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Papilliferous Keratoameloblastoma

A systematic review

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Abstract

Papilliferous Keratoameloblastoma (PKA) is a rare entity and not much is known about its clinicodemographic features or biological nature. Our review aimed to provide clarity with respect to the characterization of demographic, clinical, radiological, and histopathological features of PKA. Case reports of PKA were identified by means of a systematic search across multiple databases. The search yielded a total of 10 cases, half of which were of Indian origin. All the cases invariably occurred in the mandibular posterior region and involved the right side, except for one case which primarily involved the left side of the mandible. PKA should be considered as a variant of conventional ameloblastoma but towards the more aggressive end of the spectrum. It tends to occur in older individuals (fifth decade or older), with a marked propensity to occur in the right mandibular posterior region. Surgical resection with diligent follow-up is warranted in the treatment of PKA.

Keywords: Odontogenic tumors; Ameloblastoma; Keratin; Odontogenic keratocyst

Introduction

An array of metaplastic changes can occur in the epithelial component of ameloblastoma (AM) that are attributable to the potentiality of odontogenic epithelium. The epithelial cells within ameloblastic follicles or plexuses may exhibit squamous, basaloid cell, granular cell, clear cell or even mucous metaplasia. These metaplastic changes give rise to a polymorphic histopathological picture in AM. Consequently, numerous corresponding variants of AM such as acanthomatous, basaloid, granular, clear cell have been recognized [1].

Squamous metaplasia in the central stellate reticulum-like cells of AM is the hallmark of acanthomatous ameloblastoma (AA). The terminal fate of squamous cells is to form keratin and desquamate. As a result, extensive keratinization to the extent of keratin pearl formation may occur in AM. Four types of histopathological pictures have been reported in line with the spectrum of keratinizing AMs. These include- 1) Simple histology: Ameloblastomatous follicles filled with ortho- or para- keratin centrally, 2) Simple histology along with features of conventional Odontogenic keratocyst (OKC), 3) Complex histology: extrusion of keratin masses into the stroma along with features of simple histology with or without hard tissue formation, 4) Papilliferous histology: Papillary projections of the odontogenic epithelium into the cystic lumen or microcystic spaces [2].

The World Health Organization in 1992, recognized such AM with extensive keratinization as keratoameloblastoma (KA). While some authors consider KA as a subset of AA, others have reported it as a distinct variant of AM [2,3]. The centrally desquamated cells lead to the formation of microcystic areas within the ameloblastomatous follicles. The presence of papillary ingrowths of odontogenic epithelium within these microcysts or in the primary cystic lumen is an even rarer phenomenon. The first such case was described by Pindborg and Weinmann as a subset of AM and the term ‘papilliferous keratoameloblastoma’ (PKA) was suggested [4]. While an ample number of cases of KA displaying either simple or complex histology have been identified, the PKA variant is exceedingly rare [3,5]. As a result, not much is known about the clinicodemographic characterization and biological nature of PKA.

The question whether PKA differs from other variants of AM in its biological behavior or it belongs to spectrum of AA without any clinical significance is not yet answered. The present systematic review aims to gain a better understanding of the rare entity by identifying and analyzing all the reported cases of PKA in scientific literature. The objectives of our review are to describe the demographic, clinical, and histopathological characteristics of PKA.

Methods

Case reports of PKA were retrieved by a systematic search of the databases: Medline (Ovid), PubMed, PubMed Central, Web of Science Citation Index Expanded, (SCIEXPANDED), and Google Scholar. A systematic search with keywords ((ameloblastoma) AND (papillae)) OR (papilliferous ameloblastoma). An additional search with keywords- ((ameloblastoma) AND (keratin)) OR (keratoameloblastoma) OR (keratinizing ameloblastoma), was performed and screened for potential presence of papilliferous areas in the microscopic picture. The cross references cited in the retrieved literature were also screened for identification of possible cases of PKA, in case if any were missed by the search strategy.

Full text articles of all the cases belonging to the spectrum of keratinizing AMs were scrutinized for histopathological features of PKA. The quality of case reports was evaluated by means of JBI critical appraisal tool for case reports [6]. To further minimize bias in quality assessment, the authors were divided into two groups (SS and TC; MS and YA) which independently evaluated the case reports for their inclusion in the present review (Figure 1).

