Histopathological Variations of Radicular Cyst at Tertiary Hospital of Eastern Nepal

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ABSTRACT

Radicular cyst is the most common odontogenic cyst with diverse histopathological presentation. Diversity might mislead the diagnosis of this pathology but also at the same time provide many relevant information regarding its nature and behaviour. In total of 27 cases of radicular cyst that were observed histopathological variations in epithelial growth pattern, mucous metaplasia, cholesterol clefts, juxta-epithelial hyalinisation, Russel body, foamy macrophage, multinucleate giant cell and odontogenic epithelial rests were observed; indicating chronicity, aggressiveness and adaptive mechanism of the lesion as well as the host. Surgically excised tissue of any periapical pathology must undergo a regular histopathological evaluation retrieving information focusing on its aggressive behaviour and potential for malignant transformation.

Keywords: Cholesterol cleft; odontogenic cyst; radicular cyst.

INTRODUCTION

Radicular cyst is defined as a cyst arising from cell rests of Malassez in periodontal ligament as a result of inflammation, usually following death of dental pulp.[1] It is the most common cause of swelling associated with the jaw[2] with the incidence of 7-54% of all periapical radiolucency.[3]

Histopathologically, radicular cyst is usually lined wholly or partially by non-keratinizing stratified squamous epithelium, 6-20 cell layers thick with fibrous capsule containing chronic inflammatory cells,[2] however many histopathological variations cannot be disregarded. The case series presented here will be highlighting the histopathological variations observed during microscopic evaluation of radicular cyst, with associated clinical significance. The aim of this case series is to discuss the histopathological diversity in radicular cyst among Nepalese populations.

CASE REPORT

A total of 27 histopathologically confirmed cases of radicular cyst from the archives of department of Oral Pathology were evaluated; among which 14 were of males and 13 females. All the cases were associated with non-vital teeth of which six cases were associated with deciduous and remaining with permanent teeth. 14 cases were from maxilla of which 11 were from anterior and three from posterior region. Among seven cases associated with mandible, six were from posterior region and one from anterior region of the jaw. The age distribution of all cases was from 19-79 years involving permanent tooth and 2-10 years for deciduous tooth; with maximum number of cases in age group 20-30 years (18 cases). Most of the cases were asymptomatic and few with symptoms of mild pain and swelling. Vestibular obliteration was evident in majority of the cases. Well-defined homogenous radiolucency with radiopaque border was a common radiographic finding. Out of 27 cases, marsupialisation was done in six cases and complete excision in remaining.

Histopathological slides were obtained after routine histopathological processing and stained with routine hematoxylin and eosin. The histopathological slides of the radicular cyst were evaluated for variations

in epithelium lining and fibrous capsule. Epithelial variations were seen as arcading pattern, atrophic epithelium, ciliated columnar epithelium with goblet cells, mucous metaplasia and vacuolated cells whereas connective tissue showed presence of cholesterol clefts, odontogenic epithelial rests, juxta-epithelial hyalinisation, foamy macrophage, Russel body, and multinucleated giant cells. The presentations of above variations were either single in a case or combined in one case.

DISCUSSION

Radicular cyst, an inflammatory odontogenic cyst is usually seen in maxillary anterior region with comparatively high incidence in males.[4] Dental caries is considered the common aetiology along with trauma, heat produced during cavity preparation, etc. The pathogenesis of the cyst can be described under three stages; phase of initiation, cyst formation and enlargement and can be explained by two different concepts. First concept given by Stockdale in 1988 states that, the proteolytic enzyme formed during inflammatory process results in formation of cystic cavity and second concept states that, cavity is formed due to the degeneration and autolysis of central cells of periapical granuloma.[5] Majority of the microscopic feature in the present case series fulfilled the criteria to be called as radicular cyst along with few unusual presentations. Epithelial lining of the cyst predominantly showed non-keratinised stratified squamous epithelium but rarely exhibited ortho-keratinisation, around 2% of cases.[4] In long standing cases of radicular cyst the antigenic stimuli decreases and cystic cavity enlarges at the expense of epithelial lining converting 6-20 cell layers thick epithelium with arcading pattern (19 cases) (Figure 1-a) to quiescent lining epithelium[4] which were evident in few of our cases (7 cases) (Figure 1-b). These features at times might mislead to consider it as dentigerous cysts, when patient history is inadequate.

