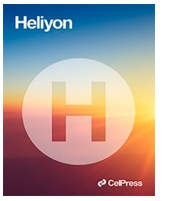
Heliyon 9 (2023) e22928

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Inflammatory myofibroblastic tumor of the submandibular gland Harboring MSN-ALK gene fusion: A case report and literature review

Limei Diao [a,b], Wen Li [a,c], Qingming Jiang [a,b], Haiping Huang [a,b], Enle Zhou [a,c], Bingjie Peng [a,c], Xiaoling Chen [d], Zhen Zeng [a,b,**], Changqing He [a,c,*]

[a] Department of Pathology, Chongqing University Cancer Hospital, Chongqing, 400030, China
[b] Chongqing Cancer Multi-omics Big Data Application Engineering Research Center, Chongqing University Cancer Hospital, Chongqing, 400030, China
[c] Chongqing Key Laboratory of Translational Research for Cancer Metastasis and Individualized Treatment, Chongqing University Cancer Hospital, Chongqing, 400030, China
[d] Department of pharmacy, Chongqing University Jiangjin Hospital, Chongqing, 402260, China

ARTICLE INFO

Keywords:
Inflammatory myofibroblastic tumor
Submandibular gland
ALK
MSN-ALK

ABSTRACT

Inflammatory myofibroblastic tumors (IMTs) are rare lesions with distinct clinical, pathological, and molecular characteristics. IMTs typically arise in the abdominal soft tissues, including the mesentery, omentum, and retroperitoneum, followed by the lungs and mediastinum, and usually affect both children and young adults. Herein, we present a rare case of an IMT in the submandibular gland of a 47-year-old male patient. Microscopically, the tumor displayed an infiltrative growth pattern with diffuse glandular tissue destruction. Their backgrounds revealed characteristic spindles and inflammatory cells. Immunohistochemistry revealed positivity for anaplastic lymphoma kinase (ALK), smooth muscle actin, and calponin in neoplastic cells. The inflammatory cells and some neoplastic cells were positive for CD68. In contrast, negative staining for cytokeratin, desmin, and CD30 was observed. Furthermore, fluorescence *in situ* hybridization revealed ALK gene rearrangements, and next-generation sequencing detected a moesin (MSN)-ALK gene fusion. This case highlights a rare and unique occurrence of IMT originating from the submandibular gland, which exhibited an MSN-ALK gene fusion.

1. Introduction

Inflammatory myofibroblastic tumors (IMTs) are neoplasms that predominantly occur in the lungs, mesentery, or omentum of young individuals; their pathogenesis is currently unknown [1]. IMTs have been reported in various locations in the head and neck region, including the salivary glands, epiglottis, parapharyngeal space, mandible, maxillary sinus, and oral cavity [2]. In the oral cavity, IMTs involve the parotid gland, submandibular salivary gland, tongue, buccal mucosa, gum, and mandible [3]. IMTs are

* Corresponding author. Department of Pathology, Chongqing Key Laboratory of Translational Research for Cancer Metastasis and Individualized Treatment, Chongqing University Cancer Hospital, No.181 Hanyu Road, Chongqing, 400030, China.
** Corresponding author. Department of Pathology, Chongqing Cancer Multi-omics Big Data Application Engineering Research Center, Chongqing University Cancer Hospital, No.181 Hanyu Road, Chongqing, 400030, China.
E-mail addresses: zengzhen0906@163.com (Z. Zeng), piaoyun_8888@163.com (C. He).

https://doi.org/10.1016/j.heliyon.2023.e22928
Received 23 April 2023; Received in revised form 20 November 2023; Accepted 22 November 2023
Available online 1 December 2023

characterized by the presence of proliferative fibroblasts and myofibroblasts along with a background of chronic inflammatory cells, including plasma cells, lymphocytes, and eosinophils, as observed microscopically [4]. Due to the heterogeneity of tumor components, different pathological names have been used, including inflammatory plasma cell granulomas and pseudotumors. In 2002, The World Health Organization officially designated this neoplasm as an "IMT" and classified it as an intermediate type, which can occasionally invade surrounding structures and cause malignant transformation, recurrence, or even metastasis [5]. IMTs in the parotid gland are relatively common, whereas those in other salivary glands are rare [6]. To date, only five cases of IMT affecting the submandibular gland have been reported in published databases. Anaplastic lymphoma kinase (ALK) gene rearrangements are found in approximately 50–60 % of all IMTs [7]. As reported previously [8], patients with IMTs and ALK gene fusion alterations may opt for treatment with tyrosine kinase inhibitors (TKIs). Therefore, detection of genetic alterations, such as ALK gene fusion, is of significant therapeutic importance in patients with IMTs. The moesin (MSN) gene, located on the X chromosome, encodes the MSN protein, which belongs to the ezrin-radixin-moesin (ERM) protein family. MSN are essential regulators of cell adhesion and migration [9]. Herein, we present a novel case of primary IMT originating from the submandibular gland and characterized by *MSN-ALK* gene fusion. This is the first reported case of an IMT with this gene fusion.

