted, and we did not require informed consent.

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