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CASE REPORT

Adenomatoid odontogenic tumor arising from a dentigerous cyst—A case report

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Summary Adenomatoid odontogenic tumor (AOT) is a benign lesion derived from the complex system of dental lamina or its remnant. It is categorized into three variants (follicular, extrafollicular and peripheral). To our knowledge, there are only six existing cases of AOT associated with dentigerous cyst. We present an additional case from a dentigerous cyst around the crown of an unerupted canine in a 15-year-old boy. We provide histological evidence of an 'odontoma-like' area, as has been described in only one other previous case report. The clinical characteristics of our patient and the six previously reported cases are also briefly discussed. We believe that this case represents an odontogenic cyst with neoplastic development, containing both epithelial and mesenchymal components. As more cases accumulate, we will be able to study these rare lesions further whether the AOTs derived from an odontogenic cyst could represent a distinct 'hybrid' variant (separate to the three variants described thus far).

1. Introduction

Adenomatoid odontogenic tumor (AOT) is a benign odontogenic lesion. Philpsen et al. [1] subdivide this condition into three groups referred to as follicular, extrafollicular and peripheral. These variants have common histologic characteristics that indicate a common origin, as derived from the complex system of dental lamina or its remnant [1]. The follicular and extrafollicular variants account for 96% of all AOT (and 71% of these are follicular variants). The peripheral variant is the rarest, with only 18 cases reported so far [2]. The former two variants are intraosseous (central) and are more commonly found in the maxilla than in the mandible at a ratio of approximately 2:1.

The follicular variant is associated with the crown and often part of the root of an impacted (unerupted) tooth. This is most commonly the maxillary

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canine and rarely the permanent molars as well as the deciduous teeth. Therefore, the follicular variant is often initially regarded as a dentigerous cyst based on clinical and radiographic evaluation. Indeed, as many as 77% of follicular variants of AOT are clinically diagnosed as dentigerous cysts [3].

The extrafollicular variant is not associated with the crown of an unerupted tooth. Instead, this variant presents as a well-defined, unilocular radiolucency between, above or superimposed upon the roots of erupted, permanent teeth. Consequently, a clinical diagnosis of a residual, radicular, globulomaxillary or lateral periodontal cyst can be made according to the definite intraosseous location of the variant. The peripheral variant almost certainly always appears as a gingival fibroma or epulis in the anterior maxilla (88%) [1,2].

Here, we present an uncommon case of AOT arising from a dentigerous cyst around the crown of an unerupted canine in a 15-year-old boy.

2. Case report

A 15-year-old boy was referred by his family pediatric dentist for evaluation of the delayed eruption of his left upper canine and delayed exfoliation of his left upper deciduous canine. At this time, a firm, non-tender swelling was noted over the left upper buccal gingiva (Fig. 1A). The swelling was painless and not associated with either paresthesia or anesthesia. Clinical examination revealed a smooth nodule in the buccal gingiva, vestibule and palatal gingiva that extended from the left upper central incisor to the first premolar (Fig. 1A and B). Three milliliters of straw-colored fluid (and no cholesterol) were aspirated from the lesion (Fig. 1C). It was also noted that the anterior teeth were crowed and a retained left upper deciduous canine with grade III mobility were present. The left upper permanent canine could not been seen on clinical examination (Fig. 1A and B). Percussion pain was not elicited overlying any of the teeth involved and electric pulp vitality testing was unremarkable.

A panoramic radiograph revealed a well-defined, unilocular, round-shaped, and circumcoronal radiolucency over an unerupted canine. This was associated with a well-developed root formation, extending from the apex of the left upper central incisor to the distal aspect of the left upper second premolar and from the apex of the retained left upper deciduous canine to the cementoenamel junction of the unerupted left upper canine, and measured approximately 3 cm $\times$ 2.5 cm in diameter (Fig. 2A). A unilocular radiolucency with an unerupted left upper canine could also be seen on the upper left occlusal film (Fig. 2B). Based on these clinical findings, a diagnosis of dentigerous cyst was made. A small bony window of approximately 5 mm $\times$ 5 mm was made within the portion of labial plate that corresponded to the upper left central incisor. An incisional biopsy was performed and a histological diagnosis of dentigerous cyst with non-keratinized epithelial lining and fibrous connective tissue was made (Fig. 3).