Mucous cells and ciliated columnar epithelium with goblet cells (Figure 1-c) observed in this case series could be described as metaplastic changes associated with radicular cyst; as explained by Shear, Browne and Smith.[4,6] They mentioned a special observational feature that the mucous metaplasia increases with increase in age.[4] In our case series we found one case of mucous metaplasia and two cases of ciliated columnar epithelium with goblet cells in patient of 47 and 19 years, respectively. Ciliated cellular differentiation is seen more in cyst associated with maxilla which is said to be a result of involvement of maxillary sinus however its considerable occurrence in mandibular area explains the metaplastic mechanism of epithelial differentiation. Vacuolated cells present in epithelial lining of radicular cyst are considered as intermediate stage of metaplastic conversion of stratified squamous epithelial lining into mucus cell (Figure 1-d).[4,7]

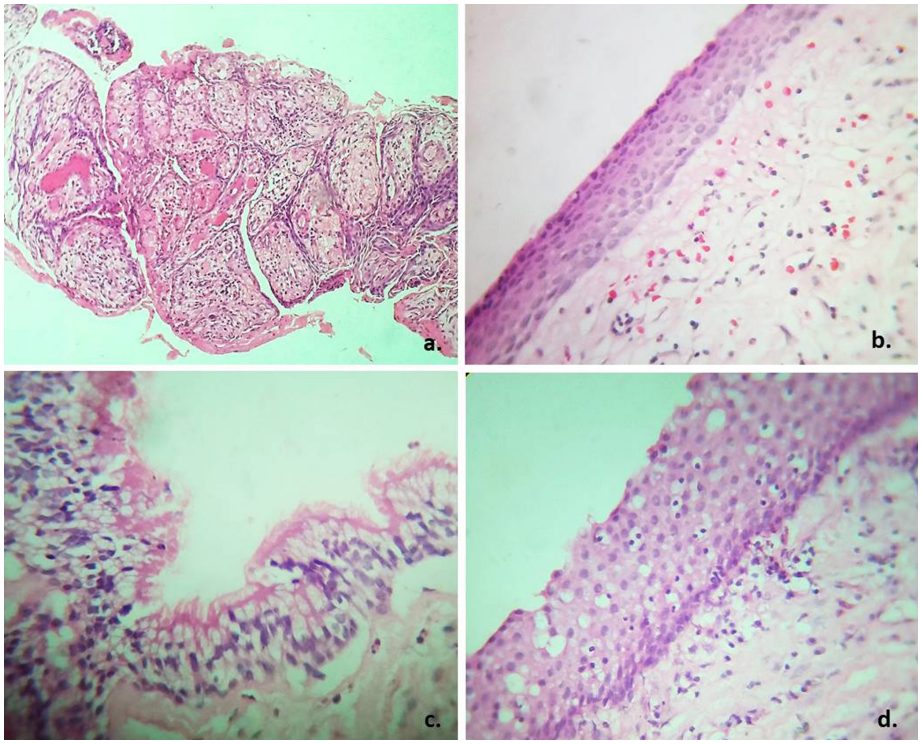

Figure 1: Radicular cyst exhibiting various epithelial patterns. a- arcading pattern; b-atrophic epithelium; c-ciliated columnar epithelium with goblet cells; d- vacuolated cells

