



# Coexistence of Adenoid Cystic Carcinoma and Sialolithiasis in Submandibular Gland: Case Report

## Case Report

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## Abstract

Sialolithiasis is the primary cause of swelling in the major salivary glands. The etiopathogenesis is not clear. Adenoid cystic carcinoma is a slow-growing salivary gland malignancy with a poor prognosis. There are only a few cases in the literature reporting the coexistence of sialolithiasis and adenoid cystic carcinoma. In this report, we present a case that was thought to have sialolithiasis in the foreground because of the calcified image on computed tomography, but was diagnosed with adenoid cystic carcinoma after excision, together with a discussion of the relationship between sialolithiasis and carcinogenesis.

**Keywords:** Salivary glands, adenoid cystic carcinoma, sialolithiasis, malignancy, tumor, case report

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## Introduction

Adenoid cystic carcinoma (ACC) is a slow-growing salivary gland malignant tumor with a poor prognosis. Its incidence is two per 100,000. It constitutes less than 1% of all head and neck cancers and less than 10% of all salivary gland neoplasms. Most of the cases are located in the major salivary glands. The 10-year survival is between 50–70%. Surgical excision and adjuvant radiotherapy (if necessary) are preferred for treatment (1).

Sialolithiasis is the primary cause of swelling in the major salivary glands. Its incidence has been reported between 1 in 30,000 and 1 in 10,000. It develops in the submandibular gland in 80–90% of the cases. Salivary gland stones are composed of a combination of organic and inorganic substances, including calcium

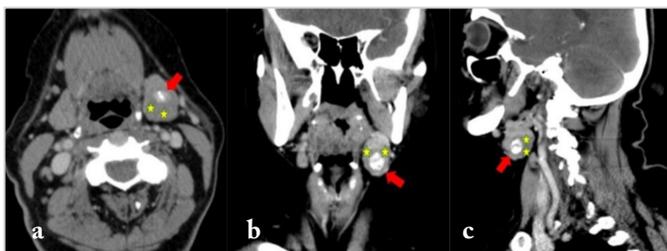
carbonates and phosphates, cellular debris, glycoproteins, and mucopolysaccharides. The pathogenesis of sialolithiasis is not clear (2).

In this article, we present the case of a patient who was thought to have sialolithiasis because of the calcified image on computed tomography (CT) but was diagnosed with ACC after excision together with a discussion of the relationship between sialolithiasis and carcinogenesis.

## Case Presentation

A 65-year-old female patient was admitted to the Ear Nose and Throat Diseases Clinic with swelling under her left chin. She stated that the swelling had existed for five years and increased in size and pain over time. The patient had hypertension and was using antihypertensive drugs.

She had no history of smoking, alcohol, or previous surgery. The patient had no history of sialolithiasis or any other salivary gland disease. There was no feature in the family history. On physical examination, a solid, fixed, painless mass lesion measuring 3x2 cm was palpated in the left submandibular area. No additional finding was found in the routine ear, nose and throat examination. The lesion was evaluated with contrast-enhanced head and neck CT. On CT, a calcified lesion with a diameter of approximately 1.5 cm in the left submandibular gland and a hypodense area reaching 4 mm in the surrounding submandibular gland tissue of this lesion was observed (Figure 1). For this hypodense area, it was decided to perform an imaging-guided fine-needle aspiration biopsy to differentiate chronic inflammation and malignancy. The biopsy was reported as suspicious for malignancy. Submandibular gland excision was performed for definitive diagnosis. During the operation, it was observed that the submandibular gland adhered to the surrounding tissue and was difficult to dissect. The salivary stone was located intraparenchymal. Histopathological examination was reported as grade 2 ACC. The tumor, measuring 2.5x2.2x2.1 cm, showed tubular and solid features, extracapsular invasion, and diffuse perineural invasion (Figure 2). Surgical margins were positive for the tumor. As a result of these findings, it was decided to perform a left supraomohyoid neck dissection. The primary lesion area was also re-excised with the neck dissection. No metastatic lymphadenopathy was observed in the histopathological examination of the neck dissection specimen. A residual invasive tumor was observed in the 3 mm area of the scar tissue. Due to capsule invasion, perineural invasion, and grade 2 tumor, a total of 66 Gy radiotherapy in 2.2 Gy/30 fractions was applied to the primary tumor area with intensity modulated radiation therapy technique as adjuvant therapy. The department of medical oncology did not recommend adjuvant chemotherapy. The patient was closely followed. No pathological finding was observed in the magnetic resonance imaging (MRI) of the neck six months after the operation.