Under general anesthesia, the mass was approached intraorally via a reflected mucoperiosteal flap. Bony perforation was noted over the apical

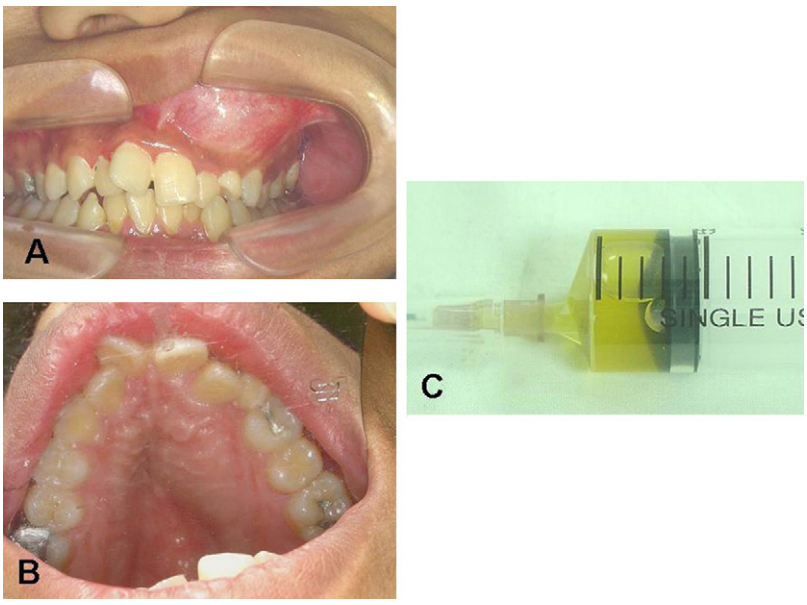

Fig. 1 Buccal (A) and palatal aspects (B) of the swelling. Aspiration of straw-colored fluid (C).

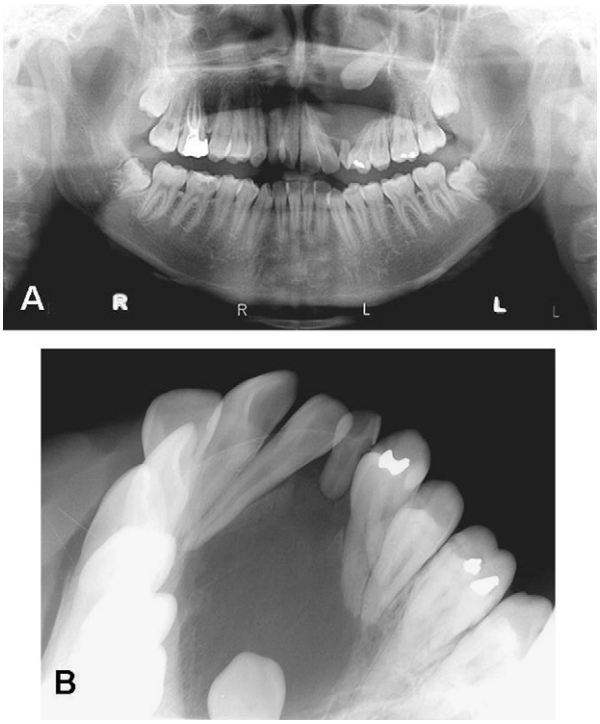

Fig. 2 A well-defined, unilocular, round-shaped circumcoronal radiolucency over an unerupted canine was noted in both panoramic (A) and occlusal radiographs (B).

region of the left upper central incisor (at the previous biopsy site) and the thin nature of the labial cortical bone was comparable to that of an eggshell. The bony window was next enlarged (Fig. 4), so that the entire lesion could be separated easily from the adjoining bone and removed together with the involved tooth. The retained deciduous upper canine was removed simultaneously. There was no evidence of oro-nasal and oro-antral communication, and the palatal mucosa was intact. Triosite (artificial bone graft, 2 ml/bottle, four bottles) was placed within the surgical defect and the wound was then sutured closed.