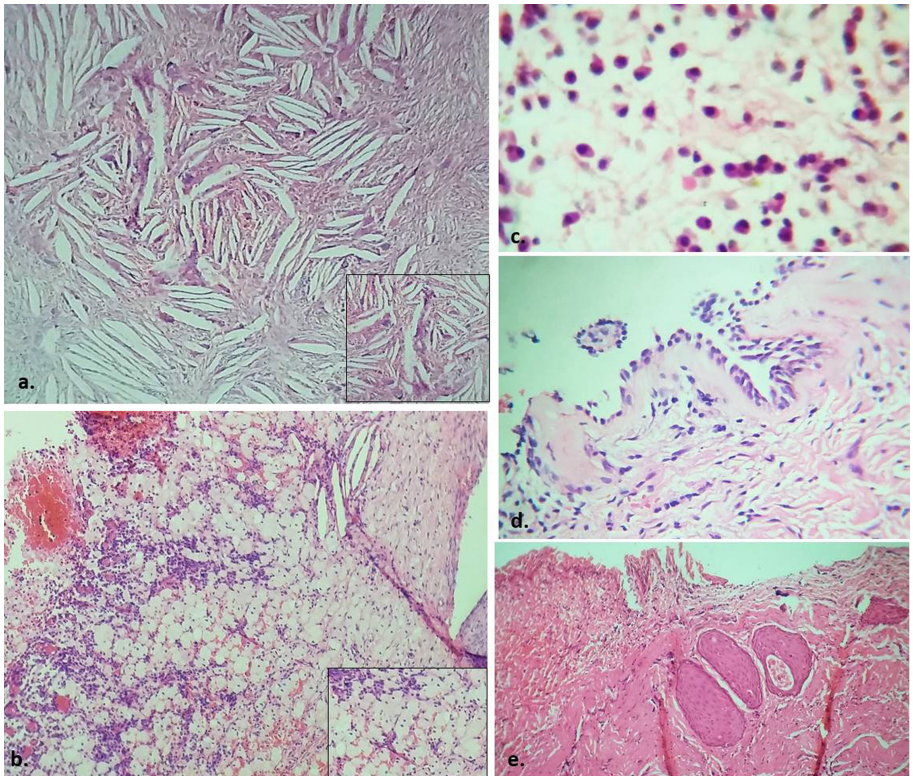

Figure 2: Radicular cyst with connective tissue variation; a- cholesterol cleft; b- foamy macrophage; c- Russel body; d- juxta epithelial hyalinisation; e- odontogenic epithelial rest

Metaplasia of epithelial lining in radicular cysts explained as either due to the change seen as cellular adaptability in response to any abnormal stimulus or as a result of reprogramming of cells by the stem cells under the influence of cytokines and growth factor generated in adjacent environment. This metaplasia which is in accordance to the stem cell is explained as desired metaplasia in literature and is justified by the fact that mucus and goblet cells secretes various glycol-conjugate like glycosaminoglycan and glycoproteins which helps in cystic expansion by maintaining the osmolality of cystic content.[7]

Deposition of cholesterol crystals depicted as clefts in fibrous capsule of radicular cyst is common yet not pathognomonic, as it may also be present in other odontogenic cysts. In total of 27 cases cholesterol clefts were evident in only five cases (Figure 2-a). Disintegration of mainly the erythrocyte (42% of cholesterol onto its membrane) and to some extent the lymphocyte, plasma cells, macrophage taking part in inflammatory process results in cholesterol deposition due to the absence of proper lymphatic channel. These deposited cholesterol crystals along with hemosiderin released from the breakdown of erythrocyte act as a foreign body and attract macrophage for their phagocytosis. Macrophages accumulate many cholesterol fragments during phagocytic process and have foamy appearance which is due to cholesterol deposition in there cytoplasm hence, called as foamy macrophage[8] as seen in one of the case (Figure 2-b). This could be justified by the fact of presence of lipofuscin or lipid pigment in macrophage.[4] Presence of foamy macrophage is representative of either a proliferative process or localised bone destruction. Many monocyte fuse together in act of phagocytosis of hemosiderin and cholesterol to form multinucleated giant cell in response to foreign body reaction.

The inflammatory process undergoing in the lesion attract many chronic inflammatory cells like lymphocyte, plasma cell and even compliment C3. Out of these, plasma cell is responsible for the formation of immunoglobulin for defense. IgG (85%) is the major immunoglobulin associated with radicular cyst followed by IgA, IgE and IgM.[4] Excessive synthesis of immunoglobulin cause plasma cells to appear as Russel body, a homogenous eosinophilic globular mass. 50% of radicular cyst can show its presence yet we were able to seen in only one case (Figure 2-c).

Juxta-epithelial hyalinisation was appreciated in two of the cases which is representative of chronic irritation and is due to fibrosis supported by rich quantity of factor VIII in fibrous capsule when host

fails to defend the chronically destructive stimuli (Figure 2-d).[4,9]

Odontogenic epithelial rests were found in four cases, (Figure 2-e) which are suggested to have reparative function.[8] This feature holds an interest because of its resemblance to squamous odontogenic tumour like proliferation (SOTLP) which shares a common cell of origin with radicular cyst.[10] It is also suggested that SOTLP is initial expression of neoplastic form yet malignant transformation has not been admitted. However its resemblance to squamous odontogenic tumour, ameloblastoma (acanthomatous, desmoplastic) and well-differentiated squamous cell carcinoma can mislead the diagnosis resulting in overtreatment.[11] Radicular cyst is usually due to chronic inflammation which on itself is well established cause of carcinogenesis. Radicular cyst has been reported to transform into primary intra-osseous squamous cell carcinoma[12] and unicystic ameloblastoma.[13] Transformation of radicular cystic lining into squamous cell carcinoma is rare but not beyond possibility.

Radicular cyst are difficult to excise in-toto and are often received in small bits usually not bigger than 4-6 mm. Irrespective of its dimension the tissue can show any of the above additional variation in the histopathology that becomes a guideline for managing the patient, depending upon nature and behaviour of the lesion.

SUMMARY

Radicular cyst, the most common inflammatory cyst can present diverse histopathological variations. Each histopathological variation in this case series or in scientific literature is indicative of valuable information about the behaviour, nature and fate of the radicular cyst. Hence, confirmatory diagnosis is not the only concern of histopathological evaluation rather extracting valuable information from each bit of tissue excised without discarding any tissue bit is also important.

Conflict of Interest: None

JNDA

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