2. Case DESCRIPTION

A 47-year-old Chinese man noticed a hard quail yolk-sized mass, without any obvious cause, in the left submaxillary region 10 days prior to his clinical presentation. The patient, a farmer, had resided in a rural region of Chongqing for an extended period. Physical examination revealed no local redness, swelling, pain, hoarseness, swallowing difficulties, shortness of breath, fever, night sweats, intraoral redness, swelling, cavity mass, or dry mouth. On May 12, 2022, ultrasonography performed at another hospital revealed a solid cystic nodule in the left submandibular gland. The patient presented to our hospital five days later for further evaluation and treatment.

The patient was referred to our hospital for computed tomography (CT) and enhanced CT. The CT scan revealed an isodense nodular shadow with a size of 1.7 × 1.6 × 1.2 cm in the left submandibular gland (Fig. 1A). Enhanced CT revealed uniform and obvious enhancement with a clear boundary (Fig. 1B and C). No abnormal density or enhancement was observed in the right submandibular or the bilateral parotid glands. Lymph nodes with diameters of 0.5 cm were detected. Combined with the patient's clinical manifestations and imaging examinations, the clinician considered the lesion neoplastic, and the patient had a strong willingness to undergo surgical treatment. Additionally, the patient declined postoperative radiotherapy or chemotherapy. After 13 months of follow-up, there was no evidence of recurrence or metastasis.

Macroscopic examination revealed that the tumor was a well-defined nodular mass with a tan, fleshy cut surface. Microscopic examination at low magnification revealed that the spindle cells were arranged in sheets and intersecting fascicles with abundant blood vessels (Fig. 2A–C). Local interstitial fibrous tissue hyperplasia with a hyalinized collagenous stroma was also observed (Fig. 2D). Under high-power magnification, spindle- and oval-shaped cells with abundant cytoplasm, vesicular nuclei, distinct nucleoli, and 1–3 small nucleoli were observed. The interstitium consisted of numerous inflammatory cells, including lymphocytes, plasma cells, and eosinophils (Fig. 2E and F). A vascular thrombus was detected around the tumor (Fig. 2G). Nerve bundles were encased by tumor cells (Fig. 2H). The surgical margins were negative.

Immunohistochemical staining showed positivity for ALK, smooth muscle actin (SMA), calponin (Fig. 3A–C), inflammatory cells, and some neoplastic cells that were positive for CD68 (Fig. 3D) but negative for cytokeratin (CK), desmin, and CD30 (Fig. 3E–G). CD34 staining reveals vascular positivity. S-100, SOX10, and TLE1 were negative, whereas vimentin was strongly positive. The Ki-67 index in the intracellular hotspots of tumor cells was approximately 20 % (Fig. 3H). Additionally, CK-L, CK-H, LCA, GFAP, and NY-ESO-1 staining results were negative. Furthermore, INI-1 has no deletions. A representative example of *ALK* gene disruption detected using fluorescent *in situ* hybridization is shown in Fig. 4A. Next-generation sequencing (NGS) results are shown in Fig. 4B. *ALK* gene fusion was detected, which was composed of an *MSN* exon 9 and *ALK* gene exon 20 rearrangement. The fusion form retained the complete kinase domain of *ALK*, which may have constitutively activated *ALK* kinase, participated in the occurrence and development of tumors, and increased sensitivity to *ALK* kinase inhibitors.

3. Discussion

IMTs are rare mesenchymal tumors composed of fusiform fibrocytes and have different degrees of lymphoplasmacytic inflammation [10]. IMTs are rare mesenchymal tumors with unique clinical, pathological, and molecular characteristics. Previously, they

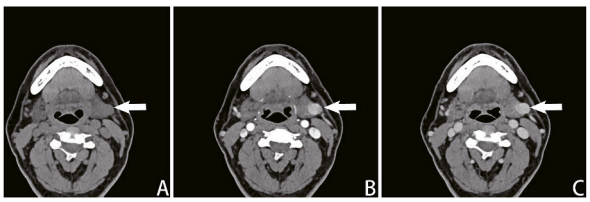


Fig. 1. (A) The image exhibits a CT scan, (B) arterial phase enhanced CT, and (C) venous phase enhanced CT.

