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CASE REPORTS

# Primary Alveolar Soft Part Sarcoma of Cheek: Report of a Case and Review of the Literature

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## Abstract

Alveolar soft part sarcoma (ASPS) is a rare soft tissue sarcoma characterized by an alveolar or organoid arrangement of polygonal tumour cells separated by fibrovascular septa. A specific fusion gene [*ASPS critical region 1* (*ASPSCR1*)—*TFE3*] was detected in ASPS. Despite being a slow-growing tumour without pain and dysfunction, ASPS is characterized by early metastasis, which leads to poor prognosis. Herein, we report a rare case of primary ASPS of the cheek harbouring *ASPSCR1* (exon 7)—*TFE3* (exon 5) fusion gene in a 21 year-old woman. This tumour was a well-circumscribed, smooth, round mass that was clinically suspected as a benign tumour. However, histologically, it was observed that the polygonal tumour cells were arranged in solid and alveolar growth patterns. Post-operative examination of the whole body excluded the possibility of metastasis at other sites. Thus, careful immunohistochemical and genetic analyses, as well as whole-body examination, demonstrated that the tumour was a primary ASPS of the cheek.

**Keywords** Alveolar soft part sarcoma · ASPS · Cheek tumour · *ASPSCR1* · *TFE3*

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## Introduction

Alveolar soft part sarcoma (ASPS) has a uniform pattern characterized by an alveolar or organoid arrangement of polygonal tumour cells separated by fibrovascular septa. Molecular studies have shown an unbalanced translocation t(X;17)(p11.2;q25) that leads to the fusion of the first seven exons of *ASPS critical region 1* (*ASPSCR1*) to exon 6 (type 1) or 5 (type 2) of *TFE3* [1]. This fusion is highly specific to ASPS [2, 3]. ASPS is a rare malignant tumour comprising of less than 1% soft-tissue sarcomas and accounting for less than 0.1% of sarcomas of the head and neck [1]. ASPS mostly occurs in the soft tissues of the lower extremities in adults and in the head and neck region in children. In the head and neck region, the most commonly affected sites are the tongue and orbit. Approximately 15 cases of ASPS of the cheek have been reported to date (Table 1) [4–12]. The presence of *ASPSCR1*—*TFE3* fusion gene was confirmed by reverse transcription-polymerase chain reaction (RT-PCR) in only one of those cases, but the fusion type was unknown [8]. Despite being a slow-growing tumour without pain and dysfunction, ASPS is characterized by early metastasis, one of the early manifestations of this disease [1]. The lungs, lymph nodes, and brain are the common sites of ASPS metastasis, thereby leading to poor prognosis [1, 13].

Herein, we report a case of ASPS of the cheek with *ASPSCR1* (exon 7)—*TFE3* (exon 5) gene fusion, as well as review the clinical and histological features of the case.

## Clinical Summary

A 21 year-old woman was referred to the Osaka University Dental Hospital with a chief complaint of painless swelling in the right buccal region. The patient had noticed a buccal mass for 5 months and had no significant medical history. Intraoral examination revealed a firm, well-circumscribed and non-tender mass on the right side of the cheek (Fig. 1a). The mass was approximately 20 mm in size. Further, contrast-enhanced T1-weighted magnetic resonance imaging (MRI) revealed a smooth and well-defined round lesion (Fig. 1b). Based on these clinical and imaging features, a benign salivary gland tumour was suspected. Then, the tumour was excised using oral approach, under the local anesthesia. The tumour mass was present under the