The criterion for inclusion of the cases was the histopathological presence of papilliferous proliferations of odontogenic epithelium into the primary cystic lumen or microcysts formed within the ameloblastoma follicles along with the formation of keratin (Figure 2). For a better understanding of the histopathological features, photomicrographs (Figure 3) were obtained from the case reported by Bedi et al.[2] Cases with an ambiguous description or unclear histopathological demonstration of a papilliferous component or keratin formation were excluded from the review. The presence or absence of additional histopathological features besides papilliferous patterns such as budding of cells, dentinoid formation, calcifications, ghost cells or OKC-like features, were also

recorded. However, these additional features were not considered definitive criteria for diagnosis of PKA as they represent variations that can occur in the odontogenic neoplasm.

*Data extraction***:**

The demographic, clinical, radiological, and histopathological features of all the cases was extracted. Additional investigations such as special stains, immunohistochemistry (IHC) or gene expression was also elicited. The treatment performed in all the cases, number of recurrences, period between the recurrences and time with no evidence of disease after treatment was recorded. The quality of articles included in the review was also assessed using the GRADE approach [7]. The extracted data was entered and tabulated in into worksheets (Microsoft Office Excel 2016, Redmond, Washington, USA).

The review title and search protocol are registered in the International prospective register of systematic reviews - PROSPERO under the registration number: CRD42021282930.

Results and Discussion

A total of 10 reported cases of PKA were found in scientific literature available in English [2-5,8-13]. Half of the patients (n=5, 50%) in these reported cases were of Indian origin [2,5,11-13]. The clinicodemographic data extracted from all the cases of PKA are tabulated in Table 1. The age of patients ranged from 18 to 76 years with a mean age of 49.7 years (S.D = $\pm$20.95). Bedi et al., in their review, reported a slightly lower mean age of 40 years for KA exhibiting papilliferous features [2]. Conventional AM shows a peak of occurrence in the third and fourth decades [1,14]. However, the cases of PKA were evenly distributed amongst all the decades with majority of cases occurring in fifth decade or later (n=7, 70%). Only three cases occurred in patients of age less than 30 years, while no case of PKA occurring in the fourth decade has yet been reported. These findings indicate that PKA may occur at any age, but commonly occurs in patients of older age groups.

There was a slight male predilection observed with 60% of the cases occurring in males (n=6) and 40% in females (n=4). The male-to-female ratio was found to be 1.5: 1. Data from a recent systematic review of the global profile of AM has suggested that conventional AM also exhibits a slight male predilection in Africa, North America and Asia [15]. A higher male predilection with

two-thirds of cases occurring in males was reported by Konda et al., and a ratio as high as 3:1 was found by Bedi et al. in their respective reviews of PKA [2,12]. On the contrary, an equal sex distribution (1:1) in reported cases of PKA was reported by Rathore et al [13]. However, the omission of certain cases or reports of additional cases after the reviews conducted by these authors has led to a variation in the sex distribution of PKA.

All the patients (n=9, unknown for one case) complained of swelling of duration ranging from 3 months to 5 years. The swelling was asymptomatic in most of the cases (n=6, 60%), which is a common mode of presentation of AM. Pain was present in 3 cases, while mobility of teeth was present in one case. Pain is an uncommon feature in AM, and is usually noted in lesions of larger size that tend to impinge on adjacent or involved nerves or due to secondary infection [16]. Infiltration of the lesions within the bony trabeculae and subsequent resorption could account for the occasional mobility of teeth noted in conventional AM or its variants such as PKA. Difficulty in mandibular movement was present in the case reported by Collini et al., which was attributable to the involvement of condylar process by the lesion [10].

All the cases invariably involved the posterior region of the mandibular jaw (n=10, 100%) and none of the reported cases of PKA to date has occurred primarily in the maxilla or in the anterior region of the mandible. This propensity of PKA to occur in the mandible is similar to that displayed by conventional AM, wherein 90% of cases involve the mandibular jaw [17]. The lesion exhibited a marked predilection to occur on the right side (n=9, 90%), while only one case primarily involving the left side of the mandible was noted. This finding was in contrast to conventional AM, which involves both sides almost equally [1]. In one case, the lesion was extensive enough to involve the entire right side of the mandible, cross the midline and involve the anterior region of the left side.

