CASE STUDY

Primary pulmonary epithelioid inflammatory myofibroblastic sarcoma: a rare entity and a literature review

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Epithelioid inflammatory myofibroblastic sarcoma (EIMS) is an aggressive subtype of inflammatory myofibroblastic tumor (IMT) harboring anaplastic lymphoma kinase (*ALK*) gene fusions and is associated with high risk of local recurrence and poor prognosis. Herein, we present a young, non-smoking male who presented with complaints of cough and dyspnoea and was found to harbor a large right lower lobe lung mass. Biopsy showed a high-grade epithelioid to rhabdoid tumor with ALK and desmin protein expression. The patient initially received 5 cycles of crizotinib and remained stable for 1 year; however, he then developed multiple bony metastases, for which complete surgical resection was performed. Histopathology confirmed the diagnosis of EIMS, with *ALK* gene rearrangement demonstrated by fluorescence in situ hybridization. Postoperatively, the patient is asymptomatic with stable metastatic disease on crizotinib and has been started on palliative radiotherapy. EIMS is a very rare subtype of IMT that needs to be included in the differential diagnosis of ALK-expressing lung malignancies in young adults.

Key Words: Epithelioid inflammatory myofibroblastic sarcoma; Inflammatory myofibroblastic tumor; Lung; Anaplastic lymphoma kinase; Crizotinib; Fluorescence in situ hybridization

Inflammatory myofibroblastic tumor (IMT) is a distinctive mesenchymal tumor composed of neoplastic myofibroblastic tumor cells associated with inflammatory infiltrate of plasma cells, lymphocytes, and occasional eosinophils or neutrophils. IMTs present mainly in children and young adults, lack significant gender bias, and occur in a variety of anatomical locations [1]; lungs are one of the most common sites, accounting for ~1% of all adults and ~50% of pediatric lung tumors [2]. Fusions of the anaplastic lymphoma kinase (*ALK*) gene with various fusions partners, most commonly tropomyosin 3 (*TPM3*) or tropomyosin 4 (*TPM4*) gene, are observed in up to 60% of IMTs, correlating with diffuse cytoplasmic staining for ALK protein in tumor cells. Conventional IMTs show low-grade spindle cell tumor morphology lacking significant atypia, mitoses, or necrosis. Surgical resection is curative, and although one-fifth of cases will recur, < 5% of all IMTs metastasize [1,2].

Epithelioid inflammatory myofibroblastic sarcoma (EIMS) is a very rare subtype of IMT that has been associated with an aggressive course, rapid local recurrence, early metastases, and fatal outcome [1,3]. Unlike the bland spindle cell morphology of IMT, EIMS is composed of plump round to epithelioid tumor cells with prominent nucleoli and myxoid stroma with neutrophil-rich infiltrate [1] and show mitoses and necrosis. They harbor *ALK* gene fusions, most commonly with *RANBP2* (Ran specific binding protein 2) or, rarely, with *RRBP1* (ribosome binding protein 1). The fusions have been associated with a peculiar nuclear membrane (*RANBP2-ALK* fusion) or perinuclear accentuated cytoplasmic immunostaining (*RRBP1-ALK* fusion) for ALK protein [3-5]. EIMS occurs mainly in children and young adults, with a male gender predilection. These tumors have been most commonly reported in the mesentery and omentum [3,6], while primary pulmonary EIMS is extremely rare [7-9]. Herein, we report a primary pulmonary EIMS in a young male who was initially treated with ALK inhibitor monotherapy and subsequent surgery in the face of metastatic progression. In addition, we discuss the challenges associated with the diagnosis and treat-

ment of this rare entity.