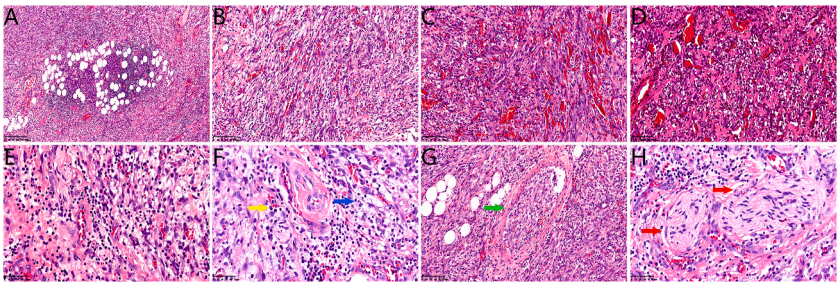


Fig. 2. (A) Infiltrative growth in the submandibular gland and adipose tissue (× 100). (B) Spindle cells arranged in sheets (× 200). (C) Arranged in intersecting fascicles with abundant blood vessels (× 200). (D) Local interstitial fibrous tissue hyperplasia with hyalinized collagenous stroma (× 200). (E) Vesicular nuclei, small nucleoli, and eosinophilic cytoplasm, with inflammatory cells (× 400). (F) Massive inflammatory cells include lymphocytes (blue arrow) and a few plasma cells (yellow arrow) (× 400). (G) A tumor embolus (green arrow) in the blood vessel (× 400). (H) Nerve tract (red arrow) was surrounded by tumor cells (× 400).

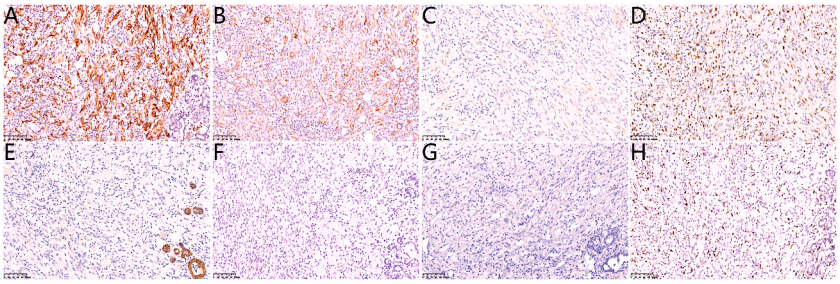


Fig. 3. Immunohistochemical staining (× 200). (A) Spindle cells showing diffuse cytoplasmic staining for ALK. (B) Spindle cells showing diffuse and intense immunoreactivity for SMA. (C) Calponin was weakly positive in a few spindle cells. (D) Inflammatory cells and some neoplastic cells were also positive for CD68. CK(E). Desmin (F) and CD30 (G) were negative in tumor cells. (H) Ki-67 counts in hot spots were approximately 20 %.

were often considered inflammatory pseudotumors because of their distinct morphological appearance. Although IMTs can occur in individuals of any age, they are more common in children and young adults, with a slightly higher incidence in women [11]. A total of 21 cases of IMTs (15 men and six women) are shown in Table 1. Interestingly, IMTs occurring in the submandibular gland have a different age distribution than other IMTs, with most cases occurring in middle-aged to elderly individuals. The histomorphology of these tumors showed typical IMT characteristics and positive immunohistochemical staining for the anaplastic marker ALK. No cases of tumor recurrence or metastasis were reported after surgical resection. However, it should be noted that gene detection was not performed in the five reported cases of IMTs in the submandibular gland. A study utilizing NGS identified ALK fusion proteins in IMT patients who tested negative for ALK expression by immunohistochemistry [7]. Therefore, genetic testing is recommended when typical IMT morphology is present, regardless of ALK immunohistochemical expression. More than 10 ALK fusion partners have been identified in IMT. According to a previous report [4], most ALK gene fusions provide a strong promoter and oligomeric domain that leads to the carcinogenic activation of ALK. This suggests that ALK inhibitors, such as crizotinib, could be effective in IMT patients with ALK fusion genes.

