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(CASE REPORT)

METASTATIC PULMONARY INFLAMMATORY MYOFIBROBLASTIC TUMOR WITH CEREBRAL INVOLVEMENT: DIAGNOSTIC CHALLENGES AND RADIOLOGICAL RESPONSE TO CRIZOTINIB

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ABSTRACT

Inflammatory myofibroblastic tumor (IMT) is a rare mesenchymal neoplasm of intermediate malignant potential, most commonly arising in the lung. Although generally indolent, distant metastases occur in a minority of cases and can generate major diagnostic uncertainty, particularly when the central nervous system is involved. We report the case of a 48-year-old chronic smoker who presented with intracranial hypertension, seizures, and weight loss. Initial contrast-enhanced thoraco-abdomino-pelvic and brain computed tomography (CT) demonstrated a left lower lobe mediastino-pulmonary mass associated with multiple intra- and extra-axial enhancing cerebral lesions, highly suggestive of metastatic disease. Three CT-guided pulmonary biopsies, two surgical pulmonary biopsies, and a stereotactic brain biopsy were non-diagnostic or only suggestive. Definitive diagnosis was achieved only after cerebral metastasectomy, which confirmed IMT on histology and immunohistochemistry. The tumor was ALK-negative by immunohistochemistry, but fluorescence in situ hybridization identified a TFG-ROS1 fusion. The baseline imaging available at our institution was obtained after metastasectomy and before initiation of targeted therapy. Under crizotinib, follow-up CT showed a marked decrease in the number of brain lesions, from four residual lesions to a single residual lesion, with reduction in lesion size, enhancement, and vasogenic edema. The pulmonary mass also partially regressed, with a decrease of its soft tissue component and progressive calcification. This case highlights the diagnostic limitations of repeated biopsy in IMT, the decisive value of surgical sampling when radiological and pathological findings remain discordant, and the central role of imaging in the post-therapeutic assessment of metastatic disease. It also illustrates the biological and therapeutic relevance of ROS1 rearrangement in metastatic IMT.

Keywords: Inflammatory Myofibroblastic Tumor; Pulmonary IMT; Brain Metastases; ROS1 Fusion; Crizotinib; Computed Tomography; Case Report.

1 INTRODUCTION

Inflammatory myofibroblastic tumor (IMT) is an uncommon mesenchymal neoplasm composed of myofibroblastic spindle cells associated with a variable inflammatory infiltrate. Once regarded as a reactive pseudotumoral process, it is now recognized as a true neoplasm of intermediate malignant potential because of its capacity for local recurrence and occasional distant metastasis [1-4].

The lung is one of the most frequent sites of involvement. On CT, pulmonary IMT usually appears as a solitary mass or nodule, sometimes lobulated and sometimes calcified, but these findings are non-specific and often overlap with those of primary lung cancer, metastasis, or other inflammatory and infectious lesions [3,5,6]. Accordingly, imaging can strongly suggest tumor aggressiveness and guide biopsy strategy, but it cannot by itself establish a secure diagnosis.

Recent molecular studies have shown that IMT may harbor actionable kinase rearrangements, most often involving ALK and less frequently ROS1, NTRK, RET, or PDGFRβ, which has major therapeutic implications in advanced disease [1,2,7-9]. We report a case of metastatic pulmonary IMT with cerebral involvement, prolonged diagnostic uncertainty despite repeated biopsies, confirmation on cerebral metastasectomy, and marked radiological response to crizotinib in a tumor harboring a TFG-ROS1 fusion.

2 CASE PRESENTATION

A 48-year-old man with chronic tobacco exposure presented with signs of intracranial hypertension and seizures in a context of weight loss.