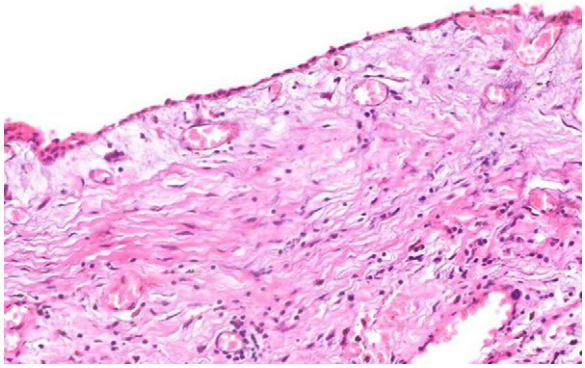

Fig. 3 Incisional biopsy revealed a non-keratinized epithelial lining and fibrous connective tissue (hematoxylin and eosin, 100×).

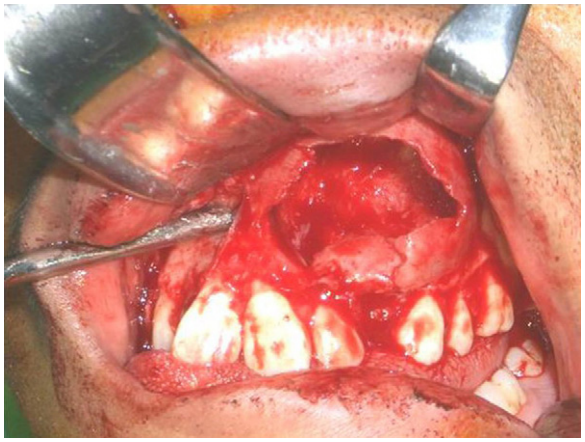

Fig. 4 Surgical view with the bony perforation of the swelling.

The surgical specimen was submitted for pathological examination. It measured approximately 3.5 cm in diameter, and as indicated by radiographic investigation of the specimen, surrounding the crown of the unerupted canine (Fig. 5A and B). Three distinct regions could be identified within the cut sections of the specimen. The most obvious

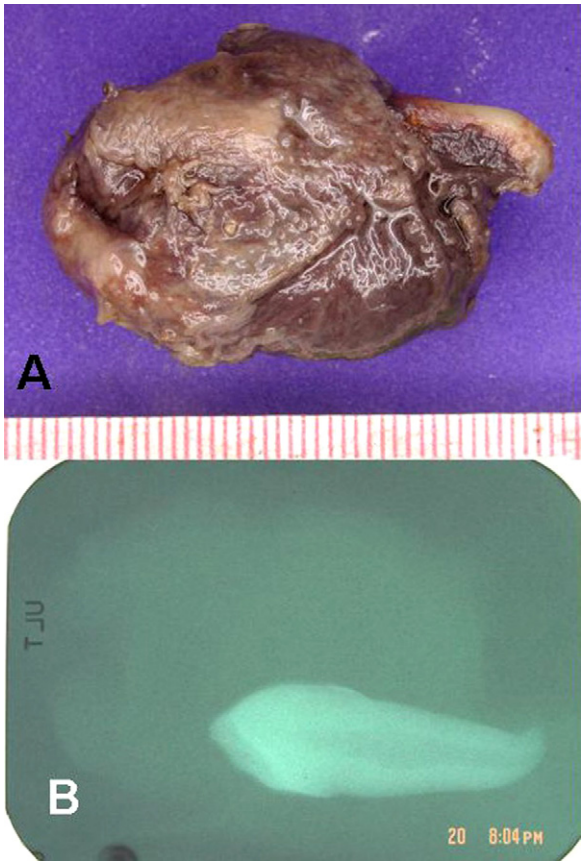

Fig. 5 Surgical specimen of the lesion (A); periapical radiograph of the specimens revealing the crown of the unerupted canine (A and B).

