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Case report

Intimal sarcoma of the pulmonary artery treated with neoadjuvant radiation prior to pulmonary artery resection and reconstruction

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ABSTRACT

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Intimal sarcoma (IS) is a rare malignancy arising in the great vessels or heart, most commonly in the pulmonary artery, primarily treated with surgical intervention. We report a case of IS of the pulmonary artery diagnosed after an endarterectomy to remove a suspected pulmonary embolism. The tumor could not be entirely resected and showed interval growth at post-operative follow up. Neoadjuvant radiotherapy was then delivered to improve resectability. Imaging confirmed decreased tumor size, and a surgical resection with pulmonary artery reconstruction and right upper lobectomy was then successfully performed. Adjuvant gemcitabine and docetaxel was later initiated. Four months post-operatively, the patient is alive without disease recurrence. While prior reports in the literature document use of adjuvant chemotherapy and radiotherapy for treatment of IS of the pulmonary artery, no prior experience has documented utility of neoadjuvant radiotherapy for improvement of resectability. Our experience suggests that neoadjuvant radiation should be considered to improve resectability in cases of borderline resectable IS of the pulmonary artery.

1. Case presentation

A 65-year-old African-American man initially presented with shortness of breath several months after knee replacement surgery. Computed tomography angiography (CTA) revealed a large filling defect thought to represent pulmonary embolism in the right main pulmonary artery and he was started on apixaban. The patient re-presented two months later with significant dyspnea and chest pressure requiring admission. Repeat CTA revealed near-complete occlusion of the right main pulmonary artery (Fig. 1A and B). After receiving 24 hours of thrombolytic therapy with no improvement on CTA, the patient underwent pulmonary endarterectomy. A chronic and organized clot was resected from the right pulmonary artery with gross residual disease in right upper lobe pulmonary artery branches that could not be resected. Histopathologic examination of the specimen documented an obstructing myxoid sarcomatoid neoplasm with atypia and variable cellularity, engendering a broad differential diagnosis (Fig. 2A and B). Immunostaining revealed only nonspecific positivity for desmin, while lack of rearrangement at *EWSR1* ruled out several other myxoid tumors, such as myxoid chondrosarcoma. Clinical SNP microarray testing documented a complex karyotype with numerous anomalies, including amplification of *MDM2*, in context establishing the classification as an intimal sarcoma. There were no post-operative complications, and the patient was discharged on warfarin. Subsequent Positron Emission Tomography (PET) imaging showed no abnormal radiotracer uptake in the lungs, mediastinum, or any distant site, favoring a diagnosis of primary pulmonary artery intimal sarcoma. CTA performed two months post-operatively revealed a hypodense mass within the right main pulmonary artery measuring 2.7×2.1 cm. One month later, the patient again presented to the emergency department with worsening dyspnea, and CTA revealed interval growth of the mass to 3.2×2.0 cm (Fig. 3A and B). The patient's pulmonary reserve suggested a right pneumonectomy would be of high risk, especially considering the evidence that right pneumonectomies are associated with higher perioperative mortality than left

pneumonectomies [1]. Given the uncertainty of obtaining an optimal resection without performing a pneumonectomy, the decision was made to first administer neoadjuvant radiation. The patient received 50 Gy in 25 fractions to the mass using a volumetric modulated arc therapy (VMAT) technique, and subsequent CTA four weeks post-radiation revealed a decrease in mass size to 2.2×1.2 cm (Fig. 4A and B). The patient underwent resection of the right pulmonary artery tumor, right upper lobectomy, and right pulmonary artery reconstruction with bovine pericardium. The vascular resection margin was purposefully close to avert the need for pneumonectomy. Histopathologic examination of the resected tumor showed evidence of radiation treatment efficacy with 70% viable tumor remaining and a negative final margin at the residual pulmonary artery stump. Post-operative course was complicated by a hemothorax requiring video-assisted thoracoscopic surgery and acute kidney injury requiring temporary hemodialysis. The patient was discharged 17 days post-operatively. One month later he was initiated on a chemotherapy regimen of gemcitabine $900\text{mg}/\text{m}^2$ (IV = 1800mg on day 1 and day 8) and docetaxel $75\text{mg}/\text{m}^2$ (IV = 150mg on day 8) every three weeks with a plan for 12 cycles total. Adjuvant doxorubicin was not selected due to patient's history of coronary artery disease and atrial fibrillation. The patient is currently 136 days out from the second operation and 80 days out from his first cycle of chemotherapy. Follow-up chest CT with contrast at this time did not reveal any evidence of recurrent disease or enlarged lymph nodes (Fig. 5A and B). The patient was provided informed consent and allowed us to publish his experience.