Initial contrast-enhanced thoraco-abdomino-pelvic and brain CT, performed before referral to our institution, revealed a left lower lobe mediastino-pulmonary tumor process associated with multiple cerebral secondary lesions. The patient underwent three CT-guided biopsies of the pulmonary lesion; all were non-contributory. Two subsequent surgical pulmonary biopsies were then performed. The first remained non-diagnostic, whereas the second was interpreted as favoring inflammatory myofibroblastic tumor. However, because of the unusual association between a presumed pulmonary IMT and multiple cerebral lesions, the initial diagnosis remained questioned during multidisciplinary discussion.

To further investigate the intracranial disease, a stereotactic biopsy of the most accessible lesion, located in the right frontal region, was performed but remained inconclusive. In view of the persistent radiopathological discordance, the patient subsequently underwent cerebral metastasectomy.

Histologically, the resected lesion showed a distinctive fascicular proliferation of spindle cells associated with a prominent inflammatory infiltrate. Immunohistochemistry showed weak, diffuse and dot-like cytoplasmic staining but was interpreted as ALK-negative. Fluorescence in situ hybridization (FISH) performed on interphase nuclei from 5-micron formalin-fixed paraffin-embedded sections demonstrated a TFG-ROS1 fusion, supporting the diagnosis of ROS1-rearranged inflammatory myofibroblastic tumor.

The patient was then referred to our institution for completion of management and oncologic imaging follow-up. Crizotinib was initiated as targeted therapy. The first imaging study available at our institution corresponded to the postoperative baseline examination, obtained after cerebral metastasectomy and before the start of crizotinib.

2.1 Imaging findings

The baseline postoperative pre-treatment examination included contrast-enhanced brain CT and thoraco-abdomino-pelvic CT.

At the cerebral level, contrast-enhanced CT demonstrated a postoperative cavity corresponding to the resected lesion. In addition, four residual enhancing cerebral lesions were identified, involving both intra- and extra-axial compartments, and associated with surrounding vasogenic edema. In the postoperative setting, these findings were highly suggestive of persistent metastatic disease burden (Figure 1).