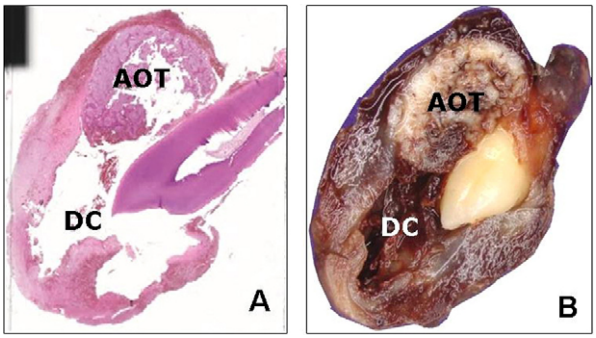

Fig. 6 Low-power view of the cystic space (DC), tooth and solid area (AOT) (hematoxylin and eosin, 4×) (A) corresponding to the macroscopic observation of the cut section of the specimen (B).

is a well-developed canine and crown portion, circumscribed by cyst (Fig. 6A). The cystic region was brownish in color and contained a little brownish fluid. It measured approximately 2 cm in diameter (Fig. 6A). There was a solid part adjacent to the tooth which was whitish in color, firm in consistency and measured about 1.5 cm in diameter (Fig. 6A).

Corresponding with gross observation, the three parts (cystic space, tooth and solid area) could also be identified microscopically (Fig. 6B). Sections of the solid tissue contained histologic characteristics of AOT (Fig. 7A and B). The tumor was composed of nodules of various sizes consisting of cuboidal or columnar epithelial cells that formed nests or rosette-like structures. Foci of eosinophilic hyaline droplet material and calcification were also observed (Fig. 7A and B). Areas of mitoses or necrosis were not observed. As previously noted from the incisional biopsy, the cystic area was composed of dense fibrous tissue lined by one to three layers of cuboidal cells. Furthermore, this lining of the cyst was in continuity with the AOT area (Fig. 8A). Interestingly, multiple areas of cementicles and osteodentin (presumed to be an 'odontoma-like' area) can be observed at the periodontal ligament of the impacted canine (Fig. 8B). The junction of the tooth and the epithelial lining is also shown in Fig. 8C. Consequently, the final histological diagnosis was AOT arising from a dentigerous cyst over the left maxilla. The postoperative course was uneventful and during the last 2 years there have been no signs of recurrence at follow-up.

3. Discussion

AOT was first described by Ghosh [4] in 1934 as an adamantinoma of the maxilla and was first recognized as a distinct pathological entity by Staphne [5] in 1948. According to the second edition of the WHO

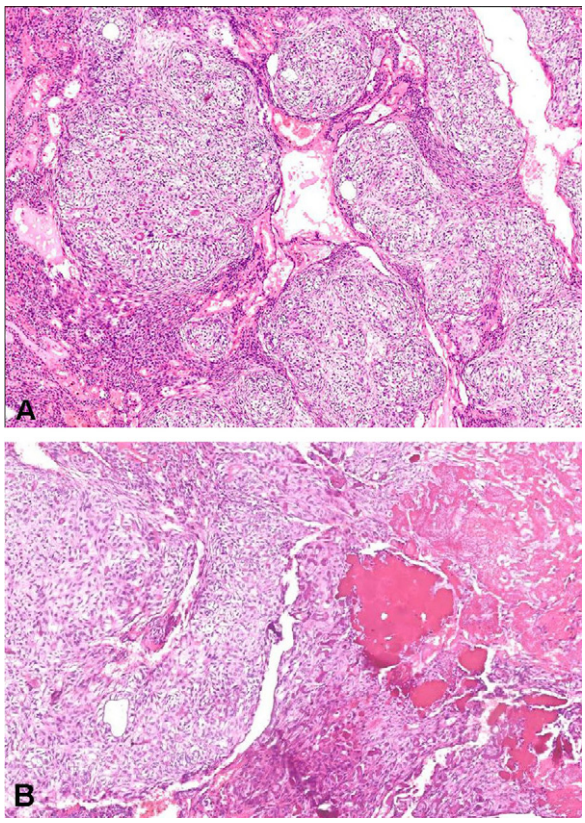

Fig. 7 The tumor consisted of solid nodules of various sizes. Within these, cuboidal or columnar epithelial cells formed nests or rosette-like structures (A); foci of aggregates of eosinophilic hyaline droplet material and calcification were also noted (B).

''Histological Typing of Odontogenic Tumors'' [6], AOT is defined as: ''A tumor of odontogenic epithelium with duct-like structures and with varying degrees of inductive change in the connective tissue. The tumor may be partly cystic, and in some cases the solid lesion may be present only as masses in the wall of a large cyst''.

