Successful treatment of inflammatory myofibroblastic tumor with surgery and radiochemotherapy and review of the literature

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Case Report

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Abstract

Background

Inflammatory myofibroblastic tumors (IMTs) are rare soft-tissue neoplasms. Accordingly, there is no standardized therapy for unresectable or advanced IMT. Chemotherapy, radiotherapy, and targeted molecular therapy play an important role in unresectable or advanced IMT.

Case presentation:

We present a 54-year-old man with a cough and chest distress case report. The positron emission tomography/computed tomography (PET/CT) showed that the occupying lesion was about 7.2 x 6.7 x 6.1 cm, with the SUVmax about 13.4. The thoracic surgeon performed the right upper pulmonary occupying lesion wedge resection and enlarged lymph node excision biopsy. Pathologic diagnosis revealed that the morphology of "right upper lung mass" was considered as Inflammatory Myofibroblastic Tumor (IMT). Radiotherapy was indicated at a high dose: 5400cGy in 27 fractions of 2Gy over 5 weeks were delivered combined with cisplatin. The side effects of concurrent radiochemotherapy were grade I myelosuppression with WBC 3.22 x10^9/L during concurrent radiochemotherapy and grade I radiation pneumonitis 6 months after radiochemotherapy. The patient was given a CT/MRI and hematological index every 3 months and experienced no more adverse events. The patient survives with no tumor recurrence as of the last follow-up. Progression-free survival (PFS) exceeded 48 months.

Conclusions

We have reviewed the literature and summarized and discussed the radiotherapy treatment options and challenges for IMT. Radiotherapy played an essential role in unresectable or advanced IMT. We first reported surgery and high-dose radiotherapy combined with chemotherapy treatment for local advanced IMT. Surgery is the first choice for IMT, Concurrent radiochemotherapy may be considered an intensive treatment for local progress, local recurrence, and nonresectable IMT patients.

Background

Inflammatory myofibroblastic tumor (IMT) is a quite rare type of soft-tissue neoplasm. The 2013 World Health Organization classification defined IMT as a mesenchymal neoplasm of intermediate malignancy [1]. IMT usually occurs in children, adolescents, and young adults with equal incidence in male and female patients [2]. Besides, it usually presents as a mass in soft tissue-composed organs and structures, such as the lung, abdomen, pelvis, retroperitoneum, head and neck, central nervous system, and others [3–5]. The clinical presentations are various, such as pain, fever, malaise, swelling, weight loss, etc., depending on the IMT location. Moreover, IMT rarely metastasizes, and distant metastatic IMT may only occur in up to 5% of all IMT patients [6].

Because IMT is locally invasive, complete surgical resection is the first choice. However, unresectable or advanced IMT does not have standard therapy. Chemotherapy, radiotherapy, and targeted molecular therapy play an important role in unresectable or advanced IMT. Radiotherapy is usually ineffective for IMT [7]. Chemotherapy is also applied in the IMT treatment with good therapeutic effect [8]. Besides, the molecular landscape of IMT is essential as they can be targeted for treatment involving several targets, such as ALK, ROS1, PDGFR β, RET, and NTRK [3, 9].

Here, we present a case of IMT located in the lung and mediastinum. This patient accepted subtotal resection and concurrent chemoradiotherapy. Additionally, we reviewed and discussed case experiences and the scientific literature.

Case Presentation

In February 2018, a 54-year-old man presented to the hospital with a cough associated with chest distress. A CT scan was performed and revealed an occupying lesion in the superior lobe of the right lung with enlarged lymph nodes in the mediastinum. The positron emission tomography/computed tomography (PET/CT) showed that the occupying lesion was about 7.2 x 6.7 x 6.1 cm, with the SUVmax about 13.4 and lymph node metastasis in the hilum of the right lung, mediastinum, and right subclavian fossa (Fig. 1).