**Table 1** Clinical characters of alveolar soft part sarcoma cases of the cheek origin

| | Age/ Sex | Location | Maximum dimension (cm) | Tumour duration (months) | Shape | Meta/Rec | Follow-up (months) |
|---|---|---|---|---|---|---|---|
| Kimi et al. [4] | 25/F | Cheek | 1.2 | – | Well-circumscribed round mass | No | 36 |
| Charrier et al. [5] | 54/F | Cheek | 10 | 2 | – | Lung, liver, spleen, kidney | 3 weeks died |
| Kim et al. [6] | 22/M | Buccal space | NA | NA | Round or ovoid shape, lobulated contour | No | 22 |
| Min et al. [7] | 37/M | Cheek | 2.3 | 9 | Well-circumscribed round mass | No | 24 |
| Argyris et al. [8] | 13/M | Buccal mucosa | 3.2 | 2 | Lobulated mass | No | 12 |
| Mullins et al. [9] | 37/F | Cheek | 2.1 | 24 | – | No | 168 |
| Wang et al. [10, 11] | 36/F | Cheek | 6 | – | Well-circumscribed multiple nodules | No | 24 |
| Wang et al. [11] | 24/F | Cheek | 1.8 | – | Lobulated multiple nodules | No | 14 |
| Wang et al. [11] | 29/F | Cheek | 2.8 | – | Lobulated multiple nodules | No | 67 |
| Wang et al. [11] | 5/M | Cheek | 5.5 | – | Lobulated multiple nodules | 6 months Rec | 60 |
| Wang et al. [11] | 57/M | Cheek | 4 | – | Lobulated multiple nodules | No | 60 |
| Asano et al. [12] | 11/F | Cheek | – | – | – | Lung, breast, cranium | – |
| This case | 21/F | Cheek | 2 | 5 | Well-circumscribed round mass | No | 14 |