The lesion was described radiologically as a radiolucency (n=9, 90%), which was unilocular in 2 cases and multilocular in 7 cases. The radiolucency was well-defined in 5 cases and ill-defined in 3 cases. In one case, it was described as an osteolytic lesion with irregular calcifications [10]. The radiological features demonstrated by PKA are not pathognomonic and are shared by several other entities [18]. Therefore, odontogenic keratocyst, various benign and malignant odontogenic tumors,

benign fibrosseous lesions and central giant cell granuloma constitute the clinicoradiological differential diagnosis of PKA. The extensively destructive nature of PKA was evident in radiographs of all the cases wherein the majority of the cases involved the body, angle and ramus of the mandible (n=7, 50%). Out of these, 2 cases exhibited extended involvement up to the sigmoid notch and condylar process.

Additionally, all the cases that reported findings of computed tomography, found that the buccal and lingual cortical plates exhibited expansion as well as perforation. AM displays a tendency to cause extensive bone destruction and aggressively invade local structures. Increased motility of neoplastic cells due to loss of Syndecan-1 coupled with increased expression of matrix metalloproteinases (MMPs) and receptor activator of nuclear factor-kappa B ligand (RANKL) has been suggested as the possible reasons for the aggressive biological nature of AM [19,20]. However, none of the authors has investigated the expression of these markers or genes involved in the reported cases of PKA. Expression of similar markers needs to be studied in cases of PKA, to further elucidate the reasons for its aggressive nature.

Histopathologically, all the lesions exhibited an AM component with keratinization and papilliferous areas. The histopathological features of PKA described by various authors in their respective cases are tabulated in Table 2. When considering the AM component, the follicular pattern of ameloblastoma was observed most commonly (n=5). The plexiform pattern of AM was predominant in the case reported by Konda et al., which also exhibited areas of desmoplastic changes within the stroma. Two cases exhibited an admixture of the follicular and plexiform pattern [12]. In one case, the papilliferous proliferations were present in the primary lumen of a Unicystic ameloblastoma (UAM) [13]. In the case reported by Collini et al., the architecture of tumor cells was described as nests, tubules, islands and even single-file pattern, which simulated the appearance of a salivary gland neoplasm [10].

Ameloblast-like cells were present in the majority of lesions wherein low to tall columnar ameloblast-like cells exhibiting nuclear hyperchromatism and reversal of polarity were present in almost all the cases (n=8, 80%). These cells were present peripherally in the tumor follicles or plexuses. Of these 7 cases exhibited stellate reticulum-like cells, while one case had granular cells

towards the centre. Besides ameloblastomatous follicles, some of the follicles were lined by only squamous cells with or without keratin formation.

One case of AM exhibiting papilliferous proliferations reported by Adeyemi et al. had basaloid metaplasia within the centre of the follicles [21]. We believe that their case represents a basaloid variant of AM exhibiting papilliferous changes or possibly a hybrid odontogenic tumor. However, since there was no keratin formation within the tumor islands, it did not fulfil the criteria for diagnosis of PKA. The earliest cases of PKA reported by Pindborg and Altini et al. did not exhibit ameloblast-like cells lining the follicles [4,8]. Instead, single to multiple layers of parakeratotic squamous epithelial cells were observed, half of which formed tumor islands while the other demonstrated papilliferous epithelium within a central cystic lumen. Similar parakeratotic stratified squamous cells were noted in the tumor islands of cases reported by Kuberappa et al. and Rathore et al., but with the presence of AM-like features in some follicles [5,13].

The majority of the cases exhibited cystic degeneration centrally within the ameloblastic follicles or plexuses (n=8, 80%) in which necrotic cell debris were present. It has been suggested that these acantholytic cells separate from the viable epithelial cells in the follicle which continue proliferating. This differential rate of proliferation and necrosis gives rise to pseudopapillary structures projecting into the microcystic lumen [8]. Such phenomena are noted occasionally in AM, but are common in odontogenic carcinomas. This suggests a closer histopathological resemblance of PKA to the more aggressive end of the spectrum of odontogenic neoplasms.