In order to identify the pathological type, endobronchial ultrasound (EBUS) and transbronchial needle aspiration (TBNA) were used to assess the lesion organization twice. However, the pathological result of the occupying lesion biopsy specimen in the right lung revealed fibrous tissue hyperplasia with a small amount of inflammatory cell infiltration, while the pathological result of enlarged lymph nodes biopsy specimens were negative. The Multidisciplinary Team discussed the case, and the diagnosis was considered a malignant tumor. Under the agreement of the patient and his family, the thoracic surgeon performed the right upper pulmonary occupying lesion wedge resection and enlarged lymph node excision biopsy assisted by thoracoscopy under general anesthesia.

Pathologic diagnosis for this patient revealed that the morphology of "right upper lung mass" was considered as inflammatory myofibroblastic tumor with endovascular changes. Immunohistochemical staining results were as follows: CD163 (+), CD68 (+), ALK (-), Desmin (-), S100 (-), SMA (+) and CD34 (blood vessels +), Vimentin (+) and STAT6 (-), CD23 (-), CD138 (plasma cells +), CD38 (plasma cells +), IgG4 (-), IgG (-), CK (Pan) (alveolar epithelium +), PAS (-), PASM (-), and acid-fast staining (-) (Fig. 2).

After recovering from the operation, the patient was transferred to the oncology department for antitumor treatment one month after surgery. Because of subtotal resection, the patient accepted concurrent radiochemotherapy. In the first stage, the radiotherapy dose was PTV: DT 3800cGy/19F. Boost CTV: DT 1600cGy/8F in the second stage. The total dose on the tumor was 5400cGy/27F (Fig. 3). The patient received weekly concurrent chemotherapy with cisplatin dosed at 40mg qw for 5 cycles during radiotherapy. The side effects of concurrent radiochemotherapy were grade I myelosuppression with WBC 3.22 x10^9/L during concurrent radiochemotherapy and grade I radiation pneumonitis 6 months after radiochemotherapy.

After therapy, the IMT did not recur. The patient was given a CT/MRI and hematological index every 3 months and experienced no more adverse events. Progression-free survival (PFS) lasted more than 48 months. Written informed consent was obtained from the patient to publish the case report and related images.

Discussions And Conclusions

We reported an IMT located in the right lung and mediastinum, which was treated with X-beam irradiation and cisplatin after subtotal resection.

IMT is a rare tumor and primarily occurs in soft tissues. Usually, IMT presents as a nodular circumscribed mass, occupying lesion, multinodular lesions in the soft tissue of chest, abdominopelvic or retroperitoneal region [2]. The definitive diagnosis of IMT is mainly based on the histopathological report. In this case, the presence of CD163, CD68 SMA, CD34, and Vimentin and the absence of ALK, S-100, Desmin, CD23, STAT6, PAS, PASM, and acid-fast staining associated with the mix of spindle cells and inflammatory cells helped the histopathological diagnosis.

Because IMT always presents local invasiveness, thus local therapy plays an important role, especially surgical resection [10]. Besides, complete surgical resection is the standard treatment for localized IMT. However, local recurrences are common with incomplete resection, which usually occurs in the presence of involved surgical margins [11]. Typically, about 23–25% of IMT recurred after surgery [12, 13]. Nonetheless, a second surgery, radiotherapy, or chemotherapy regimen can be effective in recurrent IMT [14, 15].

Because of the inflammatory features of IMT, anti-inflammatory drugs, such as steroids and non-steroidal anti-inflammatory drugs (NSAIDs), were the first applied in the treatment. However, different cases reported opposite results of anti-inflammatory drugs [16, 17]. Therefore, the effect of anti-inflammatory drugs in IMT might depend on individual patient differences and tumor heterogeneity.

Chemotherapy is reportedly effective in IMT. Moreover, it is used in neoadjuvant therapy and postoperative adjuvant therapy for unresectable, progressive, or metastatic disease. Multiple chemotherapy regimens have been described as functional, including ifosfamide, carboplatin, vincristine and dactinomycin (IVA), paclitaxel, vincristine, methotrexate and vinblastine (MTX/VBL), and vinorelbine (MTX/VNB) [2, 3]. The development of targeted drugs shows a good therapeutic effect in the IMT treatment directed towards ALK, PDGFR β, ROS1, NTRK, RET, and other molecular targets [2–4]. Thus, molecular landscape targeted therapeutics might play a more critical role in IMT.