*Meta* metastasis, *Rec* recurrent, *NA* data not available

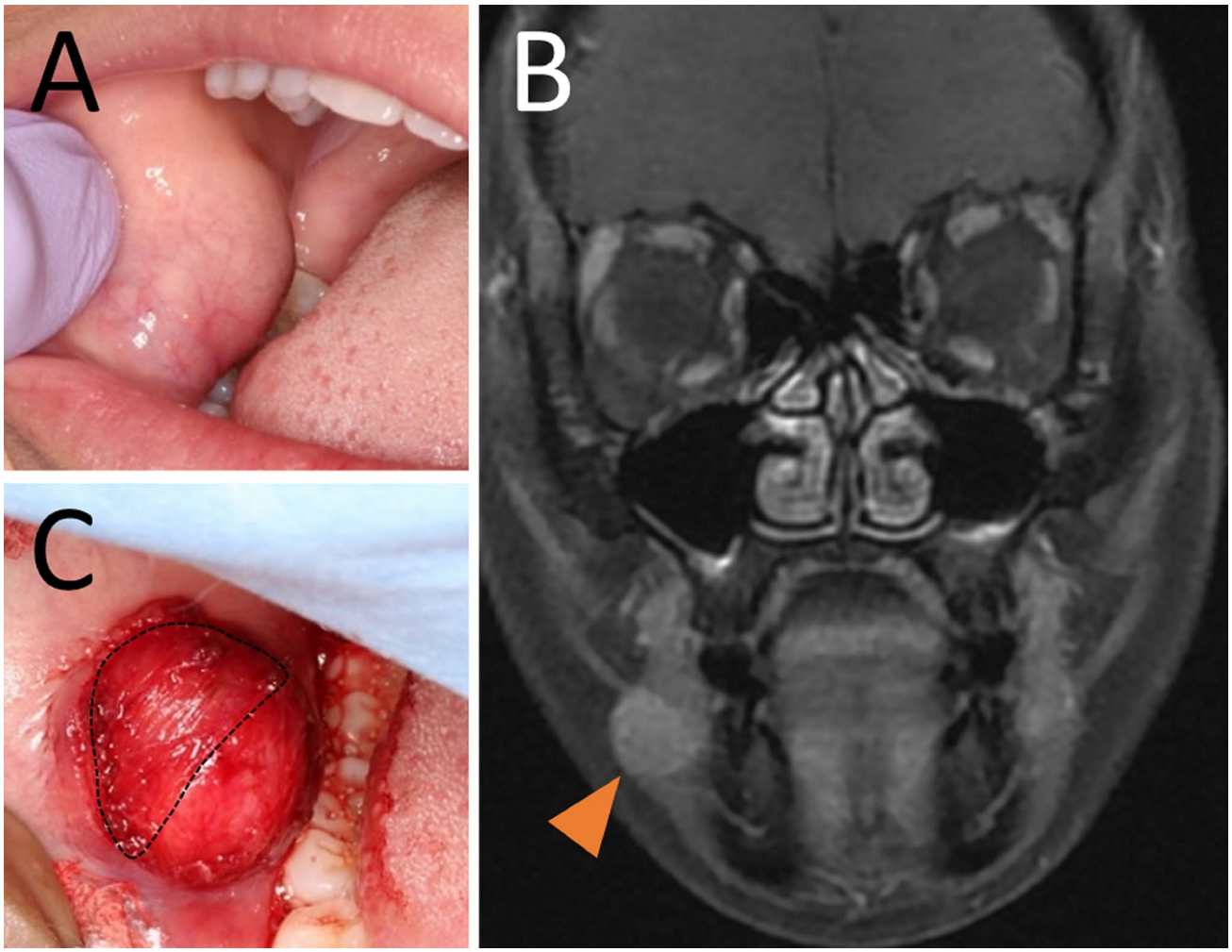


**Fig. 1** Clinical presentation. **a** Intra-oral finding. **b** Contrast-enhanced T1-weighted magnetic resonance imaging (MRI) in coronal view. **c** Surgical finding (dotted line indicated the buccinator)

buccal mucosa and was partially adhered to the buccinators (Fig. 1c, dotted line). The boundary between the tumour and the surrounding tissues was observed to be clear (Fig. 1c).

## Pathological Findings

Histological examination revealed a well-defined lesion with a solid nodular growth pattern (Fig. 2a). The lesion was encapsulated by a thin layer of fibrous connective tissue, and no invasive proliferation was observed in the adjacent tissues. The tumour showed an organoid growth pattern separated by vascularized septa (Fig. 2b, left side) and a solid growth pattern with abundant small vessels (Fig. 2b, right side). The two-patterned tumour areas were bordered and separated by an incomplete fibrous stroma, as well as had abundant eosinophilic cytoplasm and prominent nucleoli (Fig. 2b). Few mitotic figures and vascular invasions were also observed (Fig. 2c). Besides some lymphocytic aggregates observed at the periphery of the tumour (arrowheads in Fig. 2a and d). Based on these histological findings, the differential diagnosis included ASPS, paraganglioma, perivascular epithelioid cell tumor (PEComa) or metastatic tumours such as ASPS, adrenocortical carcinoma or renal cell carcinoma (RCC).

Immunohistochemical analysis showed that the tumour cells were nuclear-positive for TFE3 and cytoplasmic-positive for cathepsin K and MyoD1 (Fig. 3a–c). In contrast, the tumour cells were negative for AE1/AE3, cytokeratin (CK) 7, EMA, synaptophysin, chromogranin A, HMB45, Melan-A, and inhibin-α. The MIB1 (Ki-67) labelling index was highest at 3% (Fig. 3d). Immunohistochemical analysis of CD34 highlighted the delicate capillaries surrounding the tumour cells or nests (Fig. 3e). Additionally, the cytoplasm of the tumour cells contained periodic acid-Schiff (PAS)-positive diastase-resistant crystals (Fig. 3f). These results narrowed down the differential diagnosis to the possibility