CASE REPORT

A 25-year-old, non-smoking male presented with complaints of cough, significant weight loss, intermittent high-grade fever, and difficulty breathing for longer than 4 months. Imaging revealed a well-defined homogenous fluorodeoxyglucose (FDG)-avid mass of 6.9×4.2×6.1 cm involving the superior segment of the right lower lung lobe with no other pulmonary/pleural lesions or lymphadenopathy (Fig. 1A). Positron emission tomography scan showed another FDG-avid well-defined hypodense lesion of size 1.1×1.2 cm in segment IVA of the liver, likely metastasis. Biochemistry including serum tumor biomarkers was within normal range. A computed tomography–guided biopsy of the lung mass showed a poorly differentiated malignant tumor immunonegative for epithelial (pan-cytokeratin, epithelial membrane antigen), hematopoietic (CD45, myeloperoxidase, CD30), pneumocytic (thyroid transcription factor 1), melanocytic (human melanoma black 45, S-100), and mesothelial (calretinin, Wilms tumor protein 1) markers with retained INI-1 and BRG-1 expression. Tumor cells showed cytoplasmic ALK (VENTANA anti-ALK [D5F3] antibody developed by Roche Diagnostics [one 5 mL dispenser of VENTANA anti-ALK (D5F3) antibody contains approximately 70 µg of the rabbit monoclonal (D5F3) antibody; the antibody is diluted in 0.08 M phosphate buffered saline with 3% carrier protein and 0.05% Pro-Clin 300, a preservative]) and cytoplasmic desmin. Myogenin was
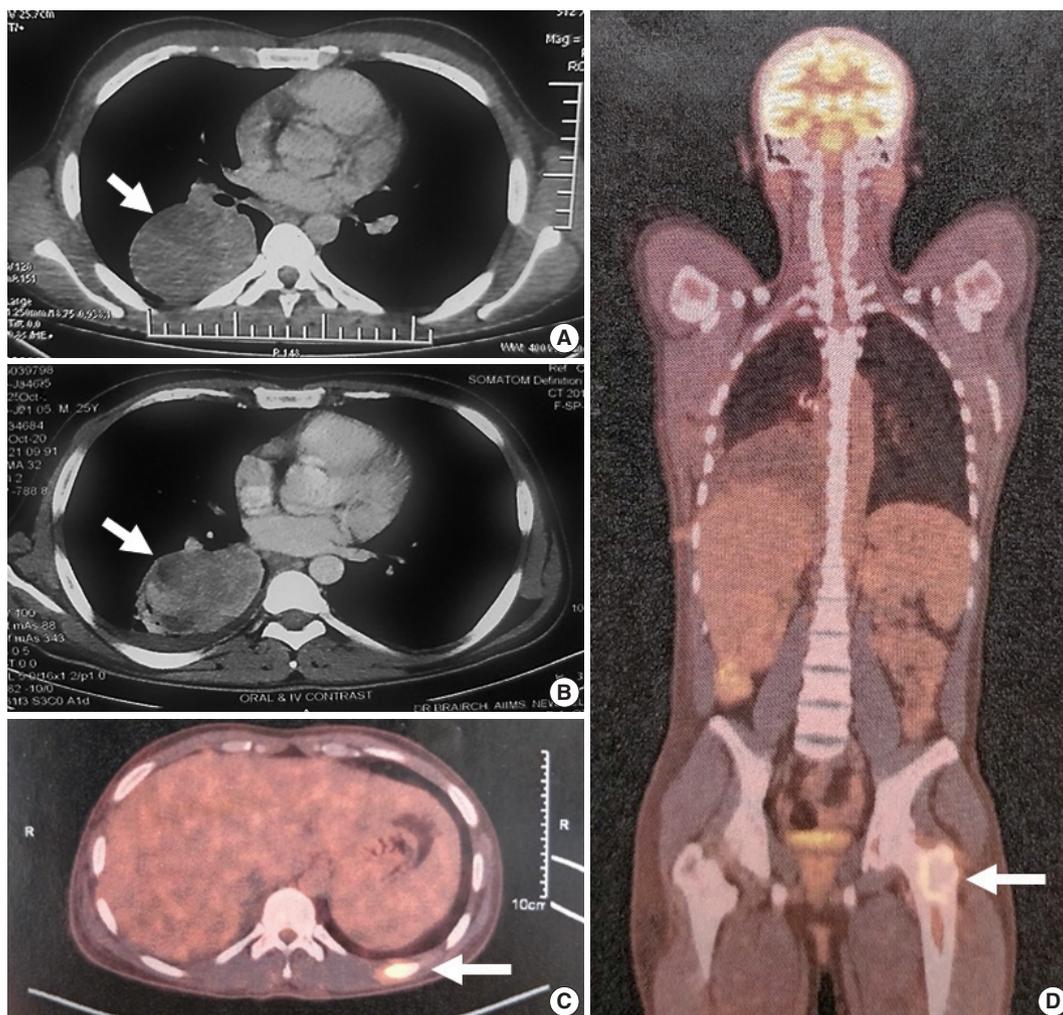