The histological features of the present case, including spindle cell and collagen fiber proliferation, rich eosinophilic cytoplasm, thin small capillary vessels, and sparse inflammatory cell infiltration, revealed nerve and vascular infiltrations without necrosis. Compared with typical IMTs, the morphology was diverse, and the disease can easily be misdiagnosed as inflammatory leiomyosarcoma, leading to overtreatment and a decline in the patient's quality of life. IMTs must be differentiated from other conditions, including nodular fasciitis, aggressive fibromatosis, solitary fibrous tumors, low-grade myofibroblastic sarcomas, spindle cell melanomas, sarcomatoid carcinomas, and IgG4-related diseases. Clinical data usually facilitate the differentiation of nodular fasciitis, which typically occurs rapidly within weeks to months. Histologically, IMTs typically exhibit more prominent inflammatory infiltration compared to nodular fasciitis. IMTs often show storiform or fascicular patterns, whereas the latter is absent in nodular fasciitis. In aggressive fibromatosis, the spindle cells are arranged in long bundles in a crisscross pattern and exhibit minimal inflammatory cell infiltration. Immunohistochemically, these tumors are typically negative for ALK. In contrast, in most cases of aggressive fibromatosis, beta-catenin is nuclear positive. The solitary fibrous tumor had a hemangiopericytoma-like structure and was positive for CD34 and STAT6 on immunohistochemistry. Low-grade myofibroblastic sarcomas have a histomorphology similar to that of aggressive fibromatosis with mild-to-moderate nuclear atypia. Immunohistochemically, the tumor was positive for SMA but negative for ALK. Immunohistochemical techniques can be used to differentiate IMT from spindle cell malignant melanoma and sarcomatoid carcinoma. Spindle cell malignant melanoma expresses melanin markers, such as HMB45 and Melan-A, but IMTs do not. Sarcomatoid carcinoma expresses epithelial markers such as CK. Histologically, IgG4-related diseases are characterized by rich lymphoplasmacytic infiltration,