Radiotherapy also showed effectiveness in IMT [18–21]. It may be a choice for localized IMT patients who cannot tolerate surgery or could be used as postoperative adjuvant therapy in unresectable, progressive, or metastatic cases. However, there is no standardized radiation dose and combined drug therapy regimen.

It was reported that Low-dose radiation therapy (2000cGy) combined with steroid therapy treatment for IMT in the skull base showed a high recurrence rate [22]. Nevertheless, low-dose radiation therapy (2000cGy) treatment for IMT in orbit showed good effect [18]. It seems that the radiation dose might vary based on the tumor's location. Reference the radiotherapy dose for common tumors in the same position might be suitable. However, it remains unknown whether radiotherapy should combine chemotherapy or steroid treatment. The last is usually offered as a combined therapy [19, 20, 23]. Chemotherapy, especially cisplatin, might sensitize the patient for the radiation and improve the radiotherapy effect [24]. For high-risk patients, chemotherapy combined with radiotherapy might be an intensive treatment.

In our case, surgery and radiochemotherapy played an essential role in treating this patient. Despite the local progress and subtotal resection, the progression-free survival (PFS) was more than 48 months. We first reported surgery and high-dose radiotherapy combined with chemotherapy treatment for local advanced IMT. In conclusion, surgery is the first choice for IMT, concurrent radiochemotherapy may be considered for local progress, local recurrence, and nonresectable IMT patients.

Abbreviations

Inflammatory myofibroblastic tumors	IMTs
Positron Emission Tomography/Computed Tomography	PET/CT
Endobronchial Ultrasound	EBUS
Progression-free survival	PFS
Transbronchial Needle Aspiration	TBNA
Non-Steroidal Anti-Inflammatory Drugs	NSAIDs

Declarations

Authors' contributions

All authors substantially contributed to the manuscript. HBZ, HWG, MYJ and RQL wrote the main manuscript text and JJC, WPY and XDL prepared figures 1-3. All authors read and approved the final manuscript.

Consent for publication

The patient was informed about the intention to publish a report of his medical.

Competing interests

All authors declare that they have no competing interests

Ethics approval and consent to participate

This study was approved by the ethics committee of Zhejiang Provincial People's Hospital. Written informed consent for this study was obtained from the patient.

Availability of data and material

These datasets generated and/or analyzed during the current study are publicly available from the corresponding author on reasonable request.

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Not applicable

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Tables

Table 1 Summary of inflammatory myofibroblastic tumor treated with radiotherapy

Reference	N	Age (y)	Sex	Tumor site	Treatments	Radiotherapy dose	Follow up
Lisi R 2019[18]	1	26	F	Trachea	FRT	4500cGy/25F	PFS≧62 months
Strianese 2018[20]	20	5-76	12M+13F	orbit	STL/TR+steroid (22/25) +radiotherapy (3/25)	2000cGy/1F	radiotherapy (1/3) recurred after 13 years
Chennouf 2017[6]	1	26	M	Left parieto-occipital	Four surgical resections and FRT+crizotinib +ceritinib	6000cGy/ 30F	PFS≧14 months
Gorolay2016[21]	1	49	M	Posterior mediastinum	thoracic surgical biopsy+external beam radiotherapy	NR	PFS≧36 months
Zhang 2015[14]	1	49	M	Right inguinal region	Surgery Second Surgery +FRT	4600cGy/23F	PFS≧6 months
Gabel 2015[19]	1	56	M	Left Sphenoid and Cavernous Sinus	STL +steroid therapy +FRT	2000cGy/10F	PFS≧24 months
Maire 2013[23]	1	38	M	Skull base	Corticosteroids+FRT	2000cGy/10F	PFS≧24 months
Lee 2006[22]	8	52-76	4M+4F	Skull base	Steroid therapy (7/8) +low-dose radiation therapy (6/8)	2000cGy (6/8) 3000cGy (1/8)	PFS NR recurrence (7/8) recurrence in low-dose group (5/6)
Present case 2022	1	54	M	right lung, and mediastinum	STL+FRT+Chenmotherapy	5400cGy/27F	PFS≧47 months