Fig. 1. Imaging features of the patient. (A) Computed tomography images show a homogeneous mass (arrow) with well-defined margin involving the superior segment of the right lower lobe. (B) Imaging at 6-months post-biopsy with the patient on crizotinib; the mass (arrow) was stable in size with few hypodense areas suggestive of necrosis. Positron emission tomography scan at 12-month post-biopsy with the patient continuing on crizotinib revealed new metastatic lesions in left 10th rib (arrow, C) and left proximal femur (arrow, D).

negative. The possibility of EIMS was suggested, and resection/re-biopsy was advised for molecular confirmation due to limited remaining biopsy material.

After multidisciplinary thoracic oncology tumor board dis-

cussion, the patient was planned for surgical excision of the lung tumor and radiofrequency ablation of the liver lesion because of the young age of the patient with good performance status, solitary metastasis, and unconfirmed primary pathological diagno-

Fig. 2. Gross features of the resected pulmonary tumor. Resection specimen shows a well encapsulated, lobulated, uncut tumor (A). A cut section shows a circumscribed, fleshy tumor with a surrounding rim of lung parenchyma (arrow, B).
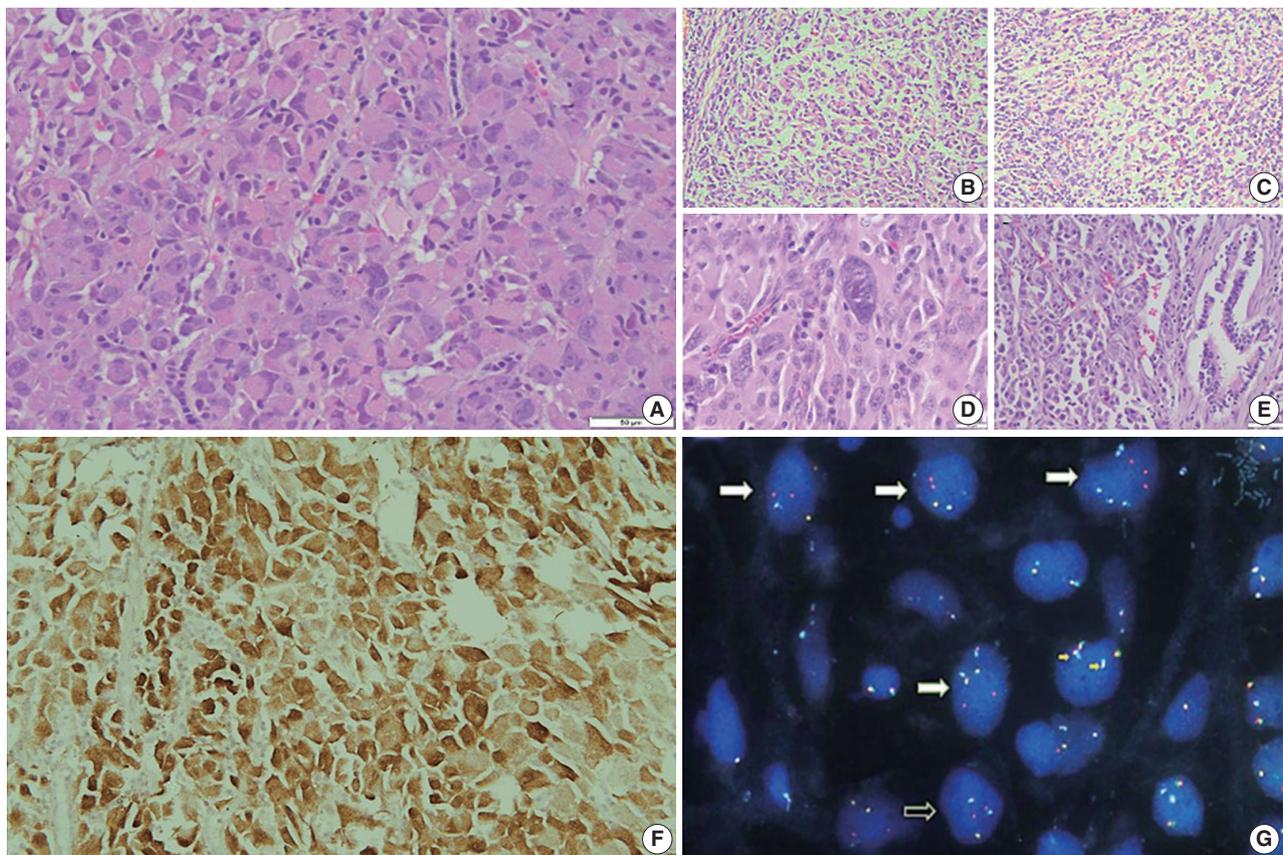