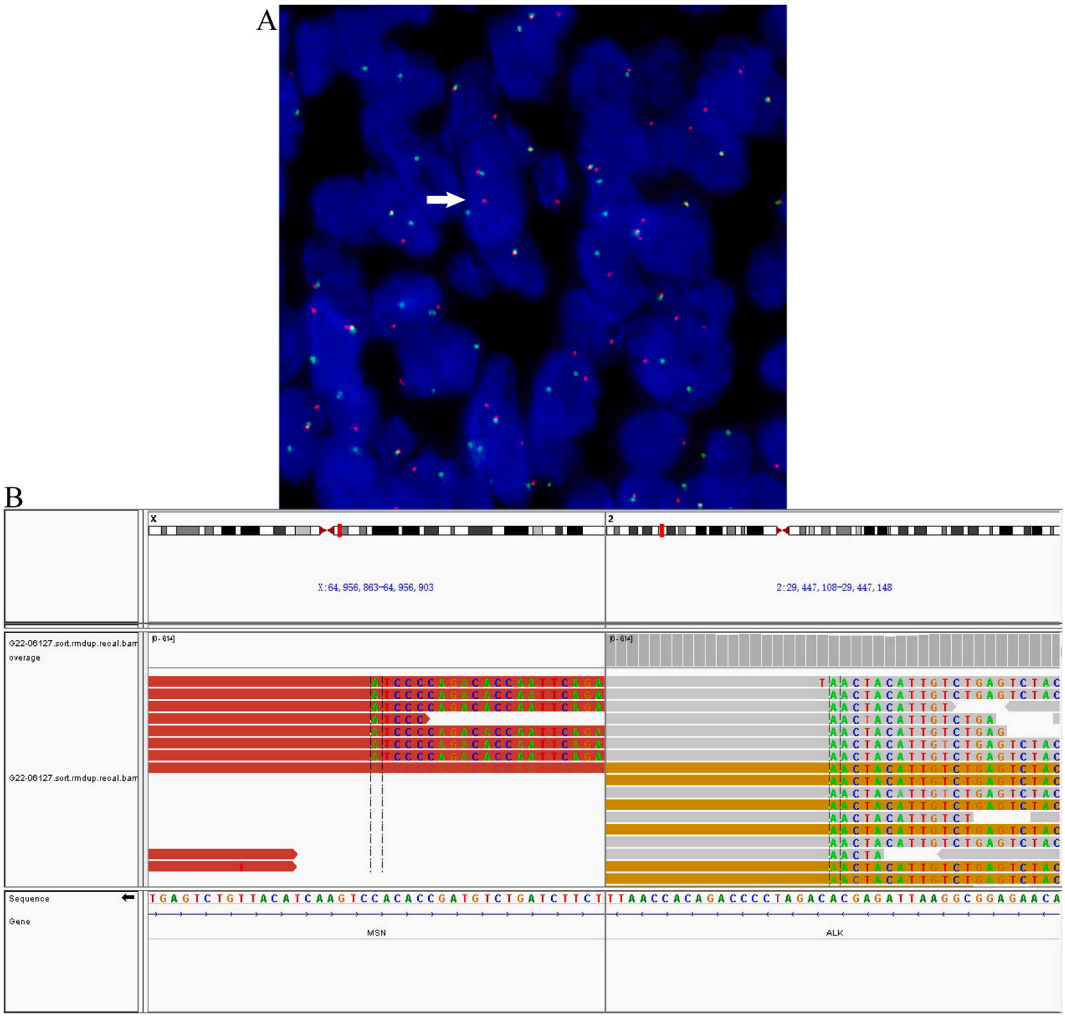


Fig. 4. (A) Fluorescent *in situ* hybridization (FISH) analysis. ALK fragmentation probe shows red-green signal separation. (B) *MSN-ALK* fusion is identified by next-generation sequencing.

mat-like fibrosis, and obliterative phlebitis. The background contains more IgG4-positive plasmacytes, and the IgG4/IgG ratio is usually >40 %.

Immunohistochemical studies show that IMTs are typically positive for smooth muscle actin [25]. In this study, the immunohistochemically positive markers included vimentin, ALK, SMA, and calponin. ALK expression in IMT is closely associated with ALK rearrangement [26].Approximately 50 % of IMTs express ALK protein [26]. According to previous studies [27], ALK can be expressed in three main ways: 1) localized in the cytoplasm, as per the typical IMT, corresponding to *TPM3/4* gene fusion isoforms; 2) localized in a granular form in the CLTC fusion gene subtype; and 3) localized in the nuclear membrane or nucleus and observed in epithelioid inflammatory myofibroblast sarcoma, corresponding to the RANBP2 fusion gene subtype. In the present case, ALK expression on the cell membrane was observed immunohistochemically. Additionally, some neoplastic cells were positive for CD68. CD68 is strongly expressed by tumor cells in hepatic IMTs but not in colorectal IMTs [28,29]. In one case of thyroid IMT, CD68 was not expressed by tumor cells, but only by focal histiocytes [30]. The expression of CD68 varies with IMT at different sites. ALK immunohistochemistry is usually positive for ALK-positive anaplastic large cell lymphoma and sometimes for neuroblastoma. In the present case, the negative morphological characteristics and immunohistochemical results for CK, CD30, S-100, SOX10, and LCA suggested that these conditions could be excluded.

In this case, NGS detected a fusion between exon 9 of MSN and exon 20 of ALK with a mutation abundance of 9.6 %. ALK, located on chromosome 2, is a potent oncogenic driver that can activate several intracellular signaling pathways such as PLCγ, JAK-STAT, PI3K-AKT, mTOR, and MAPK. This activation is closely related to the enhancement of cell growth, transformation, and anti-apoptosis, leading to the proliferation, growth, and invasion of cancer cells. Moesin, a member of the ezrin, radixin, and moesin (ERM) family, is involved in cell migration and tumor invasion by transducing signals sent to actin filaments by glycoproteins, such as podoplanin. MSN-ALK fusion occurs when ALK breaks and fuses with MSN, resulting in a conformational change in the ALK fusion protein after

Table 1
Inflammatory Myofibroblastic Tumors of the major salivary glands in the literature.