2. Discussion

Pulmonary Artery Intimal Sarcoma (PAIS) is a rare sarcoma arising from the mesenchymal cells of large vessels such as the pulmonary artery intima. The condition was first described in 1923, and there have since been around 300 cases reported in the literature as case reports and small series [2]. PAIS is a histologically variable neoplasm but

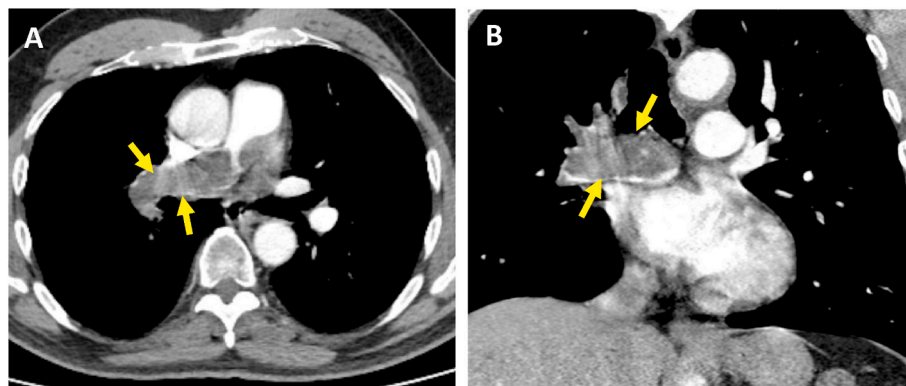


Fig. 1. CTA of pulmonary arteries prior to endarterectomy.

(A) Axial and (B) Coronal images show large occlusive filling defect in right main pulmonary artery (yellow arrows). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