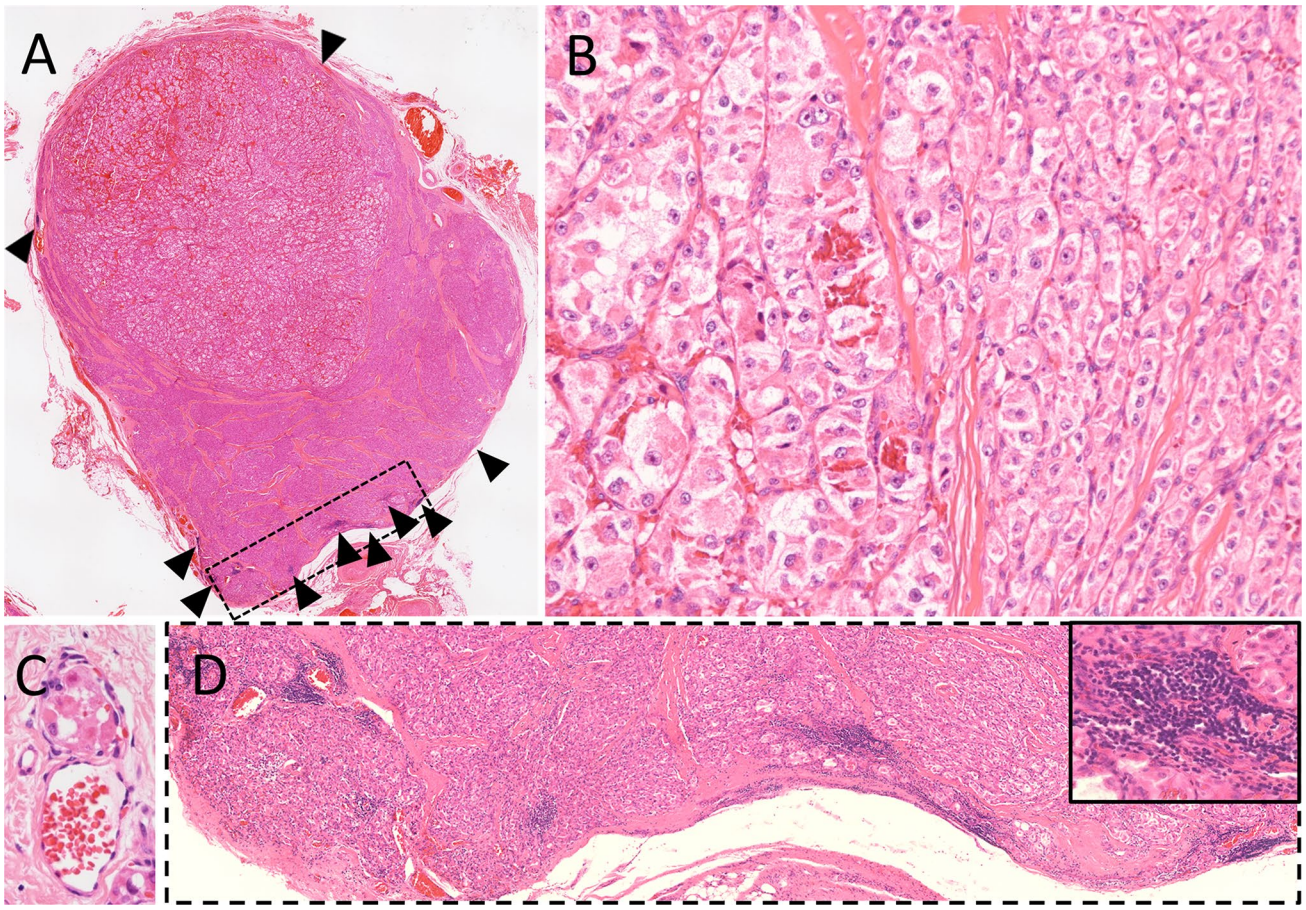


**Fig. 2** Histological findings. **a** Low-power view of the buccal tumor (arrowheads indicated lymphocytic aggregates). **b** Transitional area between alveolar growth pattern (left side) and solid growth pattern (right side). **c** Vascular invasion. **d** Lymphocytic aggregates [**d** was dotted-box area in (**a**)]

of ASPS. To confirm the diagnosis, RT-PCR using cDNA obtained from the paraffin-embedded specimen was performed followed by direct sequence analysis. The analysis revealed that exon 7 of *ASPSCR1* was fused to exon 5 of *TFE3* (*ASPSCR1—TFE3* type 2 fusion) (Fig. 3g). To differentiate between primary and metastatic ASPS in the lymph node, postoperative whole-body examination, including chest X-ray imaging and positron emission tomography-computed tomography (PET-CT) was performed. No signs of tumour were detected in the other organs. Thus, a final diagnosis of primary ASPS of the cheek was done. After 14 months of follow-up, there was no evidence of recurrence observed.

## Discussion

We reported a case of ASPS of the cheek, which was suspected to be a buccinator-lymph node metastasis. Primary ASPS of the cheek is exceedingly rare. Although approximately 15 such cases have been reported to date, only this case was confirmed to have type 2 *ASPSCR1* (exon 7)—*TFE3* (exon 5) fusion transcription (Table 1) [4–12].

Histological differential diagnosis of ASPS usually includes paraganglioma, adrenocortical carcinoma, RCC and PEComa, which are composed of solid and organoid growth patterns. These tumours are occasionally immunoreactive to TFE3 [14, 15]. In addition, *ASPSCR1—TFE3* translocation is occasionally observed in RCC and rarely in PEComa [15, 16]. Further, *TFE3* rearrangement and negative immunoreaction of synaptophysin and chromogranin A excluded paraganglioma. Similarly, *TFE3* rearrangement and negative immunoreaction of CK and inhibin-α excluded adrenocortical carcinoma, whereas that of HMB45 and Melan-A excluded PEComa. The positive immunoreaction of cathepsin K and PAS-positive cytoplasmic crystals differentiated ASPS from RCC [17]. These results led to the diagnosis of ASPS; however, it was difficult to distinguish between primary and metastatic buccinator lymph node lesions due to the following reasons: (1) ASPS mostly occurs