An extensive review of 500 cases of AOT has been conducted by Philipsen et al. [1]. Most recently, Leon et al. [7] described a multicentre study of both the clinicopathological and immunohistochemical features of 39 cases of AOT. Two-thirds of these tumors were diagnosed in the second decade of life, and over 50% occurred in adolescents between the ages of 13 and 19 years. Our patient falls into this group but it is noted that the range of occurrence is actually very wide (3—82 years) [1,2,7]. Both follicular and extrafollicular variants occur more commonly in the maxilla than in the mandible, with a ratio of 2.1:1. The female:male ratio for all age groups and AOT variants together is about 2:1, with an even higher female preponderance (approximately 3:1) among certain Asian populations. Our patient is an Asian male.

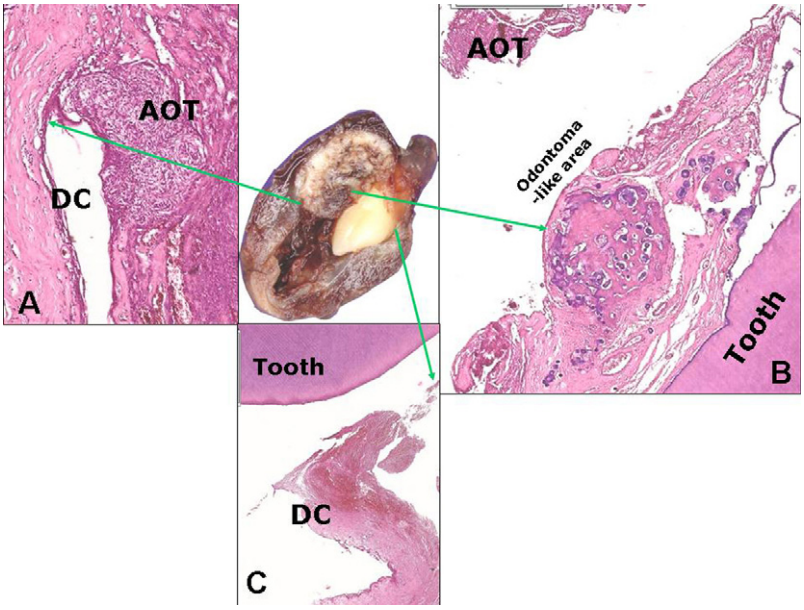

Fig. 8 Continuity between the cystic lining (DC) and the tumor (AOT) area was noted (A); multiple areas of cementicles and osteodentin, presumably as an 'odontoma-like' area can be observed at the periodontal ligament of the unerupted canine (B); the junction of the tooth and epithelial lining is also seen (C) (hematoxylin and eosin, 100×).

As previously mentioned, AOTs are usually solid but are occasionally cystic. Very few cases have been described that arise in association with a dentigerous cyst. A systematic search of the English-language medical literature revealed only six such cases (PubMed search using the keywords adenomatoid odontogenic tumor, dentigerous cyst) [8—13]. The clinical characteristics of these six cases and the current case are summarized in Table 1. It is noted that the male to female ratio is 6:1 and nearly all cases occurred during the second decade of life, ranging from 8 to 22 years old. Furthermore, four cases were patients of Asian origin, one was African and one was Caucasian. The common symptom across these seven cases was a maxillary swelling that was either painless or painful. The most commonly involved tooth was the maxillary canine (five cases); the others involved were the first premolar and the third molar. Interesting, only one case depicted a well-defined radiopaque mass; all of the others lesions appeared as a well circumscribed unilocular radiolucency around an unerupted tooth.

Tajima et al. [10] describe an AOT located in the maxillary sinus and speculate that the tumor was derived from a dentigerous cyst. Philipsen et al. [14] also postulate that the follicular type of AOT develops from nests of cells within the dental lamina, and therefore as a result surrounds the tooth. Furthermore, they suggest that the formation of the extrafollicular variant may be derived from the epithelial nests that are situated at the border of the conduit of tooth eruption. Consequently, the tooth would not be embedded in its eruption by the developing AOT.