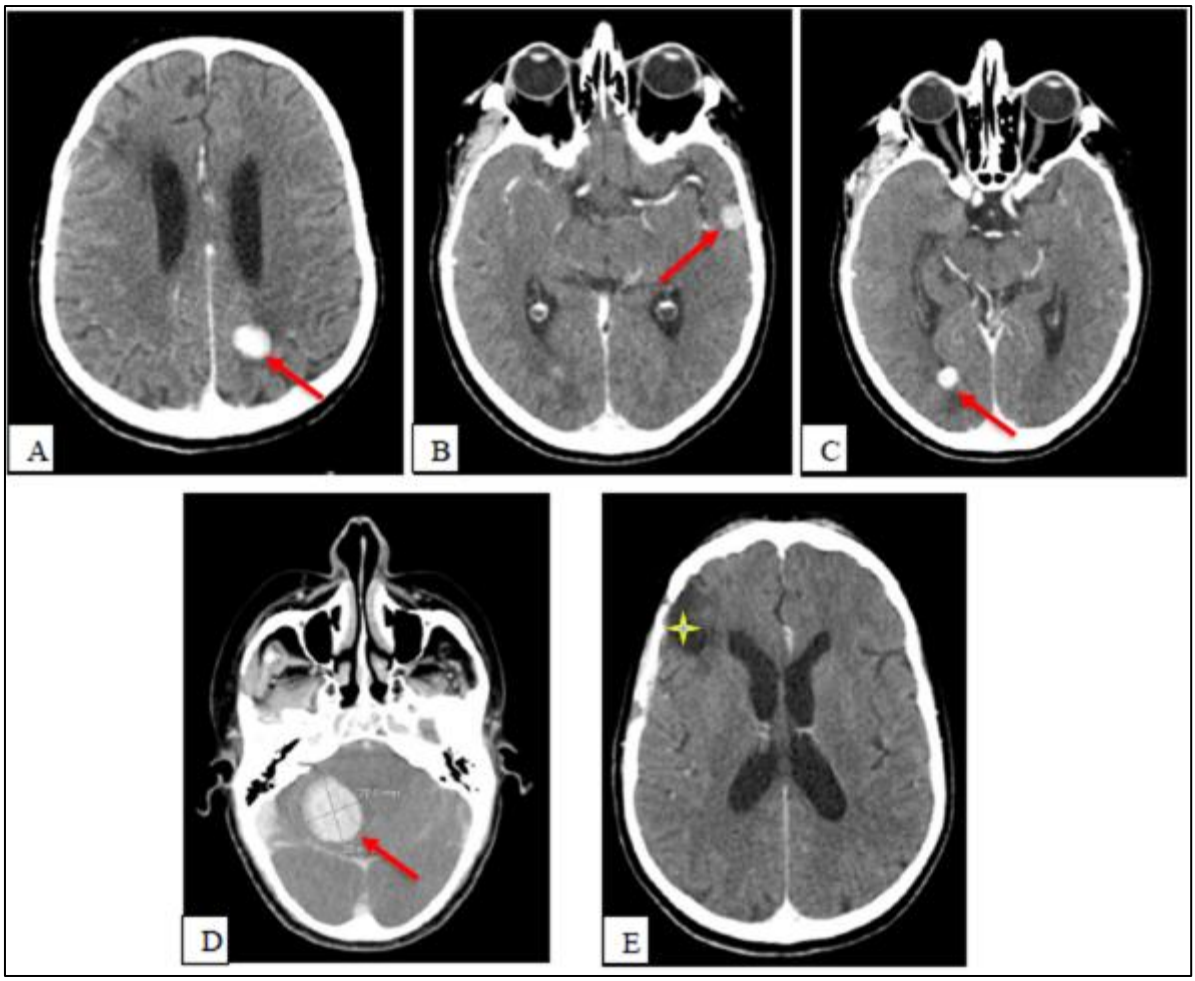

Figure 1: Baseline contrast-enhanced brain CT (axial views). Multiple enhancing lesions are identified in both intra- and extra-axial compartments, consistent with metastatic disease. Four well-defined, oval lesions show homogeneous contrast enhancement and are surrounded by vasogenic edema, including a left parietal lesion (A, red arrow), a lesion adjacent to the right occipital horn (B, red arrow), a right anterior temporal lesion (C, red arrow), and a larger extra-axial lesion along the right cerebellar tentorium (D, red arrow), measuring approximately 30 × 35 mm. A right fronto-subcortical hypodense area (E, yellow star) corresponds to postoperative changes at the prior metastasectomy site.

At the thoracic level, CT showed a persistent left lower lobe mediastino-pulmonary mass with heterogeneous attenuation and internal calcified components. The lesion retained a substantial soft tissue component at baseline (Figure 2).