Fig. 3. Histomorphological and molecular features of the tumor. Hematoxylin and eosin-stained sections show rhabdoid phenotype tumor cells with moderate to abundant inclusion-like eosinophilic cytoplasm, prominent nucleoli, and fine granular chromatin with frequent mitoses in a myxoid stroma (A).The tumor cells show rich myxoid stroma and infiltration of mixed inflammatory cells (B, C, E) and prominent nuclear pleomorphism (D). The tumor cells show strong and diffuse cytoplasmic anaplastic lymphoma kinase (ALK) immunopositivity (F). (G) Fluorescence in situ hybridization using the ALK-ROS1 FLEXISH probe shows extra 3' signals (spectrum orange) of the *ALK* gene in tumor cells (white arrows, extra red signals unfused with green and/or aqua), indicating ALK gene rearrangement. The *ROS1* gene (indicated by fused red green-aqua signals, small yellow arrows) is intact.

sis. However, the patient was started on ALK inhibitor (crizotinib), and surgical intervention was deferred due to coronavirus disease 2019. Six months later, repeat imaging showed stable pulmonary disease (Fig. 1B) and complete resolution of the liver lesion. Crizotinib was continued and the patient was re-assessed for definitive surgical management. Repeat imaging 1 year after presentation showed increase in the size of the pulmonary mass (7.2×5.3×4.2 cm), and bone scan revealed metastasis in the right humerus (mid-shaft), left 10th rib, and left proximal femur (Fig. 1C, D). Pleural effusion or mediastinal lymph node metastasis (endobronchial ultrasound-guided transbronchial needle aspiration showed reactive lymphoid hyperplasia) was absent. Despite new bony metastases, because of the young age of the patient, surgical intervention was carried out as planned by means of video-assisted thoracoscopy-assisted right lower lobectomy.

Grossly, a well circumscribed, soft, fleshy tumor was identified in the lung parenchyma with focal areas of haemorrhage and necrosis (Fig. 2). Microscopy (Fig. 3) revealed a homogeneous tumor composed of ovoid to polygonal cells arranged in fascicles and sheets. The cells showed moderate to abundant eosinophilic cytoplasm with markedly pleomorphic nuclei, prominent nucleoli, and fine granular cytoplasm showing frequent mitoses (8 per 2 mm^2). Necrosis was present that had not been seen in the biopsy. Focal areas of myxoid change and lymphoplasmacytic infiltrate were noted. The immuno-profile of the tumor was similar to that of the biopsy except for focal cytokeratin expression in the resection, while histomorphology of the tumor was similar to that of the biopsy. The Ki-67 labeling index was ~30%–35% in the highest labeled areas. There was diffuse strong cytoplasmic staining for ALK protein. Fluorescence in situ hybridization assay using the FlexISH ALK/ROS1 DistinguISH Probe (ZytoVision, GmbH, Bremerhaven, Germany) showed one or more isolated 3' signals (extra orange signals) of the *ALK* gene without corresponding 5' signals (green signals) in the majority of tumor cells, indicative of *ALK* gene rearrangements [10], confirming the diagnosis of primary pulmonary EIMS. The *ROS1* gene represented by fused aqua-green-orange signals was intact (Fig. 3). The postoperative period was unremarkable, and the patient is currently asymptomatic 4-month post-surgery. He is continuing on crizotinib and is planned for palliative radiotherapy for the bony metastases.