**Figure 1.** A calcified stone in the central part of the left submandibular gland (red arrow; AP×T×CC: 15×9×14 mm) in contrast-enhanced neck CT [a] axial, b) coronal, and c) sagittal planes]. A hypodense area (yellow stars) was observed that represent inflammatory-edematous changes caused by the stone. The left submandibular gland is larger than the right one  
CT: Computed tomography

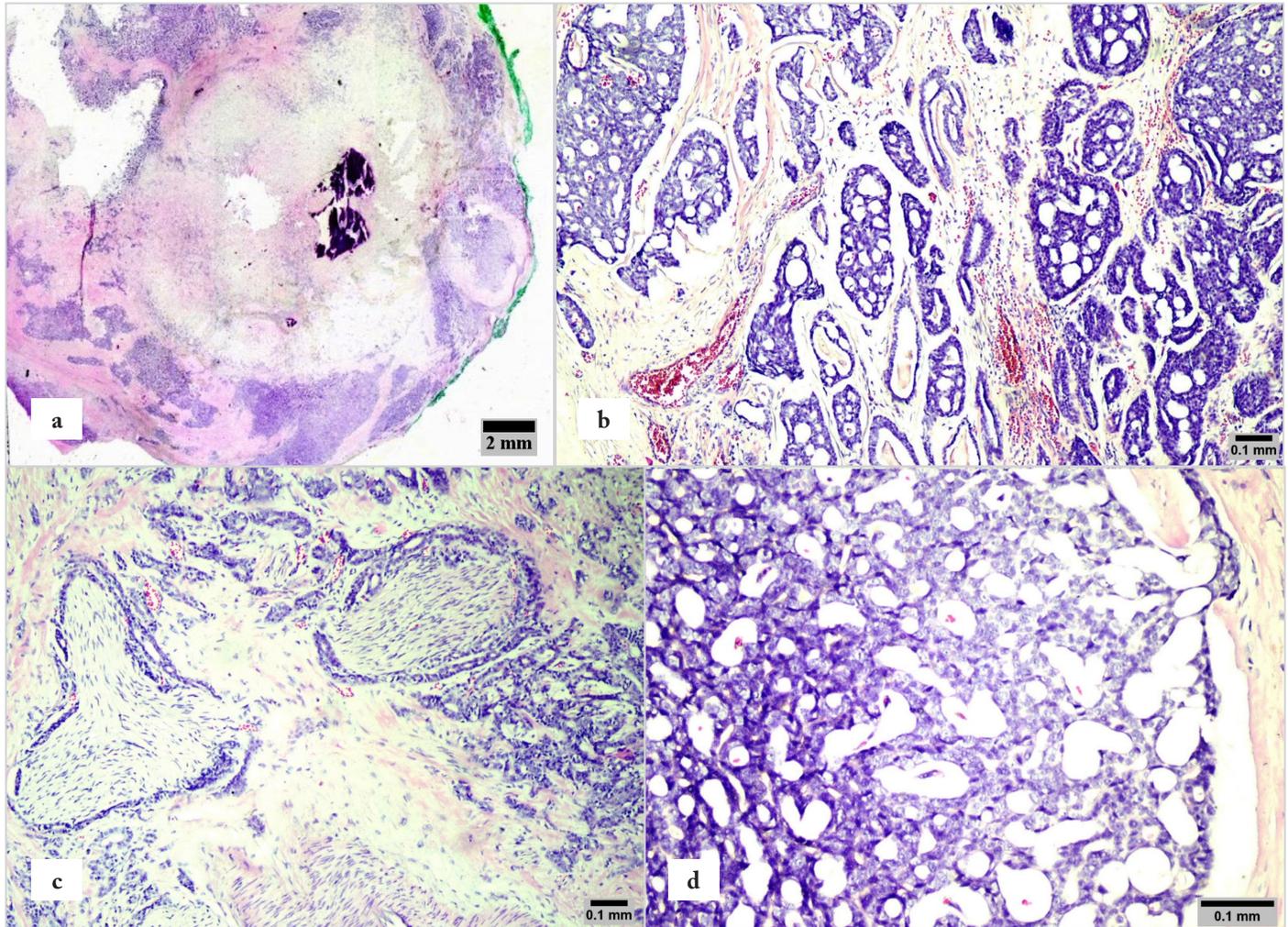
Informed consent was obtained from the patient for this report.