It has also been postulated that PKA is KA in which extensive acantholysis results in pseudopapillary projections [22]. However, true papillae consisting of ameloblastoma-like epithelium with fibrovascular core were also present proliferating in the primary cystic lumen or those formed within the follicles. The center of tumor follicles, islands, plexuses and nests were packed with stacks of para- or ortho- keratin. In three cases, the stacks of keratin were extruded into the connective tissue stroma and illustrated a Pacinian corpuscle-like architecture [3,9,12].

Classically, AM has been defined as an odontogenic neoplasm of ameloblast-like cells in which the cells do not undergo differentiation to the point of hard tissue formation [1]. Even so, formation of hard tissues is a frequent finding in KA and was also noted in three cases of PKA. It has been

suggested that the extruded stacks of keratin undergo mineralization, ultimately leading to hard tissue formation. Necrotic tissues may undergo a transition to bone with or without dystrophic calcification; a process termed 'pathologic ossification'. Takeda et al. described the hard tissue formation as a result of pathological ossification producing cellular cementum or woven bone-like material [9]. The transition between the keratin accumulated in the stroma and the forming hard tissue was also evident microscopically in their case. Dystrophic calcifications in the stroma were demonstrated in the case reported by Norval et al [3].

Another entity associated with AM that comprises hard tissue formation is adenoid ameloblastoma with dentinoid. This dentinoid-producing tumor exhibits characteristic histopathological features of AM and adenomatoid odontogenic tumor (AOT), but is not yet recognized as an official entity by the WHO. Our recent review of literature found about 30 cases of AAD reported to date [23]. Similarly, it would be possible for dentinoid formation to occur in PKA which was also described in one case by Bedi et al. Even so, the mechanism of dentinoid formation would be different for AAD (epithelial-mesenchymal induction) and PKA (pathologic ossification), considering the different pathogenesis of both entities. The term 'Kerato-odontoameloblastoma' was suggested for such KA with odontogenic hard tissue formation [2].

While OKC-like features are commonly noted in KA, they were absent in all the cases of PKA [24]. It has been suggested that OKC may occasionally serve as a source of epithelium for KA to develop since it shares a common phenotype and genetic profile, to some extent, with the cells of ameloblastic lineage [25]. Development of mural islands of AM from the lining epithelium of OKC was demonstrated by Brannon et al. Cases exhibiting combined histopathological features have been reported as 'hybrid' lesions by some authors while others have considered them within the spectrum of KA [24,26]. There is yet lack of evidence linking OKC with PKA.

Additional histopathological features such as foreign body giant cells, cholesterol clefts, ghost cells, duct-like structures and rosette-like structures were also described across the reported cases of PKA by various authors [2,5,10]. The presence of foreign body giant cells and cholesterol clefts is not surprising, and they represent the normal host tissue inflammatory response or constitute a part of the secondary infection of the tumor. The presence of abundant keratin bodies with faint nuclear

outlines was implicated as the reason for the resemblance to ghost cells [5]. The follicles with cystic degeneration are occasionally lined by a single layer of epithelium adherent to the basement membrane that imparted a hobnail appearance [8]. A cross-section of such follicles was suggested to be the reason for the apparent duct-like structures [8,21]. The presence of acantholytic cells within such follicles would also impart a rosette-like appearance, leading to misinterpretation of the lesion as AOT. A highly vascularized stroma was present in the case reported by Kuberappa et al. that resembled hemangiomatous AM [8]. Trauma or stimulation of vessels closely associated with the dental follicle has been suggested as the reason for the highly vascular transition of the stroma in AM [27].

While the tumor cells in most of the cases had a benign morphology, a high mitotic rate of 3 mitoses/ high power field was reported by Collini et al. Recurrences occurred after 39 and 58 months, respectively, in their case [10]. The patient ultimately succumbed to non-Hodgkin's lymphoma (NHL) after 6 years. They proposed that PKA should be renamed as "papillary ameloblastic carcinoma" considering its clinically aggressive nature, the microscopic abundance of necrosis and recurrence. Such cases may closely resemble ameloblastic carcinoma, well-differentiated oral squamous cell carcinoma or primary intraosseous carcinoma. Generally, PKA lacks cellular pleomorphism, vascular and neural invasion, and abnormal mitoses. The presence of these features can aid in distinguishing PKA from these other malignant epithelial or odontogenic neoplasms.