DISCUSSION

Primary pulmonary EIMS is extremely rare, with only three cases reported previously in the English literature to the best of

Table 1. Clinicopathological features of reported cases of primary pulmonary epithelioid inflammatory myofibroblastic sarcoma including the current case

No.	Study	Age (yr)/Sex	Anatomic site	Size (cm)	Clinical Presentation	Metastasis at presentation	Immunoprofile	Molecular confirmation (method)	Primary treatment	Outcome
1	Fu et al. [7]	21/M	Left lower lobe lung	10	Weight loss, fatigue	None	Desmin+, ALK (c), CD30–	*ALK* rearrangement (FISH)	Lobectomy	Bone metastases (pelvis, vertebrae) and underwent laminectomy; death 4 mo after resection
2	Sarmiento et al. [8]	71/M	Pleura based, left lower lobe	12.5	Dyspnoea, pleural effusion	None	NA	*ALK* rearrangement (FISH)	Lobectomy and adjuvant crizotinib	Progressed on crizotinib after 2 mo; near complete response to second line ALK inhibitor; remission after 1 yr at last follow-up
3	Kozu et al. [9]	57/M	Pleural cavity/chest wall	NA	Pleural effusion and dyspnoea	N/A	Desmin+, cytokeratin+, ALK+ (c), CD30–	*RANBP2-ALK* fusion (PCR)	Crizotinib	NA
4	Present case	25/M	Lung Right lower lobe	7	Cough, loss of weight, fever, dyspnoea	Liver (solitary)	Desmin+, focal cytokeratin+, ALK+ (c), CD30–	*ALK* rearrangement (FISH)	Crizotinib	Complete resolution of liver metastases and stable pulmonary disease for 6 mo; bony metastases developed at 10 mo; lobectomy done and stable metastatic disease on crizotinib for 3 mo

ALK, anaplastic lymphoma kinase; (c), cytoplasmic; FISH, fluorescent in situ hybridization; NA, not available; *RANBP2*, Ran specific binding protein 2; PCR, polymerase chain reaction.

Table 2. Differential diagnosis of poorly differentiated epithelioid to rhabdoid tumors

Entity	Incidence as lung mass	Epithelial markers	Mesenchymal markers	Other markers	ALK protein expression	Commonest *ALK* fusions
IMT [2]	Common	Pan CK+/–	SMA, Desmin+	CD30–	Cytoplasmic (50%–60%)	TPM3-*ALK*, TPM4-*ALK*
ALCL [21]	Uncommon	EMA+	SMA, Desmin–	CD30+	Nuclear and cytoplasmic	NPM-ALK
ALK+LBL [21]	Rare	EMA+	–	CD138+, CD38+, Mum1/IRF1+, IgA+, Bob1+	Cytoplasmic, nuclear and nucleolar	*CLTC-ALK ALK-SEC31A*
ALK-rearranged NSCLC	Common	CK+	–		Cytoplasmic	*EML4-ALK* [14]
Melanoma	Extremely rare	CK–	–	S-100+, Melan A+, HMB45+, SOX10+	ALK^ATI (seen in cutaneous melanoma) [22]	*EML4-ALK* [23]
Epithelioid mesothelioma [2]	Uncommon	CK5/6+/–, EMA+/–	Desmin–	Calretinin+/–, WT+, D2-40+	–	–
Rhabdomyosarcoma	Rare	CK/EMA–	Desmin+, Actin+	MyoD1+, Myogenin+ CD30–	Cytoplasmic	*NPM-ALK* [24], *EML4-ALK* [25]
Epithelioid leiomyosarcoma [1]	Rare	EMA+	SMA+, Desmin+, h-caldesmon+	CD34+/–CK+/–, EMA+/–	–	–
EIMS [2]	Rare	CK or EMA–/+	Desmin+, SMA+	CD30+	Nuclear membrane or cytoplasmic with perinuclear accentuation	*ALK-RRBP1* [3-5], *ALK-RANBP2*
Pleomorphic carcinoma [2]	<1%	NSCC component CK+, TTF-1 +, EMA+	Vimentin+	Surfactant protein A+, p53+	Rare	–