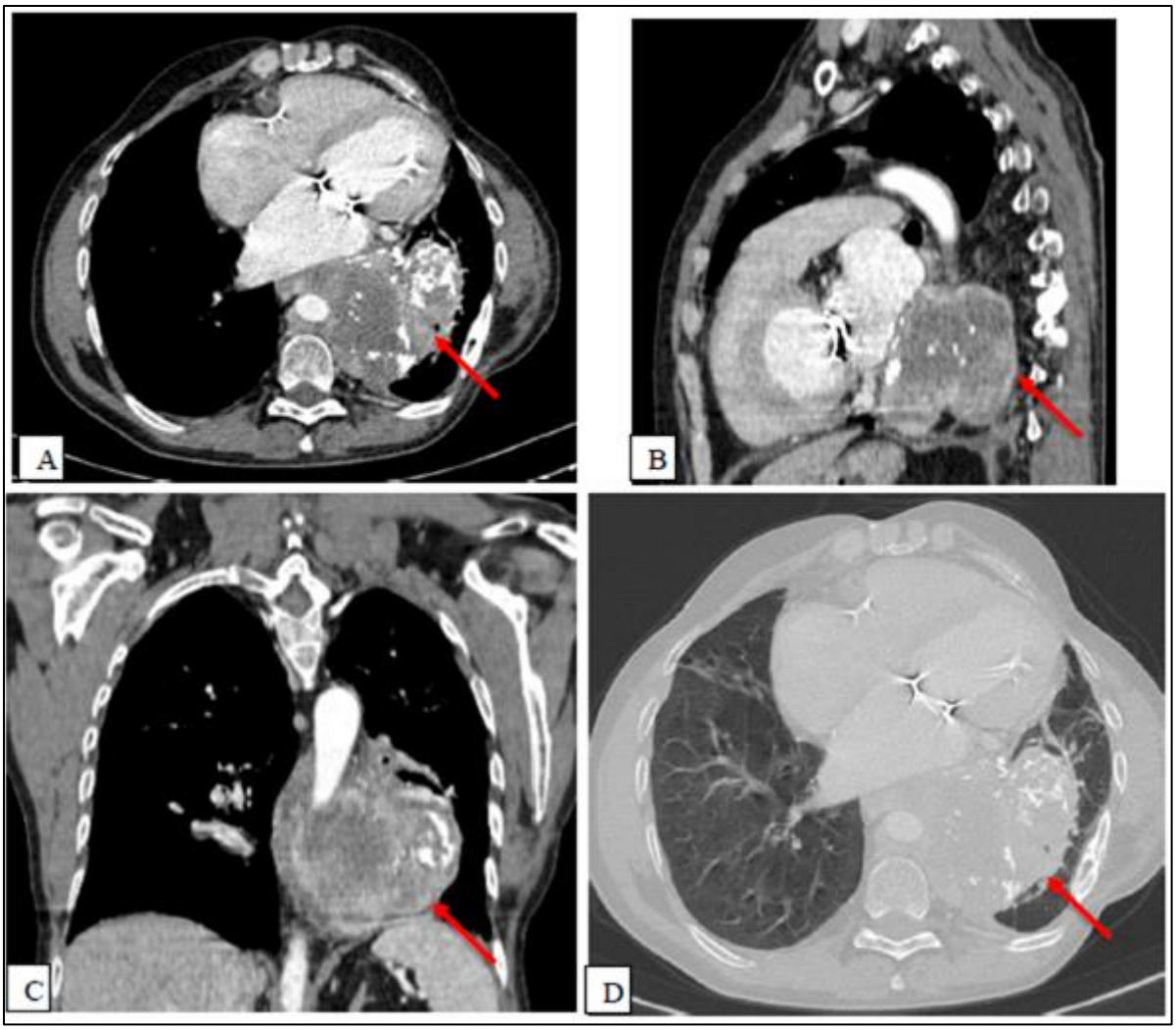

Figure 2: Baseline contrast-enhanced thoracic CT. Axial (A), sagittal (B), and coronal (C) mediastinal window images, along with an axial lung window image (D), demonstrate a large left lower lobe mediastino-pulmonary mass (red arrow). The lesion is ovoid with irregular margins, shows heterogeneous contrast enhancement, and contains internal calcifications. It measures approximately 99 × 95 mm in axial dimensions.

On follow-up imaging under crizotinib, a marked cerebral radiological response was observed. The number of residual brain lesions decreased from four to a single residual lesion. The persistent lesion itself decreased in size, with a parallel reduction in contrast enhancement and surrounding vasogenic edema (Figure 3).