Investigation of the biological chemistry of the tissue by special stains and biomarkers by means of IHC has not been extensively studied in cases of PKA. The case reported by Collini et al. resembled a salivary gland tumor owing to the presence of tubules and duct-like structures [10]. The authors investigated mucin production by Alcian blue which resulted in negative staining. The salivary gland origin of the tumor was ruled out by negative immunostaining for high-molecular-weight cytokeratins, smooth muscle α-actin, maspin, GFAP, and CD45. They found positive immunoexpression of low-molecular-weight cytokeratins in the epithelial cells, and vimentin in the stroma along with focal and weak expression of S100. Rathore et al. found intense immunoexpression of CK19 in the basal and suprabasal layers of the lining epithelium, which was indicative of its odontogenic origin [28]. Ki-67 was intensely expressed in the basal and suprabasal

layers along with infrequent positivity in the superficial cells, which was indicative of the high proliferative potential of the cells. They also found that p53 was strongly expressed in the basal and suprabasal layers, suggestive of mutation in the tumor suppressor gene. The IHC findings of Collini et al. and Rathore et al. provided further evidence for the aggressive biological potential of the neoplastic odontogenic cells in PKA [10,13].

Various authors have dealt with PKA through different approaches such as wide excision (n=4, 40%), segmental resection (n=2, 20%), hemimandibulectomy (n=2, 20%). Considering the extensive clinical involvement, presence of atypical cytological features and recurrence, Collini et al. performed modified neck dissection along with the hemimandibulectomy procedure in their case [10]. The lesion recurred 39 months after the treatment procedure, after which, no treatment was performed for the recurrent tumor owing to presence of concomitant NHL. Another recurrence was reported in the case reported by Bedi et al., which occurred three years after en bloc resection [2]. The remainder of cases showed no evidence of disease for a varying follow-up period of 2 months to 1 year. However, considering the recurrences in the case of Collini et al. and Bedi et al. after three years of treatment, the follow-up period provided by the other authors may not be sufficient to declare a successful outcome.

Except for luminal and intraluminal UAM, there is no difference in the treatment of different variants of AM [1]. Marx and Stern stated that classifying AM according to all the different types of histopathological features would only serve to complicate the classification system, ultimately confusing the clinicians [29]. Even so, the different histopathological types have academic importance and are of interest to pathologists. Therefore, as long as there is no significant difference in the biological behavior, including different histopathological types of an entity as variants seems the most rational approach. Reports of more cases in future with extensive long-term follow-up of the outcome would shed more light on the subject of whether PKA is just a variant of AM or a distinct entity. In view of the current evidence, we believe that PKA should be considered as a variant of AM within the spectrum of keratinizing AMs

Conclusion

PKA is a rare entity with only 10 reported cases to date, all of which have involved the mandibular posterior region. The clinicodemographic and radiological characteristics of PKA are much similar to AM except that it occurs more commonly in older individuals and shows a marked predilection to occur on the right side. The lesion is locally aggressive exhibiting extensive clinical involvement of the mandible and adjacent structures. The radiological features of PKA are not pathognomonic and resemble other odontogenic neoplasms. Histopathological presence of papilliferous proliferations of the odontogenic epithelium, along with extensive keratin production which may even occur in the stroma are characteristic of PKA. Based on the presence of necrotic areas, the high proliferating potential of cells, and possible recurrence, we recommend it to be considered within the spectrum of keratinizing AMs, towards the more aggressive end. Further studies pertaining to biomarkers in PKA such as Syndecan—1, MMPs and RANKL, will aid in elucidating the biological potential of the lesion. With an increasing number of reported cases, more insights could be gained with respect to the possible links between the pathogenesis of OKC, AA, KA, and PKA.

Authors' Contribution

SS and TC conceptualised the idea and designed the review. All the authors were responsible for data collection, analysis and resolution of any issues. SS, YA and TC prepared the manuscript while the content was critically reviewed and edited by MS, AT and RJ. All authors approved the final version of the manuscript.