ALK, anaplastic lymphoma kinase; ALK ATI, anaplastic lymphoma kinase with alternative transcription initiation; IMT, inflammatory myofibroblastic tumor; CK/PanCK, cytokeratin; SMA, smooth muscle actin; TPM, tropomyosin; ALCL, anaplastic large cell lymphoma; EMA, epithelial membrane antigen; NPM, nucleophosmin; Mum1/IRF1, multiple myeloma 1/interferon regulatory factor 4 protein; CLTC, clathrin heavy chain; NSCLC, non–small cell lung carcinoma; EML4, echinoderm microtubule-associated protein-like 4; HMB45, human melanoma black 45; EIMS, epithelioid Inflammatory myofibroblastic sarcoma; *RRBP1*, ribosome binding protein 1; RANBP, Ran-binding protein; NSCC, non-small cell lung cancer; TTF-1, thyroid transcription factor 1.

our knowledge (Table 1) [7-9]. Including the present case, primary pulmonary EIMS occurs across a wide age range (21–71 years at diagnosis) with a male preponderance. The tumor presents as a solitary parenchymal mass or as pleural mass with a relatively short symptom duration (< 6 months) and is not uncommonly metastatic at presentation, with brain and skeleton appearing to be the preferred sites of metastases (Table 1).

Diagnosis of EIMS is challenging. The poorly differentiated epithelioid morphology can mimic anaplastic large cell lymphoma (ALCL), malignant melanoma, alveolar rhabdomyosarcoma, alveolar soft part sarcoma, epithelioid leiomyosarcoma, undifferentiated sarcoma, malignant mesothelioma, poorly differentiated carcinoma, and pulmonary pleomorphic carcinoma (containing a minimum 10% spindle and/or giant cells) and needs to be differentiated by relevant immunohistochemical markers (Table 2). Conventional IMTs are more common in the lung but are differentiated from EIMS by their bland spindle morphology, prominent lymphoplasmacytic cellular infiltrate, and absence of mitoses and pleomorphism. Rare cases of otherwise conventional IMTs that show increased mitotic activity, necrosis, and aggressive biological behavior are reported [11,12]; these should not be designated as EIMS in the absence of distinctive

morphology of round to epithelioid cells, myxoid stroma, and mixed inflammatory infiltrate, as was observed in the present case. ALK protein expression is essential for diagnosis but is not specific as many other lung tumors express ALK protein due to underlying *ALK* gene rearrangements, as in ALCL, conventional IMTs, and non-small cell lung carcinoma (NSCLC), or to ALK copy number alterations as in rhabdomyosarcomas [13]. *ALK*-rearranged lung adenocarcinoma/NSCLC shows a variety of histological characteristics ranging from cribriform pattern, mucin-containing cells, presence of psammoma bodies, and solid signet-ring cells. None of the histological parameters are specific for a particular genotype [14-19]. Fluorescence in situ hybridization using break-apart probes is useful to confirm *ALK* gene rearrangements; however, polymerase chain reaction and/or sequencing of RNA transcripts is required for delineating *ALK* fusion partners. ALK protein expression in a nuclear membranous or perinuclear cytoplasmic pattern gives a clue to the presence of underlying *RANBP2* or *RRBP1* fusion partners with ALK, which are the most common fusions in EIMS; however, these fusions can also be observed in IMTs and ALCLs [20]. On the other hand, other fusion partners including *EML4*, the most common fusion partner in *ALK*-rearranged NSCLC, have also been report-

ed in EIMS associated with the more common cytoplasmic ALK staining pattern [26]. The various *ALK* gene rearrangement seen in NSCLC are EML4, TFG, KIF5B, KCL1, and multiple EML4 isoforms [27].

Thus, due to considerable genetic overlap with other ALKomas, EIMS is essentially a histopathological diagnosis, and definitive diagnosis can be difficult on a small biopsy, even with ancillary testing.

