Received: 10 April 2023 | Revised: 24 April 2023 | Accepted: 1 May 2023

DOI: 10.1002/ccr3.7348

Clinical Case Reports Open Access WILEY

CASE REPORT

Paraneoplastic acute eosinophilic pneumonia due to carotid angiosarcoma: A rare case

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Key Clinical Message: This case report emphasizes that we should analyze a patient's signs and symptoms as a whole rather than relying exclusively on a common pattern to diagnose the condition and indicates that thorough histological investigation and sample collection are needed to accurately diagnose this malignancy.

Abstract: Angiosarcoma is a rare, fatal, and poorly understood malignant tumor of vascular endothelial cells which is a challenging disease to diagnose in the clinical settings and requires early diagnosis to achieve a favorable prognosis. Paraneoplastic syndromes associated with angiosarcoma can include hypercoagulability, thrombocytopenia, anemia, fever, weight loss, and night sweats. In some cases, the paraneoplastic syndrome can be the first sign of the underlying malignancy. Here, we present a 47-year-old individual with angiosarcoma over the right scapula accompanied by hemoptysis and other pulmonary complaints whom at first was thought to be metastatic polmunary involvement. However, the patient's dramatic response to corticosteroids, in addition to further imaging and paraclinical studies, led us to an acute eosinophilic pneumonia (AEP) diagnosis which is an eosinophilic infiltrations of alveolar spaces. The patient received chemotherapy for angiosarcoma and radiation, since the brachial nerve network was disrupted, leaving the tumor unresectable. After 3 years of continuous follow-up, the patient is now completely cured.

KEYWORDS
acute eosinophilic pneumonia, angiosarcoma, bronchoalveolar lavage, eosinophilic lung disease, eosinophilic pneumonia, paraneoplastic disorder

1 | INTRODUCTION

Angiosarcoma is a rare, fatal, and poorly understood malignant tumor of vascular endothelial cells which is a challenging disease to diagnose in the clinical settings and requires early diagnosis to achieve a favorable prognosis.[1] Angiosarcomas are exceedingly rare, and the epithelioid variant is even rarer. Skin, spleen, liver, breast, coronary heart, bone, and gastrointestinal angiosarcomas are the most prevalent types. Paraneoplastic syndromes associated with angiosarcoma can include hypercoagulability, thrombocytopenia, anemia, fever, weight loss, and night sweats. In some cases, the paraneoplastic syndrome can be the first sign of the underlying malignancy.[2]

When eosinophils infiltrate the alveolar space and the interstitium, it can result in eosinophilic pneumonia.[3] Acute eosinophilic pneumonia (AEP) and chronic eosinophilic pneumonia (CEP) are two additional notable subtypes of eosinophilic pneumonia, both of which are distinguished by a significant accumulation of eosinophils in lung tissues and/or BAL fluid.[3] AEP and CEP share similarities in terms of pathogenesis, radiological findings, and corticosteroid therapy response. However, the disease's etiology, medical symptoms, and nature vary considerably between them.[3] Here, we present a rare and complicated case of a 47-year-old man with both AEP and epithelioid carotid angiosarcoma who was entirely treated following an accurate and prompt diagnosis.

2 | CASE PRESENTATION

The patient was 47-year-old male with no previous medical history. In the superior-posterior region of his right scapula, he observed a painful, tender mass with no secretion, and erythema. The right arm, chest, and anterior area of the neck were all affected. The mass doubled in size within a day, and 2 weeks later, the right side of the neck swelled. He had neither a fever nor the chills. Two weeks following the onset of symptoms, the patient visited a hospital in Urmia, Iran, in March 2018 and underwent an ultrasound, a biopsy, and a CT scan with a "necrotic mass congestion" or "neck abscess" impression. The diagnosis following the biopsy was "cystic mass". The patient was discharged from the hospital with the following lab results after recovery: WBC = 6.6 (poly = 56 percent); Hb = 12.8; Plt = 105; Cr = 0.08; BUN = 23.8; and ESR = 3.

One week later, he returned to the same hospital, complaining of right shoulder and neck pain and swelling. He noticed a loss of sensation and strength in his fingers, but his right upper extremity exhibited neither redness nor bruising. During a physical examination, a 50 × 80 mm palpable mass was detected in the right posterior cervical triangle and carotid triangle without erythema. It was a soft, immobile mass without lymphadenopathy or bruit.

A scapular biopsy revealed the presence of a vascular tumor. He also underwent a bronchoscopy due to hemoptysis, but the cause of the bleeding was not identified. After being admitted, the patient was transferred to us in Shohadaye Tajrish Hospital, Tehran, Iran. During his hospitalization, incisional biopsies were conducted on the patient's right shoulder and neck tumor. The pathologist reported that the cervical mass was a benign vascular lesion with localized papillary endothelial hyperplasia. Clusters of highly atypical epithelial-like cells were discovered in a hematoma in the right shoulder's soft tissue. The day after surgery, coarse crackles were audible at the bases of the lungs; thus, the patient received a chest CT scan without contrast, which revealed multiple opacities in the fields of both lungs (Figure 1). In addition, an MRI of the orbit, face, neck, and thorax was performed with and without contrast for the mass. Enhancement revealed a signal change center of 123 by 46 mm near the lateral aspect of the right neck anteroposterior triangle, but no intrathoracic extension or vascular encasement was identified.