Fractionated radiotherapy (FRT), F=female, M=male, NR=not reported STL=subtotal resection, TR=total resection

Figures

Figure 1

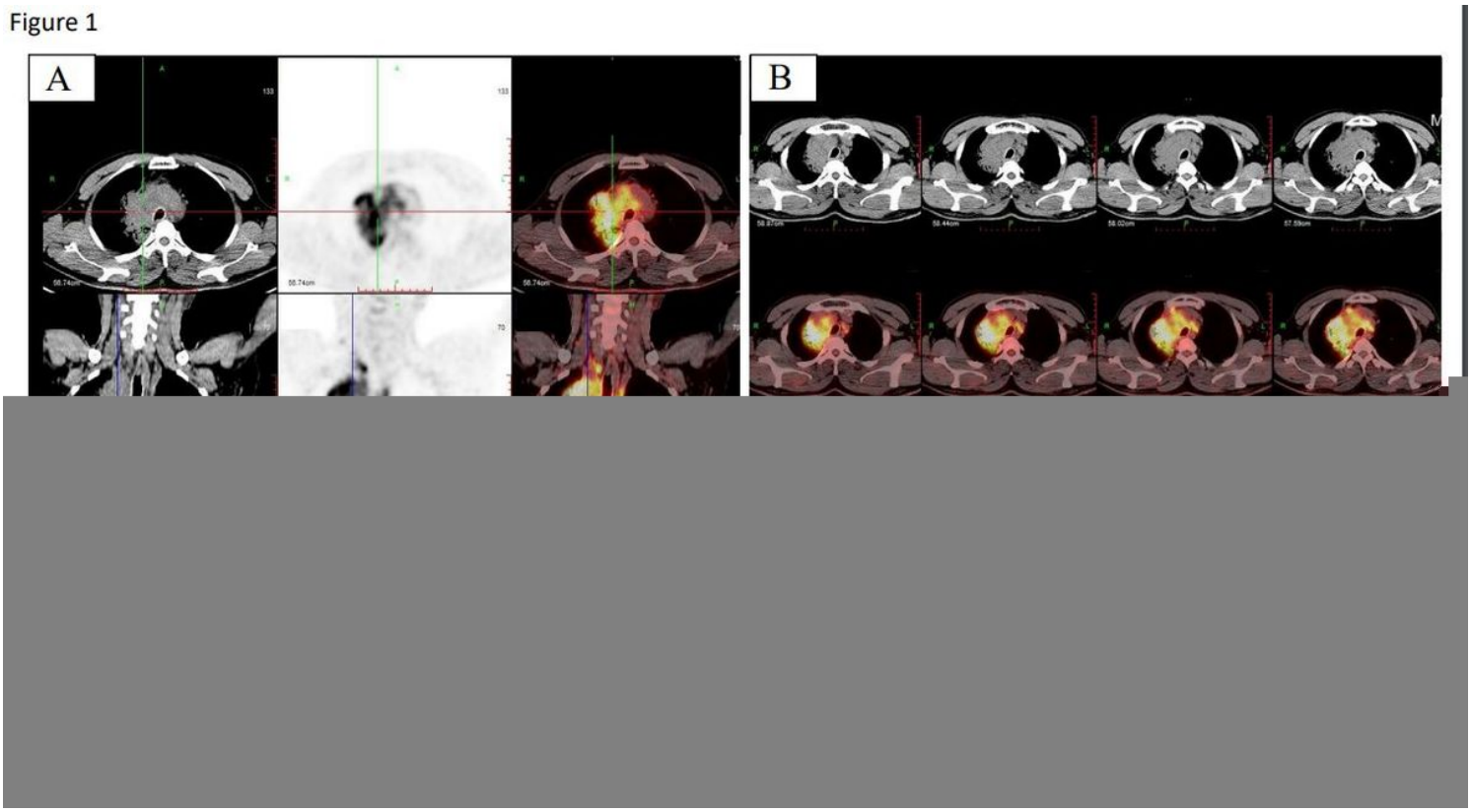

Figure 1

PET\CT images showed a mass (about 7.2 x 6.7 x 6.1 cm) in the superior lobe of right lung with the SUVmax was about 13.4 and lymph node metastasis in hilum of right lung, mediastinum, and right subclavian fossa.