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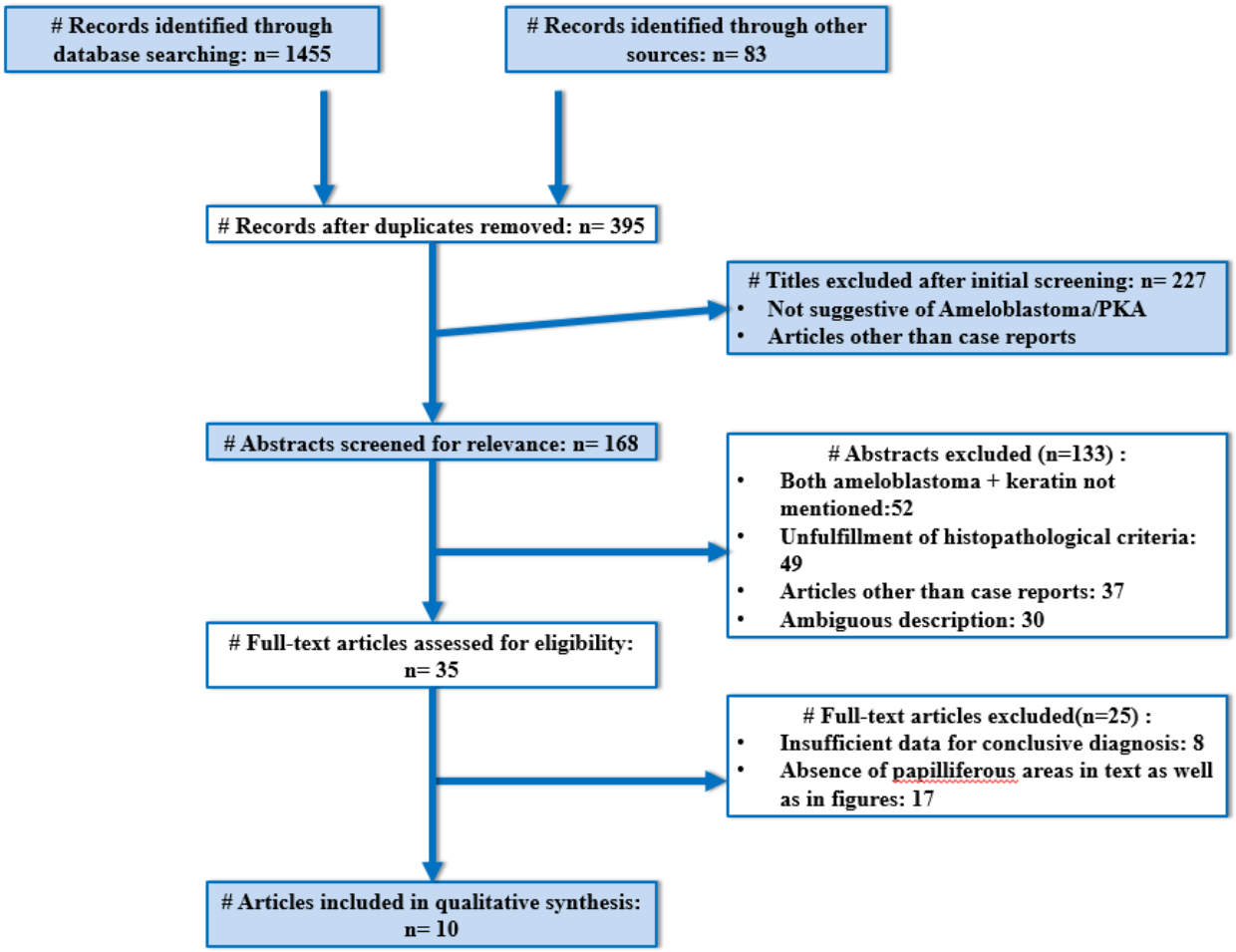

Figure 1: PRISMA Flow Chart indicating selection process of articles for final qualitative synthesis of the present systematic review.