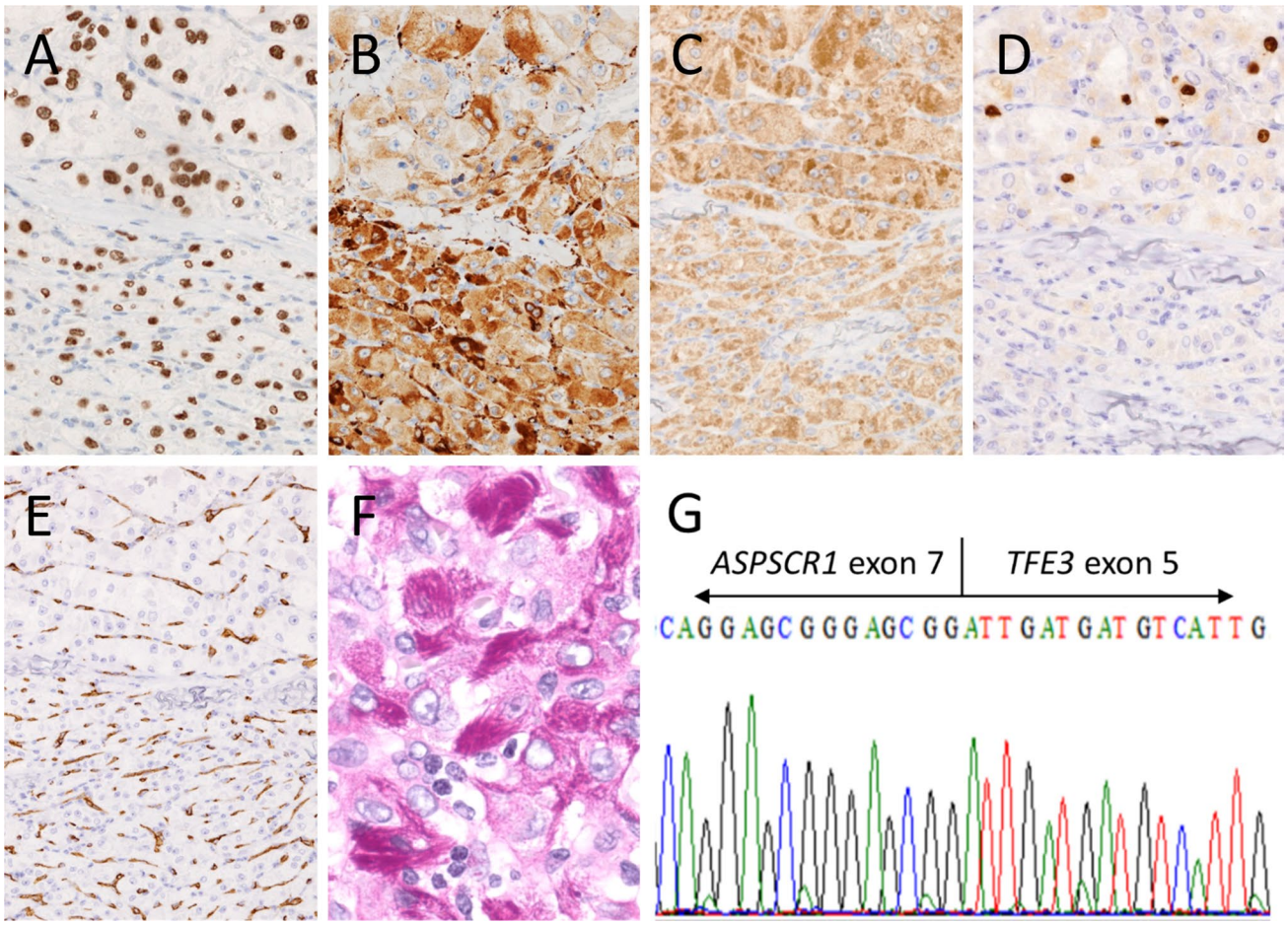


**Fig. 3** Immunohistochemical and genetic analyses. **a** TFE3, **b** cathepsin K, **c** MyoD1, **d** MIB1 and **e** CD34 immunostaining. **f** Periodic acid schiff (PAS) with diastase staining. **g** Direct gene sequencing