As noted from microscopic and macroscopic observations, the tumor portion in the current case is continuous with the cystic lining and protrudes into the lumen it creates. Given that the tumor portion is separated from the unerupted canine, we believe that a dentigerous cyst with an unerupted canine would develop first and through a stimulus that is yet to be determined, the AOT would subsequently arise from the epithelial rests of the dental lamina within the odontogenic cystic lining. The tooth is enveloped within the dentigerous cyst but the subsequent AOT is not. On the other hand, Curran et al. [15] describe an extrafollicular AOT that presented with periapical disease and has histologic features that reveal a cystic configuration with a central cavity lined by stratified squamous epithelium that is interrupted by the growth of the AOT. Indeed, AOT has also derived from a calcifying epithelial odontogenic cyst (a difference type of odontogenic cyst) [16]. Furthermore, the epithelium of an odontogenic cyst may transform into other odontogenic neoplasms such as an ameloblastoma [17] or even transform into other malignancies such as squamous cell carcinoma or mucoepidermoid carcinoma [18,19]. Significantly, Leon et al. [7] have demonstrated the positivity of CK13 in the cystic epithelium of AOT, which was negative in all other areas of AOT, implying that the cystic epithelial lining may be different to epithelial cells of the areas of AOT. Given that the number of reported cases to date is so small and that the

Table 1 Clinical data of the reported cases of adenomatoid odontogenic tumor arising from a dentigerous cyst

Case no. (authors)	Age (years)	Sex	Race	Symptom	X-ray finding	Other finding
(1) Valderrama [8]	16	Female	Philippians	Right facial asymmetry	Unilocular radiolucency, tooth 14 crown surrounded	Presence of complex odontoma
(2) Warter et al. [9]	8	Male	Nigerian	A tender swelling	Unilocular radiolucency, tooth 13 crown surrounded	Contained melanocytes and melanin-laden epithelial cells
(3) Tajima et al. [10]	15	Male	Japanese	Asymptomatic lesion	A well-defined radiopaque mass and crown of uneruption 28	
(4) Garcia-Pola Vallejo et al. [11]	12	Male	Spanish	Swelling	Unilocular radiolucency, tooth 23 crown surrounded	Agenesis of tooth 15 and 24
(5) Takahashi et al. [12]	22	Male	Japanese	Painless swelling, nasal obstruction	Unilocular radiolucency, tooth 28 crown surrounded	Expanding to sinus
(6) Bravo et al. [13]	14	Male	Not-stated	Swelling, sharp pain	Unilocular radiolucency, tooth 23 crown surrounded	Expanding to sinus
(7) Chen et al. (this case)	18	Male	Chinese	Swelling	Unilocular radiolucency, tooth 23 crown surrounded	Retained deciduous tooth 63

stimulus acting on the cell rests of the dental lamina in the epithelium of an odontogenic cyst is not known, we are unable to speculate whether the AOTs derived from an odontogenic cyst could represent a distinct 'hybrid' variant (separate to the three variants described thus far). This single case report cannot answer this question; however, further investigation into this possibility would take place as more cases of AOT arising from an odontogenic cyst occur.

Clinically, the manifestation of a delayed tooth eruption or exfoliation (as in the current report) deserves particular attention from a family pediatric dentist. It is of utmost importance that such patients are promptly referred for further radiographic and histologic investigation to clarify the underlying cause (including AOT arising from a dentigerous cyst) at the soonest opportunity.

Interestingly, a premature 'odontoma-like' area is noted at the periodontal ligament of the impacted canine. Valderrama [8] has reported a case of dentigerous cyst with intracystic AOT and complex odontoma. The dimension of this area in the current case is small and cannot be regarded as an odontoma, but its presence is still quite unique. Although AOT has been found to have the ability to produce enamel proteins and extracellular matrix molecules [20], this interesting area is indeed located at the periodontal ligament of the tooth portion (but not at the AOT portion). One may speculate that with time to evolve this area could develop and fuse into a mature complex odontoma.

The AOT and dentigerous cyst are both benign, encapsulated lesions and conservative surgical enucleation or curettage is the treatment of choice. The prognosis for a dentigerous cyst is good, and recurrences are very rare after complete removal of the lesion. There have been no reports of aggressive behavior on the part of AOT and recurrences are very rare.

4. Conclusion

Very few case reports of AOT arising from a dentigerous cyst with histological identification have previously been reported. We believe that the present case represents an odontogenic cyst with neoplastic development, containing both epithelial and mesenchymal components.

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