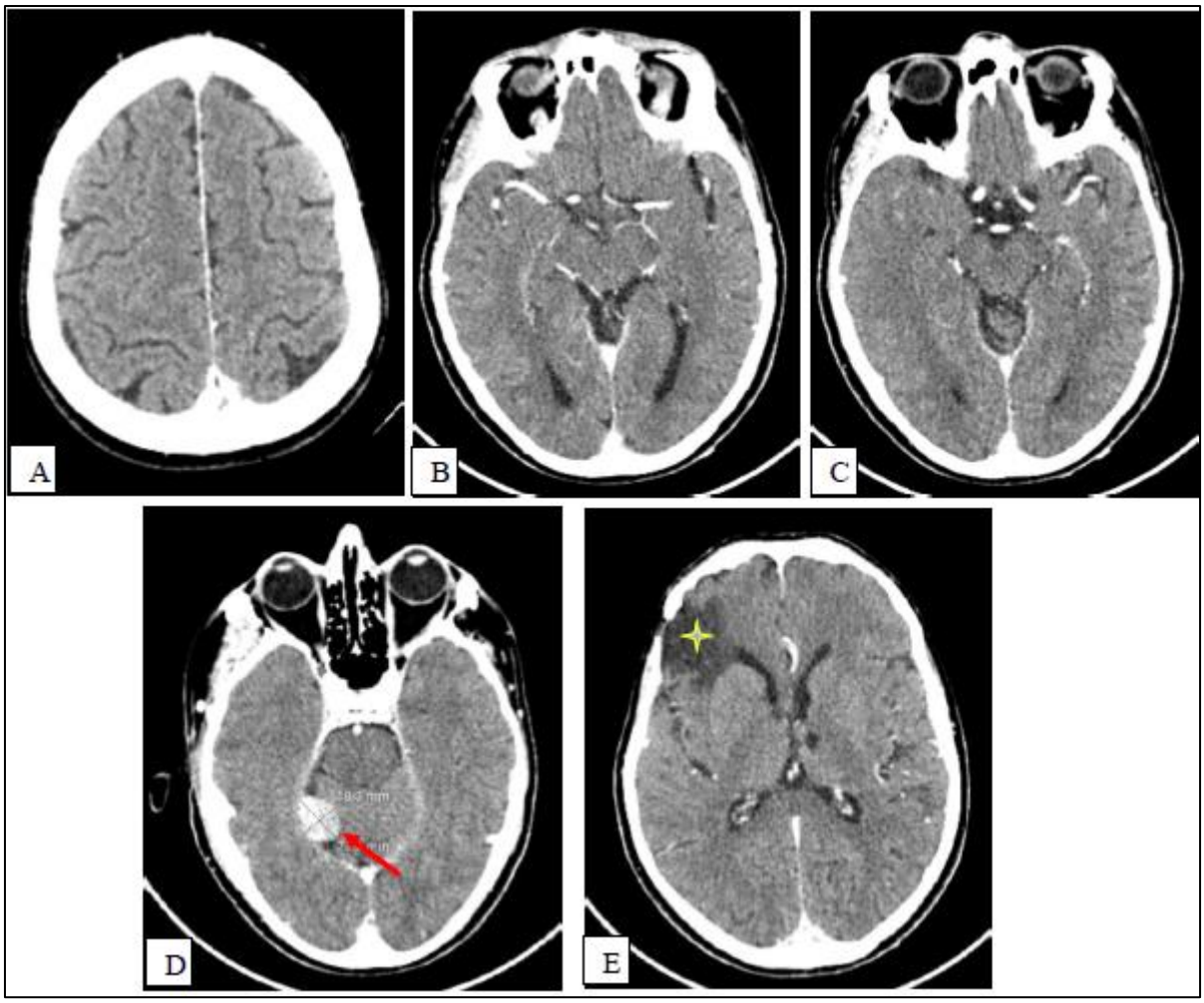

Figure 3: Follow-up contrast-enhanced brain CT (axial views, same levels as Figure 1). Compared with baseline, there is a marked radiological response with complete resolution of three previously described lesions (A–C). The remaining extra-axial lesion along the right cerebellar tentorium shows partial regression (D), now measuring approximately 18 × 23 mm in axial dimensions (red arrow). The right fronto-subcortical hypodense area (E, yellow star) persists, consistent with postoperative changes.