EIMS is an aggressive tumor with poor prognosis and local recurrence [1,3]. Review of previous reported pulmonary EIMS showed that surgical resection remained the mainstay of treatment when feasible (Table 1). These tumors do not respond to chemotherapy or radiotherapy [28,29]. Most ALK fusion proteins including those resulting from *RANBP2-ALK* fusions are sensitive to ALK tyrosine kinase inhibitor (TKI) inhibition in pre-clinical models [30], suggesting a role for targeted therapy. From the limited data available, EIMS does appear to respond to the ALK TKI crizotinib, as in our patient who experienced complete resolution of liver metastases. However, long-term responses or remissions are rare, with most EIMS patients progressing with metastatic disease within 3 to 6 months of crizotinib monotherapy [7-9], likely due to secondary resistance mechanisms [10]. A recent study demonstrated prolonged survival with a combination of ALK and CD30 targeted therapies [31]; however, CD30 expression appears to be uncommon in pulmonary EIMS (Table 1). EIMS is a very rare subtype of IMT that presents as a primary lung mass in young non-smokers, posing a considerable diagnostic challenge due to aggressive behavior with frequent metastases. There are limited data on treatment protocols; in the present case, targeted ALK inhibitor therapy combined with surgery achieved considerable disease control.

Ethics Statement

Availability of Data and Material

All data generated or analyzed during the study are included in this published article (and its supplementary information files).

Code Availability

Not applicable.

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Author Contributions

Conflicts of Interest

Funding Statement

References

1. Yamamoto H. Inflammatory myofibroblastic tumor. In: WHO Classification of Tumours Editorial Board. WHO classification of tumors: soft tissue and bone tumours. Lyon: IARC Press, 2020; 109-11.
2. Tavora F, Glass C, Hornick JL, Jain D, Sheppared MN, Yi ES. Inflammatory myofibroblastic tumor. In: WHO Classification of Tumours Editorial Board. WHO classification of tumors: thoracic tumours. Lyon: IARC Press, 2021; 288-9.
3. Marino-Enriquez A, Wang WL, Roy A, et al. Epithelioid inflammatory myofibroblastic sarcoma: an aggressive intra-abdominal variant of inflammatory myofibroblastic tumor with nuclear membrane or perinuclear ALK. Am J Surg Pathol 2011; 35: 135-44.
4. Xu P, Shen P, Jin Y, Wang L, Wu W. Epithelioid inflammatory myofibroblastic sarcoma of stomach: diagnostic pitfalls and clinical characteristics. Int J Clin Exp Pathol 2019; 12: 1738-44.
5. Lee JC, Li CF, Huang HY, et al. ALK oncoproteins in atypical inflammatory myofibroblastic tumours: novel *RRBP1-ALK* fusions in epithelioid inflammatory myofibroblastic sarcoma. J Pathol 2017; 241: 316-23.
6. Garg R, Kaul S, Arora D, Kashyap V. Posttransplant epithelioid inflammatory myofibroblastic sarcoma: a case report. Indian J Pathol Microbiol 2019; 62: 303-5.
7. Fu X, Jiang J, Tian XY, Li Z. Pulmonary epithelioid inflammatory myofibroblastic sarcoma with multiple bone metastases: case report and review of literature. Diagn Pathol 2015; 10: 106.
8. Sarmiento DE, Clevenger JA, Masters GA, Bauer TL, Nam BT. Epithelioid inflammatory myofibroblastic sarcoma: a case report. J Thorac Dis 2015; 7: E513-6.
9. Kozu Y, Isaka M, Ohde Y, Takeuchi K, Nakajima T. Epithelioid inflammatory myofibroblastic sarcoma arising in the pleural cavity. Gen Thorac Cardiovasc Surg 2014; 62: 191-4.
10. Yoshida A, Bubendorf L, Varella-Garcia M. ALK testing with FISH. In: Tsao MS, Hirsch FR, Yatabe Y, eds. IASLC atlas of ALK and ROS1 testing in lung cancer. 2nd ed. North Fort Myers: Editorial Rx Press, 2016; 41-52.
11. Parker BM, Parker JV, Lymperopoulos A, Konda V. A case report: pharmacology and resistance patterns of three generations of ALK inhibitors in metastatic inflammatory myofibroblastic sarcoma. J Oncol Pharm Pract 2019; 25: 1226-30.