Reference number	Age (yrs)	Gender	Location, Size (cm)	Follow up
[12]	63	M	Right submandibular (5.0)	No recurrence at 3 years
[13]	53	F	left submandibular (6.0)	No recurrence at 10 months
[14]	58	M	Right submandibular (several centimeters)	Lost to follow-up
[15]	72	M	Left submandibular region (8.0)	No recurrence at 2 years
[16]	70	M	right submandibular gland (3.0)	No recurrence at 6 years
[17]	68	M	parotid	No recurrence at 21 months
	35	F	parotid	No recurrence at 14 months
	74	M	parotid	No recurrence at 3 years
[18]	46	M	Right parotid (2.0)	Lost to follow-up
	87	F	Left parotid (2.7)	No recurrence at 8 years
	83	F	Right parotid (1.8)	No recurrence at 1 years (then lost to follow-up)
	61	M	Left parotid (1.5)	No recurrence at 7 months
	69	F	Left parotid (1.0)	No recurrence at 4 months
	76	M	Right parotid (1.1)	No recurrence at 3 months
[19]	N. R.	M	parotid	N. R.
[20]	59	M	Right parotid (2.5)	N. R.
[21]	64	M	Left parotid (4.0)	No recurrence was obvious on follow-up
[6]	66	M	Left parotid (4.0)	No recurrence at 3 years
[22]	48	M	Right parotid (2.0)	No recurrence at 5 years
[23]	45	F	Right parotid (3.5)	No recurrence at 1 year
[24]	41	M	Left parotid tail (3.0)	No recurrence at 10 months

N.R., not reported; M, Male; F, Female.

translation, affecting its own phosphorylation and leading to tumor development. In the present case, the tumor was primarily caused by an ALK fusion mutation.

ALK rearrangement, which usually involves fusion with the tropomyosin 3 (*TPM3*) gene (*TPM3-ALK*), is the main cause of IMT [31]. Other partner genes have been found, including *CARS*, *CLTC*, *TPM4*, *ATIC*, *SEC31L1*, *RANBP2*, *PPFIBP1*, *EML4*, *NUMA1*, *MLNA*, *NF1*, *LRRFIP1*, *TFG*, *TNS1*, *THBS1*, *DCTN1*, *PRKAR1A*, *GCC2*, *ATIC*, *KIF5B*, *and HNRAPN1* [32,33]. These results confirm the repeated participation of ALK in IMT and further demonstrate the diversity of ALK fusion partners with homologous dimerization ability as a common feature [32]. Fusion of the ALK gene with TPM3 or other partner genes leads to overexpression of the ALK protein, which can be detected by immunohistochemistry [34]. In this study, we identified IMT using NGS and identified an uncommon fusion gene between MSN and ALK. Most IMTs are associated with fusion genes, including *ALK*, *ROS1*, and *PDGFRβ* fusions [35]. *MSN-ALK* fusion was created from (X; 2) (q11-12; p23), which was first reported in anaplastic large-cell lymphoma [36]. In this study, we found that the breakpoint of the *MSN-ALK* fusion was in exon 9 of MSN and exon 20 of ALK, which differs from the breakpoint reported in the literature. The *MSN-ALK* fusion gene sequence was ATCCCCAGACACCAATTCAGAG and the *ALK* gene sequence was AACTACATTGTCTGAGTCTAC. The *MSN* mutant chromosomal site was identified as X:64956863. *MSN* may act as a fusion partner for *ALK* activation, leading to abnormal phosphorylation of the ALK protein and kinase activity, ultimately resulting in tumor development.

We found that *MSN-ALK* fusion has not yet been reported in IMT. In this study, the cloning of a similar *MSN-ALK* fusion in the IMT was first observed in the submandibular gland. The mechanism of IMT remains unclear; however, because most IMTs can detect ALK rearrangement, it is speculated that the occurrence of IMT may be related to ALK rearrangement. In this case, a new fusion gene, MSN-ALK, was identified, which may have caused IMT via ALK activation. The MSN-ALK fusion effectively complements the genetic changes that cause IMT.

The patient remained untreated after the surgery and exhibited no signs of tumor recurrence or metastasis during the 13-month follow-up period. The reported rates of local recurrence and metastasis range from 15 to 37 % and 5–11 %, respectively [4]. He et al. [33] reported a case of IMT with bone metastasis in a patient who underwent *GCC2-ALK* fusion and achieved clinical benefits after treatment with ensartinib. Schöffski et al. [37] discovered that crizotinib was effective and showed a durable response in patients with locally advanced or metastatic ALK-positive IMT. Studies have shown that TKI inhibitor-targeted therapies and/or new immune-targeted drugs may be effective in patients with recurrent or metastatic IMT. Therefore, chemotherapy, targeted therapy (e.g., tyrosine kinase inhibitors), and immunotherapy may be considered in cases of recurrent or metastatic IMT. For instance, PD-L1 expression was observed in 80 % of recurrent or metastatic tumors and 88 % of ALK-negative IMTs [38]. As the follow-up time in this case was only 13 months, further follow-up data and prognostic evaluation of the patient were lacking. In addition, the patient did not receive further treatment after surgery, and treatment experience for this patient was lacking. This report presents a case of an IMT of the submandibular gland. Owing to the rarity of this tumor, there is limited knowledge and experience regarding its treatment, necessitating further accumulation of cases for better understanding.