Thoracic follow-up CT also showed a partial response of the pulmonary lesion, with reduction of the soft tissue component and increased conspicuity of internal calcifications (Figure 4). No new thoracic, abdominal, or cerebral lesions were identified on the available follow-up studies.

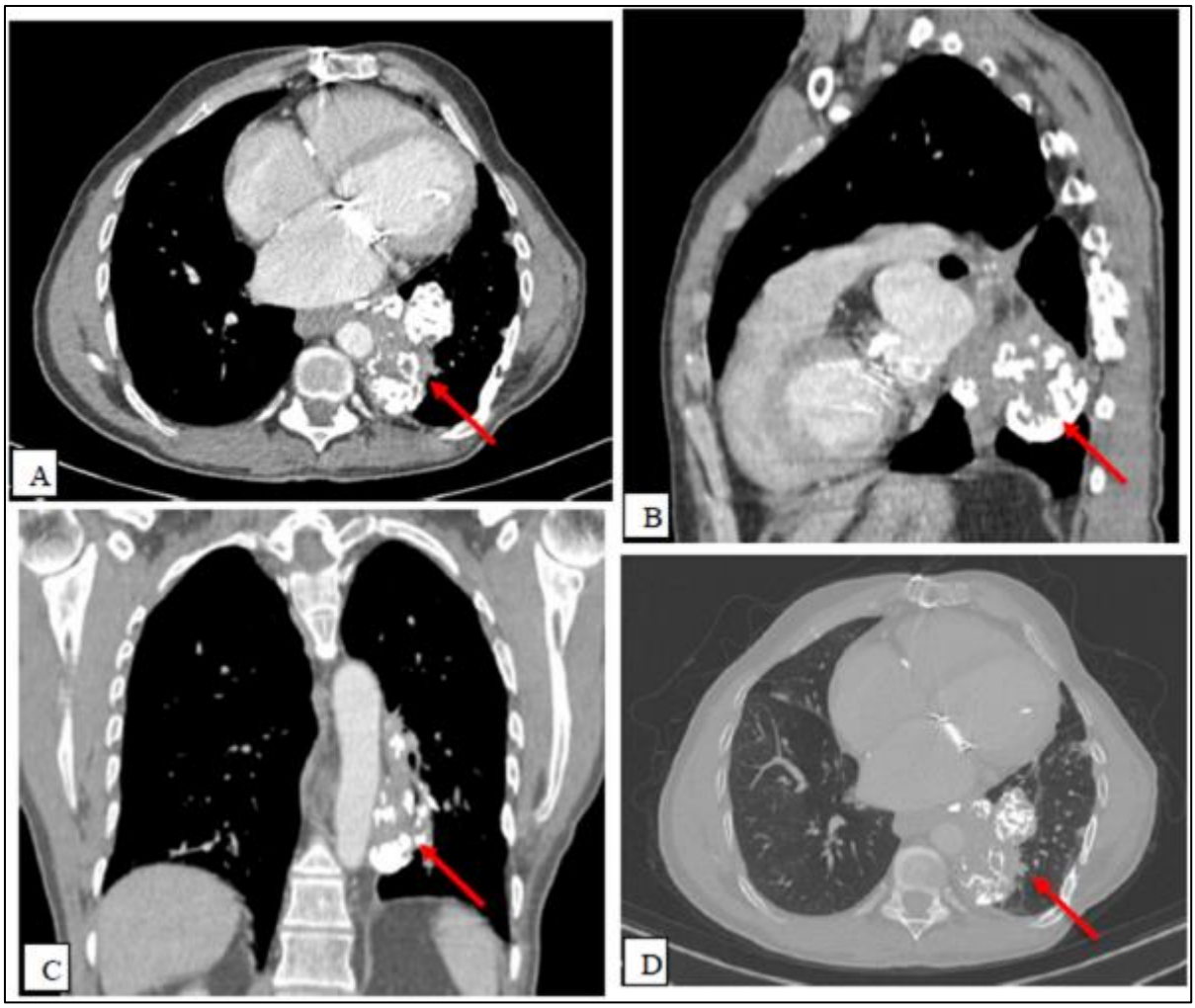

Figure 4: Follow-up contrast-enhanced thoracic CT (same planes and window settings as Figure 2). Axial (A), sagittal (B), and coronal (C) mediastinal window images, along with an axial lung window image (D), demonstrate interval partial regression of the left lower lobe mediastino-pulmonary mass (red arrow). The lesion has decreased in size, now measuring approximately 80 × 58 mm in axial dimensions, and shows a marked reduction of its soft tissue component with predominance of internal calcifications, consistent with treatment response.

Taken together, serial CT examinations documented a clear systemic treatment response, more striking at the cerebral level than at the thoracic level, underscoring the value of imaging not only for lesion detection but also for dynamic treatment assessment.

3 DISCUSSION

This case is noteworthy for the conjunction of four elements: metastatic pulmonary IMT with cerebral involvement, repeated inconclusive biopsies, identification of a TFG-ROS1 fusion, and marked radiological response to crizotinib. Each of these features adds distinct value to the report, and together they make the case particularly relevant to both radiologists and multidisciplinary oncologic teams.

From an imaging standpoint, pulmonary IMT remains a classic mimicker. Reviews and thoracic imaging series have shown that pulmonary IMT usually presents as a solitary, often well-defined peripheral mass or nodule, sometimes with calcifications, but without truly specific CT features [3,5,6,10]. In our patient, the pulmonary lesion was retrospectively compatible with IMT because of its persistent mass-like appearance and internal calcifications; however, these findings were not discriminatory. In the actual clinical context, the simultaneous presence of multiple cerebral lesions strongly shifted the radioclinical impression toward metastatic malignancy, which was entirely reasonable at presentation.