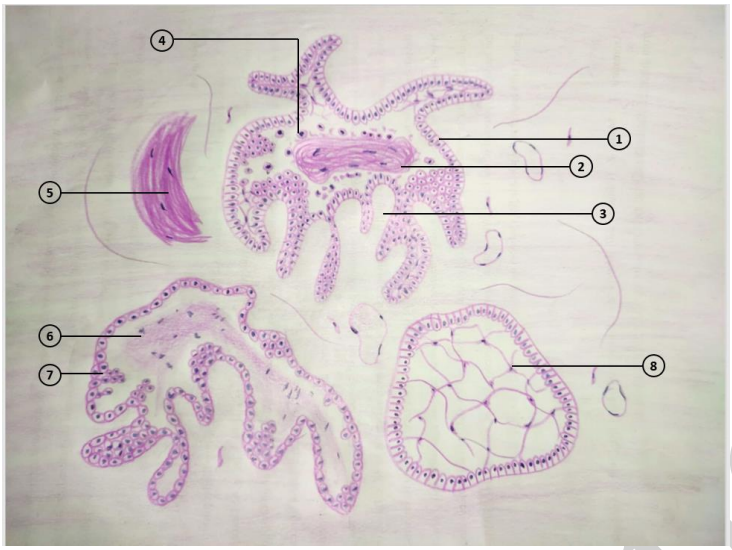

Figure 2: Line diagram illustrating histopathological features of PKA. Ameloblast-like cells (1), Stacks of keratin within cystic degeneration in the follicle (2), Papillary projections into the follicle (3), Acantholytic cells (4), Keratin extruded into the stroma (5), Necrotic material within the follicle (6), Micropapillary structures in a follicle lined by squamous epithelial cells (7), Normal ameloblastoma-like follicle with central stellate reticulum-like cells (8)

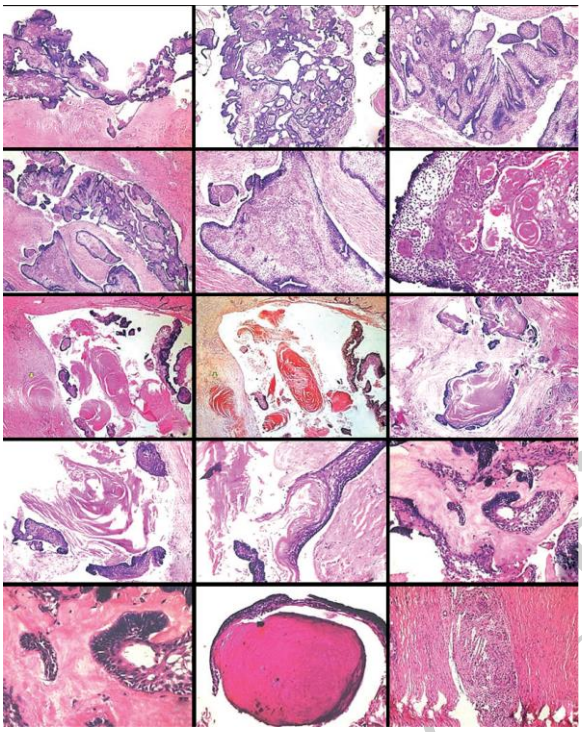

Figure 3: "(A) Photomicrograph exhibiting proliferating odontogenic epithelium lining the cystic lumen (H&E, ×40); (B) odontogenic epithelium proliferating in plexiform pattern of odontogenic epithelium (H&E, ×100); (C) papillary projections from odontogenic epithelium (H&E, ×100); (D) papillary proliferation of odontogenic epithelium within a collagenous connective tissue stoma (H&E, ×40); (E) extensive squamous metaplasia with in odontogenic islands lined by tall columnar ameloblast-like cells (H&E, ×100); (F) squamous metaplasia with keratin pearl formation (H&E, ×100); (G) "keratin filled cystic spaces" with keratin production in the stroma (H&E, ×100); (H) "keratin filled cystic spaces" with keratin production in the stroma (Krebergs Stain, ×100); (I) "curvilinear ribbons" of odontogenic epithelium within collagenized stroma, which is extruding a "lamellar stack of keratin" into the stroma without foreign body response (H&E, ×100); (J) "pacinian-like" stack of keratin (H&E, ×100); (K) parakeratin packed elongated epithelial follicles showing lamellar arrangement of keratin forming "hair-like structures" (H&E, ×100); (L) formation of dentinoid-like material adjacent to odontogenic epithelium (H&E, ×100); (M) dentinoid-like material (H&E, ×1,000); (N) dentinoid-like material with tubular structures (H&E, ×1,000); (O) granuloma with cholesterol cleft formation (H&E, ×100)." (Picture obtained from the case reported by Bedi et al.[2])

453 **Table 1:** Summary of demographic, clinical, radiological features and management of cases of PKA by various authors