in the deep soft tissues of the lower extremities and rarely in the cheek [1]; (2) most ASPS tumours have poorly defined margins and have lobulated or irregular contours [1, 13, 18], but well-defined margins and smooth round contours were observed in our case; (3) lymphocytic infiltration within the ASPS is uncommon [1], but in our case, some lymphocytic aggregates were observed at the periphery of the tumour lesion (Fig. 2d); (4) lymph node metastasis is rare in most types of sarcomas, but it is relatively common in ASPS [13]. It is important to distinguish between primary and metastatic lesions, as ASPS metastasis is a majorly poor prognostic factor [1, 13]. Sood et al. [13] reported that lung metastasis is always observed in all patients with metastatic ASPS. However, in our case, postoperative chest X-ray imaging and PET-CT did not detect any tumour in other organs. Thus, we concluded that the tumour in our case was primary ASPS of the cheek.

Cheek ASPS is usually diagnosed at an earlier stage because of its superficial location, easy visibility, and obvious functional impairment [6, 10]. In contrast, general ASPS usually presents as a painless and slow-growing mass that rarely causes functional impairment, and it is considered as a high-grade sarcoma by definition [1]. Previous studies have reported that the cheek ASPS sometimes exhibited well-circumscribed margins (4/10, 40%) and round contours (4/10, 40%), while general ASPS had ill-defined margins and lobulated or irregular contours [1, 4–13, 18]. In the cheek ASPS, the mean size was 3.7 cm (range 1.2–10 cm) and mean age was 33.7 years (range 5–57 years), whereas, in general ASPS, the mean size was 6.5 cm (range 1.2–24 cm) and mean age was 25 years (range 1–78 years) [1, 4–12]. The median size of lingual ASPS was 2.5 cm and that of orbital ASPS was 2.85 cm [19, 20]. The median age of lingual ASPS was 5 years and that of orbital ASPS was 12 years [19, 20]. The rarity of ASPS in the head and neck region makes the determination of prognostic factors for survival difficult. Lingual and orbital ASPS have very high survival rates, which could be one of the possible reasons for the identification of only a small size of patients of young age during diagnosis [1, 21]. Compared to ASPS that usually

occurs in the tongue and orbit in the head and neck region of children, cheek ASPS occurs in older patients and is not very different in size [1, 19, 20].

General ASPS shows an alveolar growth pattern, whereas ASPS occurring in the tongue of younger patients often shows a solid morphology without alveolar appearance [20]. In our case, the tumour was composed of solid and alveolar growth patterns. Fanburg-Smith et al. [20] proposed that the architecture of ASPS may be an age-related feature—the spectrum from solid growth pattern in very young patients to alveolar pattern in older children. A few cheek ASPS cases have also been reported to exhibit a solid to sheet-like growth pattern of tumour cells, as described in our case [8, 9]. In these cheek cases, the mean size was 2.43 cm (range 2–3.2 cm) and mean age was 23.7 years (range 13–37 years) [8, 9]. Thus, ASPS occurring in the tongue of children and in the cheek of adults tends to show a more solid growth pattern [20].

In summary, we reported the primary ASPS of the cheek. This tumour was a well-circumscribed, smooth, round mass that was clinically suspected as a benign tumour. Histologically, the tumour cells were arranged in solid and alveolar growth patterns. Some lymphocytic aggregates were present at the periphery of the tumour, which was suspected to be a metastatic lesion in the lymph node. Thus, careful immunohistochemical and genetic evaluation, as well as whole-body examination, demonstrated that the tumour was cheek ASPS.

**Author Contributions** All the authors contributed to this work. KH designed the study. KH, KN, YU, KO, YF, YH, EM, and ST interpreted the H&E and immunohistochemical findings. KH and MK performed the experiments and assembled the data. KH, YH, and ST contributed to the writing of the manuscript. TU, ST, SY, YI, and SM reviewed the clinical and radiological data. All authors reviewed and approved the manuscript for submission.

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## Declarations

**Conflict of interest** All authors state that they have no conflict of interest.

**Ethical Approval** This case report was approved by the Ethical Review Board of the Graduate School of Dentistry, Osaka University (No. R1-E46) and was performed in accordance with the Committee guidelines and regulations.

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