The prolonged diagnostic uncertainty in this case is also highly instructive. Multiple tissue samplings were performed before a definitive diagnosis was reached: three CT-guided pulmonary biopsies, two surgical pulmonary biopsies, one stereotactic brain biopsy, and finally cerebral metastasectomy. Such a sequence illustrates the well-recognized

limitations of small samples in IMT. Owing to marked intratumoral heterogeneity, variable proportions of spindle cells and inflammatory cells, and overlap with inflammatory, infectious, and malignant lesions, biopsies may be inconclusive or misleading [2,4,10,11]. Sakurai et al. emphasized that preoperative diagnosis of pulmonary IMT is seldom confirmed and that small biopsy specimens are generally insufficient because of the predominance of inflammatory cells in some samples [11]. Our case reproduces that problem in an extreme but clinically realistic manner.

For radiologists, the practical lesson is important: when imaging strongly suggests aggressive disseminated disease but pathology remains non-diagnostic, the radiologist should not remain confined to descriptive reporting. Imaging-pathology discordance must be explicitly emphasized at multidisciplinary discussion, because it may justify escalation toward more representative tissue sampling. In our case, the persistence of radiological suspicion ultimately supported the decision to proceed to metastasectomy, which proved diagnostically decisive.

The molecular profile is the strongest scientific aspect of the case. The tumor was ALK-negative by immunohistochemistry, yet FISH demonstrated a TFG-ROS1 fusion. This finding has two major implications. First, it confirms that ALK-negative IMT should not be considered molecularly uninformative, particularly in advanced or atypical presentations. Second, it provides a biologically coherent explanation for the observed response to crizotinib, since ROS1-rearranged tumors are known to be sensitive to this agent [1,2,7-9]. Recent reviews of IMT biology have highlighted that, beyond ALK, less common kinase fusions such as ROS1 can define clinically actionable subsets and should be actively sought when morphology and clinical behavior support the diagnosis [1,7-9].