## Discussion

ACC is a slow-growing salivary gland malignancy with a poor prognosis, the mean age at diagnosis is 57 years, and it is more common in women. Patients often present with complaints of swelling (1). Its association with sialolithiasis is very rare and there are only a few reported cases (3, 4). The relationship of sialolithiasis with salivary gland neoplasms is unknown (3). Some studies in the literature suggested that sialoliths might cause tumor formation or, conversely, that sialoliths might form in the presence of tumors (5). It is also stated that chronic inflammation due to obstruction by sialoliths could be related to oncogenesis (3-5). Another view suggests that sialolite and tumor formation could be caused by common predisposing factors rather than a cause-and-effect relationship (6). Hasegawa et al. (4) reported a case with the coexistence of ACC and sialolithiasis. They drew attention to the relationship between lithiasis and related inflammation and carcinogenesis in organs other than salivary glands with examples of cholangiocarcinoma-hepatolithiasis, pancreatic carcinomas-pancreatitis/pancreatolithiasis. The authors stated that dysplasia detected histopathologically in the bile duct epithelium of patients with hepatolithiasis could also be present between sialolithiasis and salivary gland carcinogenesis, although an objective relationship could not be demonstrated between them (4). The relationship between chronic inflammation and various epithelial malignancies has been known for many years. Increased risk of malignancy in patients with inflammatory bowel and esophageal carcinoma that may develop after reflux esophagitis are examples of this relationship (7). A case of squamous cell carcinoma occurring from the Wharton's duct epithelium in a patient with sialolithiasis has also been reported (8). In this case, squamous metaplasia of ductal epithelial cells surrounding the stones and histopathological indicators of malignant transformation foci suggested a relationship between carcinogenesis and chronic inflammation (7).

The duration of symptoms in some cases with the coexistence of sialolithiasis and salivary gland neoplasm in the literature is remarkable. The swellings duration was 10 years in Miyabe et al.'s (9) and Hasegawa et al.'s (4) cases, 3 years in Gallego et al.'s (7) case, and 1.5 years in Nanda and Mehta's (10) case. In our study, as in these cases, the swelling was present for a long time (5 years). This may support the hypothesis of malignant development as a result of prolonged exposure to inflammation.

Ultrasonography is frequently used as the first-line radiological examination of salivary gland lesions. CT and MRI provide more detailed imaging. CT can successfully show the features of the stone in a patient



**Figure 2.** Images of the histopathological examination of the material after submandibular gland excision. a) Tumoral lesion consisting of centrally dystrophic calcification and hyalinization, peripheral solid islands, and scattered cells in between (x40, full slide scanning; H&E), b) Tubular cell groups with tubular and cribriform structure (x100; H&E), c) Perineural invasion areas (x100; H&E), d) Tumoral cells with large vesicular nuclei, prominent nucleoli, and extensive eosinophilic cytoplasm (x200; H&E)

with sialolithiasis. MRI, on the other hand, shows soft tissue lesions in more detail (2, 3). Batzakakis et al. (3) argued that ultrasonography alone was not sufficient in the planning of operations in patients with sialolithiasis and that such cases should be evaluated with MRI in the presence of suspected malignancy. However, contrast-enhanced CT can also successfully distinguish soft tissue lesions, as in our case. Therefore, we believe that MRI or contrast-enhanced CT may be preferred as an advanced imaging technique in these cases. If solid lesions other than stones are detected in the salivary gland in radiological examinations, we recommend performing a biopsy with suspicion of malignancy.

## Conclusion

The coexistence of ACC and sialolithiasis is extremely rare. Especially in cases with long disease duration, the entire salivary gland should be carefully examined via imaging. In

the presence of suspicious solid areas, imaging-guided fine-needle aspiration biopsy can be performed in these areas before surgical treatment. More comprehensive studies are needed to clarify the cause-effect relationship in these cases.

**Informed Consent:** Informed consent was obtained from the patient for this report.

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## Authorship Contributions

Surgical and Medical Practices: V.A., M.E.S., Concept: V.A., M.E.S., V.A.A., M.K., Design: V.A., M.E.S., V.A.A., M.K., Data Collection and/or Processing: V.A., M.E.S., V.A.A., M.K., Analysis and/or Interpretation: V.A., M.E.S., V.A.A., M.K., Literature Search: V.A., M.E.S., V.A.A., M.K., Writing: V.A., M.E.S., V.A.A., M.K.

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### Main Points

- The coexistence of adenoid cystic carcinoma and sialolithiasis is extremely rare.
- Especially in cases with long disease duration, the entire salivary gland should be carefully examined via imaging.
- In the presence of suspicious solid areas, imaging-guided fine-needle aspiration biopsy can be performed in these areas before surgical treatment.
- More comprehensive studies are needed to clarify the cause-effect relationship in these cases.

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