12. Rush NI, Sinnott M. Malignant inflammatory myofibroblastic tumor of the lung with IgG4-positive plasma cells. Ann Clin Pathol 2016; 4: 1069.
13. Du X, Shao Y, Qin HF, Tai YH, Gao HJ. *ALK*-rearrangement in non-small-cell lung cancer (NSCLC). Thorac Cancer 2018; 9: 423-30.
14. Kim H, Jang SJ, Chung DH, et al. A comprehensive comparative analysis of the histomorphological features of *ALK*-rearranged lung adenocarcinoma based on driver oncogene mutations: frequent expression of epithelial-mesenchymal transition markers than other genotype. PLoS One 2013; 8: e76999.
15. Inamura K, Takeuchi K, Togashi Y, et al. EML4-ALK lung cancers are characterized by rare other mutations, a TTF-1 cell lineage, an acinar histology, and young onset. Mod Pathol 2009; 22: 508-15.
16. Rodig SJ, Mino-Kenudson M, Dacic S, et al. Unique clinicopathologic features characterize *ALK*-rearranged lung adenocarcinoma in the western population. Clin Cancer Res 2009; 15: 5216-23.
17. Yoshida A, Tsuta K, Watanabe S, et al. Frequent *ALK* rearrangement and TTF-1/p63 co-expression in lung adenocarcinoma with signet-ring cell component. Lung Cancer 2011; 72: 309-15.
18. Nishino M, Klepeis VE, Yeap BY, et al. Histologic and cytomorphologic features of *ALK*-rearranged lung adenocarcinomas. Mod Pathol 2012; 25: 1462-72.
19. Popat S, Gonzalez D, Min T, et al. *ALK* translocation is associated with ALK immunoreactivity and extensive signet-ring morphology in primary lung adenocarcinoma. Lung Cancer 2012; 75: 300-5.
20. Cook JR, Dehner LP, Collins MH, et al. Anaplastic lymphoma kinase (ALK) expression in the inflammatory myofibroblastic tumor: a comparative immunohistochemical study. Am J Surg Pathol 2001; 25: 1364-71.
21. Campo E, Gascoyne RD. ALK-positive large B-cell lymphoma. In: Swerdlow SH, Campo E, Harris NL, et al. eds. WHO classification of tumours of haematopoietic and lymphoid tissues. Revised 4th ed. Lyon: IARC Press, 2017; 319-20.
22. Busam KJ, Vilain RE, Lum T, et al. Primary and metastatic cutaneous melanomas express ALK through alternative transcriptional initiation. Am J Surg Pathol 2016; 40: 786-95.
23. Couts KL, Bemis J, Turner JA, et al. ALK inhibitor response in melanomas expressing *EML4-ALK* fusions and alternate ALK isoforms. Mol Cancer Ther 2018; 17: 222-31.
24. Cessna MH, Zhou H, Sanger WG, et al. Expression of ALK1 and p80 in inflammatory myofibroblastic tumor and its mesenchymal mimics: a study of 135 cases. Mod Pathol 2002; 15: 931-8.
25. Gasparini P, Casanova M, Villa R, et al. Anaplastic lymphoma kinase aberrations correlate with metastatic features in pediatric rhabdomyosarcoma. Oncotarget 2016; 7: 58903-14.
26. Soda M, Choi YL, Enomoto M, et al. Identification of the transforming *EML4-ALK* fusion gene in non-small-cell lung cancer. Nature 2007; 448: 561-6.
27. Kim H, Chung JH. Overview of clinicopathologic features of *ALK*-rearranged lung adenocarcinoma and current diagnostic testing for *ALK* rearrangement. Transl Lung Cancer Res 2015; 4: 149-55.
28. Fabre D, Fadel E, Singhal S, et al. Complete resection of pulmonary inflammatory pseudotumors has excellent long-term prognosis. J Thorac Cardiovasc Surg 2009; 137: 435-40.
29. Sakurai H, Hasegawa T, Watanabe S, Suzuki K, Asamura H, Tsuchiya R. Inflammatory myofibroblastic tumor of the lung. Eur J Cardiothorac Surg 2004; 25: 155-9.
30. Childress MA, Himmelberg SM, Chen H, Deng W, Davies MA, Lovly CM. ALK fusion partners impact response to ALK inhibition: differential effects on sensitivity, cellular phenotypes, and biochemical properties. Mol Cancer Res 2018; 16: 1724-36.
31. Fordham AM, Xie J, Gifford AJ, et al. CD30 and ALK combination therapy has high therapeutic potency in *RANBP2-ALK*-rearranged epithelioid inflammatory myofibroblastic sarcoma. Br J Cancer 2020; 123: 1101-13.