The identification of a TFG-ROS1 fusion is particularly relevant because ROS1-rearranged IMTs are much less common than ALK-rearranged cases and remain underrepresented in the literature. In the present case, this molecular alteration transforms the interpretation of treatment response from merely descriptive to mechanistically meaningful. Before molecular clarification, one might simply note that an ALK-negative IMT responded to crizotinib. After ROS1 characterization, the response becomes expected and biologically grounded. This substantially strengthens the case report and raises its scientific level beyond that of a simple rare-case description.

Metastatic behavior in IMT is uncommon but well documented. Older clinicopathological series already established that IMT is not purely benign and may occasionally recur or metastasize [2,4]. Contemporary reviews confirm that metastatic spread occurs in a minority of cases, generally below 5% overall, but may be enriched in specific molecular and anatomical subsets [1,7,8]. Cerebral involvement remains distinctly unusual. In that context, our case contributes radiologically useful information because it documents residual postoperative metastatic burden at baseline and objective response on serial CT under targeted therapy.

A major strength of the present report is therefore its dynamic imaging component. The first examination available for review at our institution was obtained after metastasectomy and before treatment initiation. This postoperative study defines the true baseline for treatment evaluation. Although the absence of directly reviewable preoperative brain imaging is a limitation for initial lesion characterization, it does not prevent robust assessment of therapeutic response. On the contrary, the baseline-follow-up comparison remains methodologically valid and clinically relevant, since it reflects the state of measurable disease immediately before crizotinib.

The cerebral response was particularly striking, with a decrease in lesion number from four to one, accompanied by reduction in lesion size, enhancement, and surrounding edema. The pulmonary lesion also showed partial response, with reduction of the soft tissue component and progressive internal calcification. This evolution suggests that, in metastatic IMT, treatment response may be more meaningfully captured by serial imaging than by static lesion morphology. It also underlines that increased calcification within the pulmonary lesion, when associated with reduction in viable-appearing soft tissue, may reasonably be interpreted as treatment-related change rather than progression.

This report has limitations. Preoperative brain imaging was not available for direct review, which precludes detailed radiological characterization of the original intracranial lesions. In addition, a complete broad molecular panel was not available beyond the demonstration of TFG-ROS1 fusion. Nonetheless, the core messages remain strong: imaging was central to detection of disseminated disease, repeated biopsy was insufficient for diagnosis, metastasectomy provided definitive tissue, and serial CT objectively documented treatment response in a ROS1-rearranged metastatic IMT.

Overall, the case supports a pragmatic radiology-centered conclusion. In rare neoplasms such as IMT, imaging should not be reduced to lesion inventory. It also structures clinical reasoning, reveals radiopathological discordance, supports strategic biopsy decisions, and provides the most objective framework for response assessment once targeted therapy is initiated.

4 CONCLUSION

ROS1-rearranged metastatic pulmonary inflammatory myofibroblastic tumor with cerebral involvement is an exceptionally uncommon presentation that may closely mimic metastatic malignancy and remain diagnostically elusive despite repeated biopsy attempts.

In the present case, definitive diagnosis required cerebral metastasectomy after multiple inconclusive pulmonary and cerebral biopsies. For radiologists, the main lessons are threefold: pulmonary IMT has no specific CT signature; persistent mismatch between imaging behavior and pathology should prompt reconsideration of sampling strategy; and serial postoperative pre-treatment and follow-up CT examinations are indispensable for documenting treatment response.

The demonstration of a TFG-ROS1 fusion and the marked radiological response to crizotinib substantially strengthen the biological and therapeutic coherence of this case, and support the value of actively seeking actionable kinase rearrangements in atypical or advanced IMT.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Disclosure of conflict of 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.

Statement of informed consent

Written informed consent was obtained from the patient for publication of this case report and the accompanying images.

Declaration of the use of generative AI and AI-assisted technologies in the writing process

During the preparation of this manuscript, the authors used a large language model (generative AI) for language editing and improvement of clarity. The authors critically reviewed, revised, and approved the final version of the manuscript and take full responsibility for its content.

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