4. Conclusion

This study reports a rare case of IMT in the submandibular gland with a novel *MSN-ALK* gene fusion detected using genetic testing. The identification of *ALK* fusion genes is particularly important in patients with recurrent or metastatic IMT. The findings of this study

provide valuable insights into the genetic changes underlying IMTs and could potentially guide future research in this area.

5. Ethics statement

The patient provided informed consent for the publication of his anonymised case details and images.

Data availability statement

The data associated with this study has not been deposited into a publicly available repository. Data will be made available on request, from the corresponding author, ZZ or CH.

CRediT authorship contribution statement

Limei Diao: Writing – original draft. **Wen Li:** Software, Methodology. **Qingming Jiang:** Formal analysis. **Haiping Huang:** Formal analysis, Data curation. **Enle Zhou:** Methodology. **Bingjie Peng:** Methodology. **Xiaoling Chen:** Methodology, Formal analysis. **Zhen Zeng:** Writing – review & editing, Writing – original draft. **Changqing He:** Writing – review & editing, Writing – original draft.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] A.K. Dhua, et al., Inflammatory myofibroblastic tumor of parotid in infancy–a new entity, Int. J. Pediatr. Otorhinolaryngol. 77 (5) (2013) 866–868.
[2] R. Korlepara, et al., Inflammatory myofibroblastic tumor of mandible: a rare case report and review of literature, J. Oral Maxillofac. Pathol. 21 (1) (2017) 136–139.
[3] S. Palaskar, et al., Inflammatory myofibroblastic tumor, Contemp. Clin. Dent. 2 (4) (2011) 274–277.
[4] L. Gros, et al., Inflammatory myofibroblastic tumour: State of the Art, Cancers 14 (15) (2022).
[5] S. Eldaabossi, et al., Common Presentation of Uncommon Disease: inflammatory myofibroblastic tumor of the lung, case report, Respir Med Case Rep 37 (2022), 101656.
[6] S. Van Weert, J.J. Manni, A. Driessen, Inflammatory myofibroblastic tumor of the parotid gland: case report and review of the literature, Acta Otolaryngol. 125 (4) (2005) 433–437.
[7] C.M. Lovly, et al., Inflammatory myofibroblastic tumors harbor multiple potentially actionable kinase fusions, Cancer Discov. 4 (8) (2014) 889–895.
[8] B.S. Rich, et al., Inflammatory myofibroblastic tumor: a multi-institutional study from the pediatric surgical oncology research collaborative, Int. J. Cancer 151 (7) (2022) 1059–1067.
[9] A.G. Abdou, et al., Immunohistochemical assessment of ezrin and moesin in colorectal carcinoma, Ultrastruct. Pathol. 40 (4) (2016) 181–188.
[10] V.Y. Jo, C.D. Fletcher, WHO classification of soft tissue tumours: an update based on the 2013 (4th) edition, Pathology 46 (2) (2014) 95–104.
[11] G. Piarulli, et al., Gene fusion involving the insulin-like growth factor 1 receptor in an ALK-negative inflammatory myofibroblastic tumour, Histopathology 74 (7) (2019) 1098–1102.
[12] M. Inui, et al., Inflammatory pseudotumor in the submandibular region. Clinicopathologic study and review of the literature, Oral Surg. Oral Med. Oral Pathol. 76 (3) (1993) 333–337.
[13] D.L. Cross, D.J. Switter, Fibroinflammatory pseudotumor of the submandibular gland, Head neck-j sci spec 18 (5) (1996) 465–468.
[14] R.A. Monteil, et al., Oral inflammatory pseudotumour: immunohistochemical investigation of a case involving the submandibular gland and review of the literature, Oral Oncol. 33 (3) (1997) 215–219.
[15] J. Mathews, A. Nicol, A.F. Dingle, Inflammatory pseudotumour in the submandibular region, J. Laryngol. Otol. 115 (6) (2001) 502–503.
[16] M. Kojima, et al., Inflammatory pseudotumor of the submandibular gland: report of a case presenting with autoimmune disease-like clinical manifestations, Arch. Pathol. Lab Med. 125 (8) (2001) 1095–1097.