Sr. No.	Author	Year	Age years	Sex	Race	Duration	Jaw	Side	Region	Extent	Symptoms	Radiographic features	Final Diagnosis	Treatment and Follow-up	GRADE System
1	Pindborg et al.	1970	57	F	Unknown	Unknown	Mn	Right	Posterior	Body, Angle, Ramus	Unknown	ML RL	PKA	Unknown	Low
2	Altini et al.	1991	76	F	South African	12 months	Mn	Right	Posterior	PM to Sigmoid notch	Swelling	WD ML RL	PKA	Hemimandibulectomy 1 year, NED	Moderate
3	Norval et al.	1994	26	F	South African	60 months	Mn	Right	Posterior	PM To 3M	Swelling, Pain	WD ML RL	Unusual variant of KA	Segmental resection + iliac crest graft	High
4	Takeda et al.	2001	76	M	Japanese	Several months	Mn	Left	Posterior	C to 2M, body	Swelling	WD ML RL	KA	Surgical resection	High
5	Collini et al.	2002	62	M	Italian	3 months	Mn	Right	Posterior	Ramus and condyle	Swelling, difficulty in mandibular movement	Osteolytic lesion with irregular calcifications	PKA	Hemimandibulectomy + Modified neck dissection Recurrence after 39 months Resection Recurrence after 18 Died after 6 years due to concurrent lymphoma	High
6	Mohanty et al	2013	46	M	Indian	12 months	Mn	Right	Posterior	C to Ramus	Swelling	ID ML RL	PKA	Unknown	Moderate

7	Bedi et al.	2015	27	F	Indian	7 months	Mn	Right	Posterior	2PM to sigmoid notch	Swelling	ID ML RL	KA complex histology	Wide excision recurred once after 3 years of en bloc resection	High
8	Konda et al.	2016	44	M	Indian	6 months	Mn	Right	Posterior	C to 1M	Swelling, intermittent pain, mobility of teeth	WD UL RL	papilliferous keratinizing variant of solid multicystic ameloblastoma	In toto excision 1 year, NED	High
9	Kuberappa et al.	2017	65	M	Indian	4 months	Mn	Right	Antero-Posterior	31 to 47	Swelling, pain	ID ML RL	PKA	Wide excision 2 months, NED	High
10	Rathore et al.	2017	18	M	Indian	3 months	Mn	Right	Posterior	C to 3M	Swelling	WD UL RL	PKA	Wide excision 2 years, NED	High

Legends for Table 1:

M = Male, F = Female; Mn = Mandible

C = Canine, PM = Premolar, M = Molar

WD = Well-defined, ID = Ill-defined, ML = Multi-locular, UL = Unilocular, RL = Radiolucency

PKA = Papilliferous keratoameloblastoma, KA = Keratoameloblastoma

NED = No evidence of disease

463 **Table 2:** Summary of histopathological features observed in cases of PKA reported by various authors

Author	Epithelial component							Connective tissue component	
	Type	Cystic Degeneration	Necrotic material	Desquamated keratin	Papillary projections	Ameloblast-like features	Stratified squamous lining in follicles	Extruded keratin	Hard tissue formation
Pindborg et al.	Follicles/islands	Present	Present	Present	Present	Present	Present	Absent	Absent
Altini et al.	Follicles	Present	Present	Present	Present	Absent	Present	Absent	Absent
Norval et al.	Follicles	Present	Present	Present	Present	Present	Questionable	Present	Dystrophic calcification
Takeda et al.	Follicles	Absent	Absent	Present	Present	Present	Present	Present	Cellular cementum / woven bone-like
Collini et al.	Nests, tubules, islands, Indian file	Present	Minimal	Present	Present	Present	Absent	Absent	Absent
Mohanty et al.	Follicles	Present	Present	Present	Present	Present	Absent	Absent	Absent
Bedi et al.	Follicles, nests, chords, plexuses	Present	Present	Present	Present	Present	Absent	Absent	Dentinoid material
Konda et al.	Plexiform	Absent	Absent	Present	Present	Present	Absent	Present	Absent
Kuberappa et al.	Follicle, plexiform	Present	Present	Present	Present	Present	Present	Absent	Absent
Rathore et al.	UAM with mural islands	Present	Present	Present	Present	Present	Present	Absent	Absent

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