Figure 2

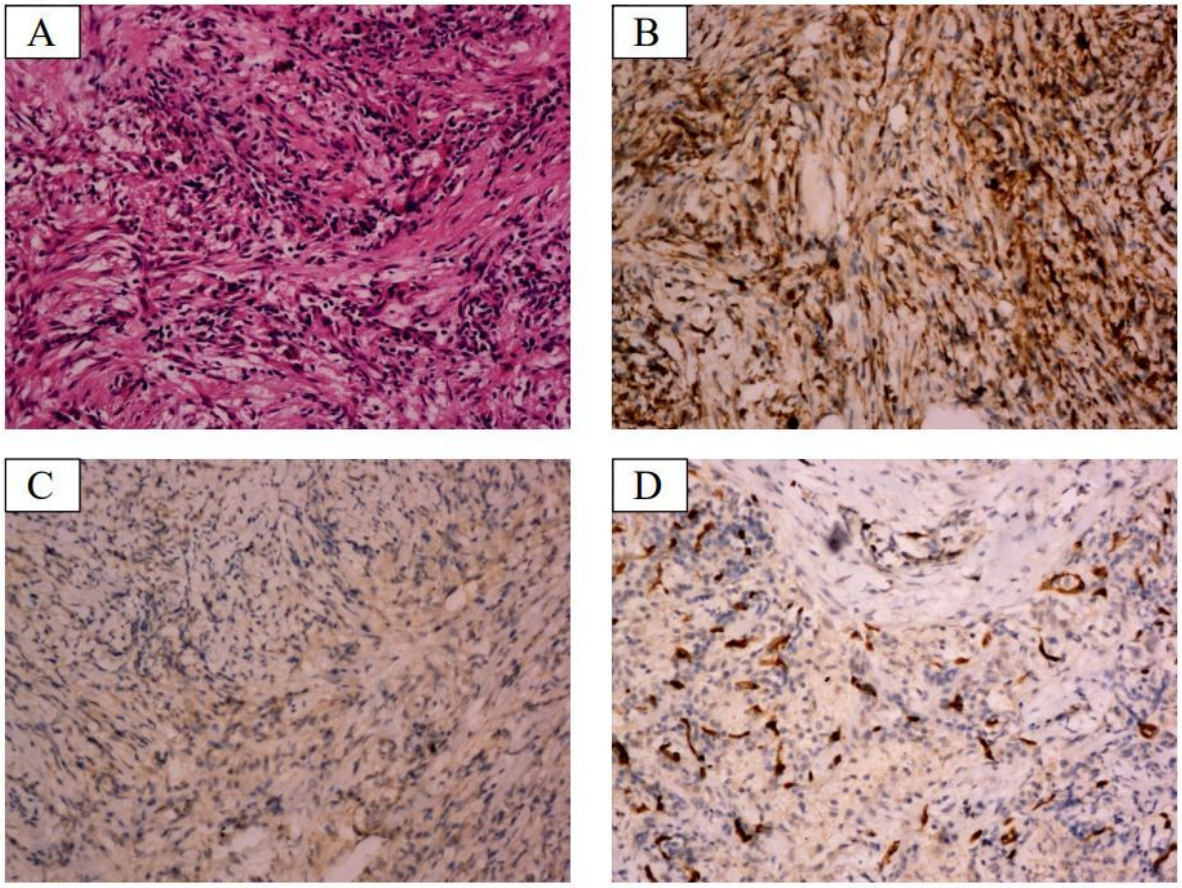

Figure 2

The microphotographs of the histopathological.

A. Spindle cells mixed with inflammatory cells. The spindle cells are epithelioid and mixed with chronic inflammatory cells. There is increased vascularity in the IMT. (H&E, 200x).