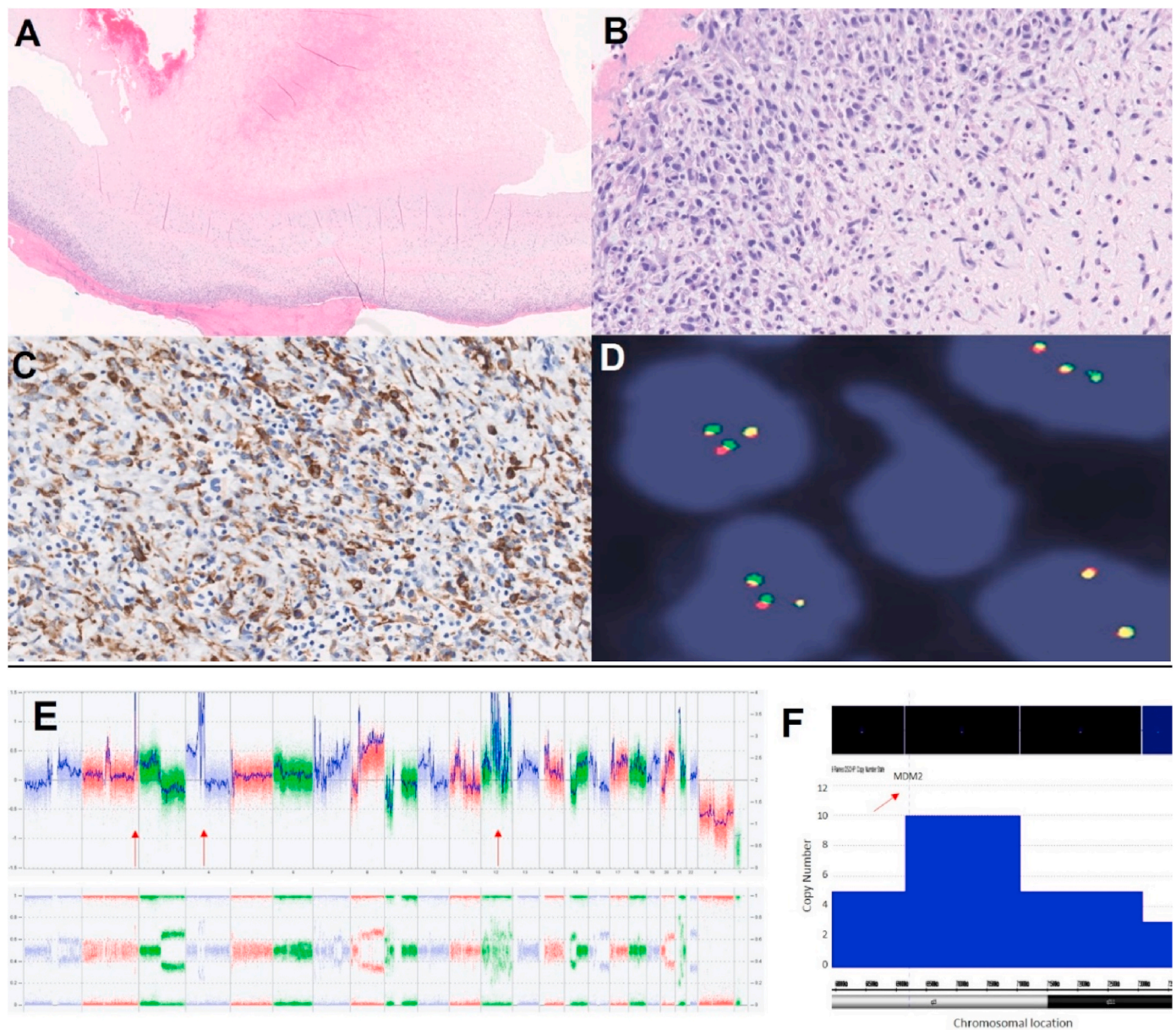


Fig. 2. Histopathology of the intimal sarcoma of the pulmonary artery

(A) Low power view of the neoplastic proliferation arising from the vessel wall (H&E, 20x) (B) High power view shows the pleomorphic cells in a myxoid matrix (H&E, 200x) (C) Immunohistochemical stain, desmin shows reactivity within the cells (200x) (D) Fluorescent in-situ hybridization of probe for Ewing sarcoma breakpoint region 1 (EWSR1) locus (22q12) showed no rearrangement (the signals for the nucleus near the center of the field were on a different focal panel) (E) Genome-wide view of the copy number findings that were present in this tumor, with the data presented as the weighted log₂ ratio (top); and the beta allele frequency pattern (bottom). The tumor had a complex karyotype with multiple copy number gains and losses. The red arrows highlight regions with amplification (noted on chromosomes 2, 4, and 12). The patterns noted on chromosome 12 were consistent with a chromothripsis-like pattern (multiple peaks). (F) The copy number patterns for the region that encompasses the MDM2 gene are shown (portions of band 12q15 and band 12q21.1). The dashed line (highlighted by a red arrow) denotes the location of the MDM2 gene. Note that the locus is coincident with the presence of a “peak” of high copy number gain (approximately 10 copies). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

consistently demonstrates gains and amplifications at the 12q12-q15 locus, including *MDM2*, amplification of which is a helpful diagnostic feature [3]. As we observed in this case, the presentation commonly mimics pulmonary embolism and features dyspnea and chest pain. Pulmonary hypertension and resulting right-sided heart failure have been documented in several case series. Most reported cases have shown Fluorodeoxyglucose (FDG) avidity on PET/CT [2,4,5]. Notably, this case diverged from the literature as the tumor did not show increased FDG uptake.

While there is no standard of care for PAIS due to a lack of published evidence, surgeries such as pulmonary endarterectomy, lobectomy, and

pneumonectomy are the most common treatment options [2,4,5]. Prognosis of PAIS is very poor even with treatment, with one group describing a survival of 1.5 months without surgical resection and 10 months with surgical resection [2]. Most literature indicates significant symptomatic improvement among PAIS patients with endarterectomy, which likely undergirds its role as a mainstay of treatment despite a lack of robust survival benefit. Adjuvant therapy is often used, the most common being doxorubicin and ifosfamide chemotherapy either alone or in combination with radiotherapy [2,4,5]. One case series of 20 patients from a single center showed a trend towards improved survival among patients receiving adjuvant chemotherapy and radiotherapy as

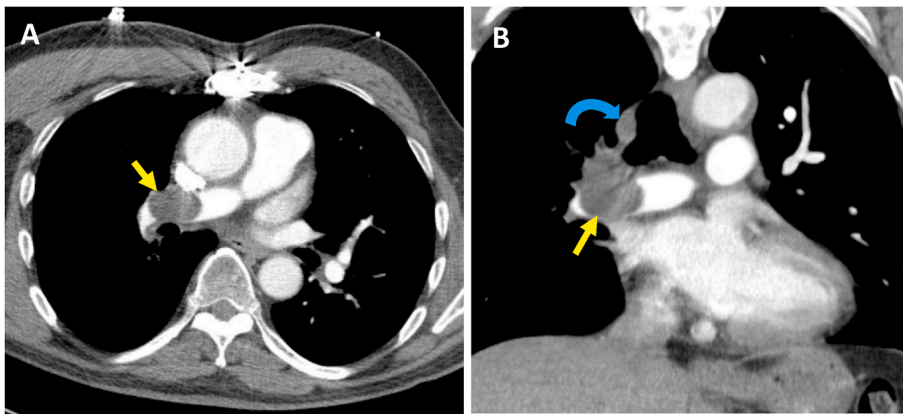


Fig. 3. CTA of pulmonary arteries performed at emergency department visit three months after end-arterectomy.