[17] L.E. Wold, L.H. Weiland, Tumefactive fibro-inflammatory lesions of the head and neck, Am. J. Surg. Pathol. 7 (5) (1983) 477–482.
[18] S.B. Williams, R.D. Foss, G.L. Ellis, Inflammatory pseudotumors of the major salivary glands. Clinicopathologic and immunohistochemical analysis of six cases, Am. J. Surg. Pathol. 16 (9) (1992) 896–902.
[19] R. Frankenthaler, J.G. Batsakis, P.A. Suarez, Tumefactive fibroinflammatory lesions of the head and neck, Ann oto rhinol laryn 102 (6) (1993) 481–482.
[20] S. Rahimi, B. Mafera, M.G. Vigili, Inflammatory pseudotumor of the parotid gland: report of a case with fine needle aspiration cytology, Acta Cytol. 48 (4) (2004) 574–576.
[21] M.W. Mielcarek, et al., Benign inflammatory pseudotumour of the parotid gland: a case report and literature review, Int. J. Clin. Pract. 58 (5) (2004) 527–529.
[22] D. Hellín Meseguer, et al., Inflammatory pseudotumor of the parotid gland, An. Otorrinolaringol. Ibero-Am. 23 (6) (1996) 631–640.
[23] E. Kilic, et al., Inflammatory myofibroblastic tumor of the parotid gland, J. Craniofac. Surg. 23 (6) (2012) e557–e558.
[24] S. Kansara, et al., Head and neck inflammatory pseudotumor: case series and review of the literature, NeuroRadiol. J. 29 (6) (2016) 440–446.
[25] D. Dosemane, et al., Seek the spindle tumor in submandibular space, Iran J Otorhinolaryngol 31 (104) (2019) 181–184.
[26] J.A. Bennett, et al., Inflammatory myofibroblastic tumor of the uterus: an immunohistochemical study of 23 cases, Am. J. Surg. Pathol. 44 (11) (2020) 1441–1449.
[27] Q. Han, et al., Case report: early distant metastatic inflammatory myofibroblastic tumor harboring EML4-ALK fusion gene: study of two typical cases and review of literature, Front. Med. 9 (2022), 826705.
[28] H. Shi, et al., Primary colorectal inflammatory myofibroblastic tumour: a clinicopathological and immunohistochemical study of seven cases, Pathology 42 (3) (2010) 235–241.
[29] Y. Xiao, et al., Radiological and histopathological features of hepatic inflammatory myofibroblastic tumour: analysis of 10 cases, Clin. Radiol. 68 (11) (2013) 1114–1120.
[30] C.X. Zhang, et al., Inflammatory myofibroblastic tumour of thyroid: a case report, Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi 31 (9) (2017) 720–721.
[31] Y. Amano, et al., Oncogenic TPM3-ALK activation requires dimerization through the coiled-coil structure of TPM3, Biochem bioph res co 457 (3) (2015) 457–460.
[32] J. Cools, et al., Identification of novel fusion partners of ALK, the anaplastic lymphoma kinase, in anaplastic large-cell lymphoma and inflammatory myofibroblastic tumor, Genes Chromosomes Cancer 34 (4) (2002) 354–362.

[33] W. He, et al., Case Report: efficacy of ensartinib treatment in pulmonary inflammatory myofibroblastic tumor with a rare GCC2-ALK fusion, Front. Oncol. 12 (2022), 934887.
[34] F. Tort, et al., Heterogeneity of genomic breakpoints in MSN-ALK translocations in anaplastic large cell lymphoma, Hum. Pathol. 35 (8) (2004) 1038–1041.
[35] A.S. Mansfield, et al., Chromoplectic TPM3-ALK rearrangement in a patient with inflammatory myofibroblastic tumor who responded to ceritinib after progression on crizotinib, Ann. Oncol. 27 (11) (2016) 2111–2117.
[36] F. Tort, et al., Molecular characterization of a new ALK translocation involving moesin (MSN-ALK) in anaplastic large cell lymphoma, Lab. Invest. 81 (3) (2001) 419–426.
[37] P. Schöffski, et al., Long-term efficacy update of crizotinib in patients with advanced, inoperable inflammatory myofibroblastic tumour from EORTC trial 90101 CREATE, Eur. J. Cancer 156 (2021) 12–23.
[38] T.R. Cottrell, et al., PD-L1 expression in inflammatory myofibroblastic tumors, Modern pathol 31 (7) (2018) 1155–1163.