B. Immunostaining positive for vimentin (200x).

C. Immunostaining negative for ALK (200x).

D. Immunostaining positive for CD34 (200x).

Figure 3

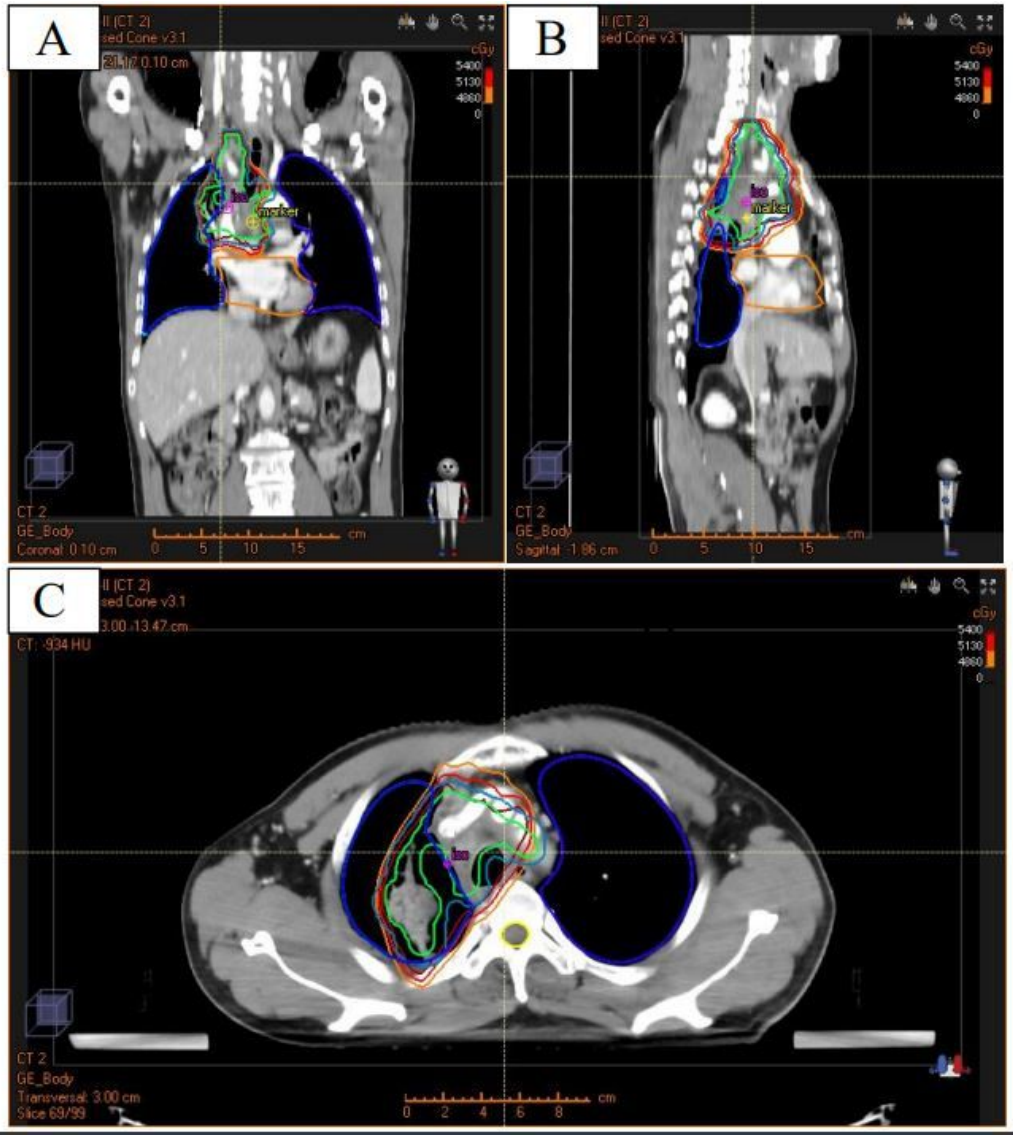

Figure 3

Intensity Modulated Radiation Therapy (IMRT) plan for the patient showing conformal radiation dose delivery to the tumor.