(A) Axial view of a 3.2×2.0 cm filling defect (yellow straight arrow) in the right main pulmonary artery extending into the truncus anterior and apical segmental artery. (B) Coronal view of the same filling defect (yellow straight arrow) also showing involvement of the right upper lobe (blue curved arrow). . (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

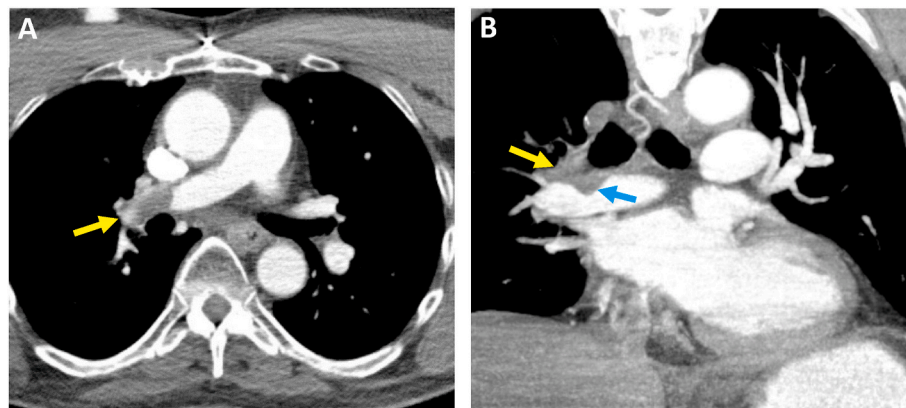


Fig. 4. CTA of pulmonary arteries performed one month after completion of radiotherapy.

(A) Axial and (B) Coronal sequences through right pulmonary artery shows residual tumor only located along superior margin of artery (yellow and blue arrows). . (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

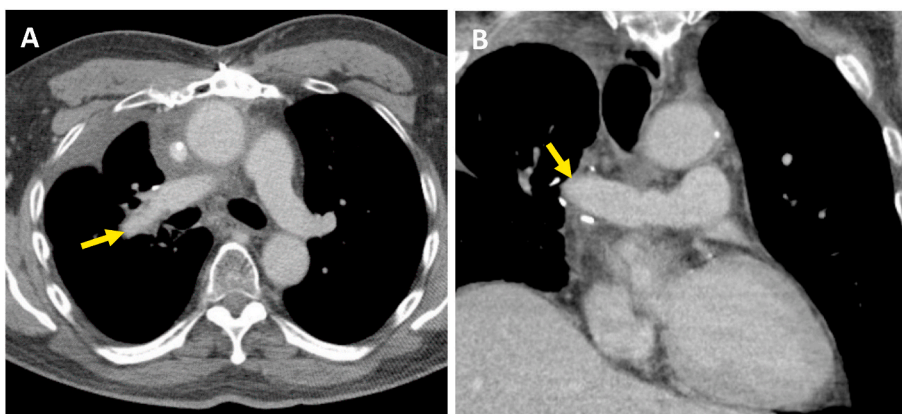


Fig. 5. CT with contrast of pulmonary arteries four months after intimal sarcoma resection, right pulmonary artery reconstruction, and right upper lobectomy.

(A) Axial view of right main pulmonary artery (yellow straight arrow) reconstructed with bovine pericardium after resection of mass. Chronic loculated hemothorax also present in right upper pleural space. (B) Coronal view of same reconstructed right main pulmonary artery (yellow straight arrow) with visible surgical clips. . (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

compared to surgery alone [5]. Our experience with this case was unique in that radiation was used neoadjuvantly to decrease tumor size and improve resectability. Evidence suggests that patients with PAIS who undergo complete resections have improved overall survival compared to those with incomplete resections [5]. Continued clinical and imaging follow-up for our patient will definitively determine the long-term clinical impact of neoadjuvant radiation, but the conversion of the tumor from unresectable to resectable is very encouraging. To our knowledge, there have been no reported cases of PAIS treated with neoadjuvant radiation. We hope that our reporting of this novel treatment paradigm may better inform management of this rare disease.

3. Conclusions

Neoadjuvant radiation can be used to improve resectability for borderline resectable PAIS. The findings of this case suggest the need for larger studies to evaluate treatment paradigms, and specifically the role of neoadjuvant radiation, in treating PAIS.

Declaration of competing interest

All authors of the case report, "Intimal Sarcoma of the Pulmonary Artery Treated with Neoadjuvant Radiation Prior to Pulmonary Artery

Resection and Reconstruction” have no conflicts of interest to report.

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