The differential diagnoses based on the patient's medical history, CT scan, and MRI, were "vascular tumor

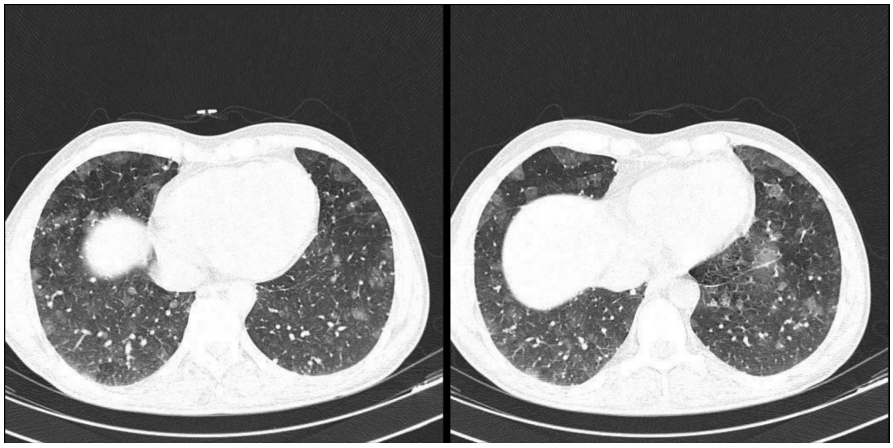

FIGURE 1 Initial chest CT scan representing wide-spreading opacities in lungs.

metastases", "BOOP in response to a neck vascular lesion", and "vasculitis". Accordingly, we reviewed the patient's clinical response and chest X-ray two days following the methylprednisolone infusion, as instructed by the pulmonary consultation. During the supplementary studies, no evidence of tuberculosis, HIV, or vasculitis was found. The incisional cervical biopsy eventually found the tumor to be benign. Therefore, these lung opacities could not have been the outcome of a probable metastasis. 15% eosinophils were found in the peripheral blood sample and 20% in the BAL sample. The patient's cough and hemoptysis improved dramatically after receiving methylprednisolone. The evidence strongly showed that the opacities in the patient's lungs were caused by AEP, based on the lung CT scan and the patient's general recovery following treatment (Figure 2). The original nondiagnostic result prompted the pathologist to seek a second opinion on the incisional right shoulder biopsy samples from another specialist. A significant hemorrhage and hematoma development were reported by the second pathologist in an epithelioid angiosarcoma (Figure 3).

Due to the involvement of the brachial nerve network, which made the tumor unresectable, chemotherapy and radiotherapy were ultimately chosen as the treatments for the patient. The patient underwent an initial three courses of 3-day ifosfamide/adriamycin/MESNA chemotherapy in addition to 35 sessions of radiotherapy, followed by a secondary three courses of 3-day chemotherapy. Currently, after 3 years of continuous follow-up, the patient is completely cured, and there are no signs of the primary tumor.

3 | DISCUSSION AND CONCLUSION

Angiosarcomas are malignant endothelial cell tumors of vascular or lymphatic origin, accounting for approximately 2% of all soft tissue sarcomas.[4] The skin and subcutaneous tissue of the head and neck are the most commonly affected sites.[2,4] Almost always, metastatic lung involvement occurs.[4] Angiosarcoma is a rare malignant tumor, making it challenging for physicians to make a diagnosis. For an early diagnosis and better prognosis, a high level of suspicion is necessary. Angiosarcoma diagnosis requires a biopsy and immunohistochemical examinations. However, case-specific histological features may differ.[1,5] Angiosarcoma is characterized by abnormal, pleomorphic, cancerous endothelial cells. The morphology of these cells might be fusiform, polygonal, or spherical.[5] PET imaging can aid in the diagnosis, staging, monitoring, and follow-up of patients with angiosarcoma.[6] Numerous peripheral pulmonary nodules, a single mass with an adjacent alveolar pattern and/or varying degrees of consolidation, and ground glass opacity may be noticed on a typical radiograph.[7] However, a chest radiography or a CT scan cannot differentiate between epithelioid angiosarcoma of the lung and other pulmonary malignant neoplasms; therefore, the conclusive diagnosis is based on histological and immunohistochemical findings.[5,7] For patients with isolated lesions, surgery is the most effective treatment option. Due to the rarity of angiosarcoma, there is no specifically defined standard of care.[5] Symptoms of primary angiosarcoma include chest pain, hemoptysis, dyspnea, coughing, and weight loss. However, up to 20% of cases show no symptoms and are only detected at autopsies.[8]

Dyspnea, cough, and fever/chills are present in more than 80% of AEP patients. The majority of symptoms appear a few days after the acute onset.[9] Admission blood tests show elevated C-reactive protein and white blood cell counts. Only 30% have peripheral eosinophilia (>500/mm^3).[9,10] Because most AEP patients do not have peripheral eosinophilia, CT scans, and a comprehensive disease history are further clues to suspect AEP.[10] AEP patients often have significant respiratory failure, making pulmonary function tests impossible. Therefore, an AEP diagnosis requires BAL eosinophilia over 40% and a lymphocyte proportion of 10%–30%.[9,10] Transbronchial lung biopsy usually yields tissue eosinophilia; hence, surgery for lung

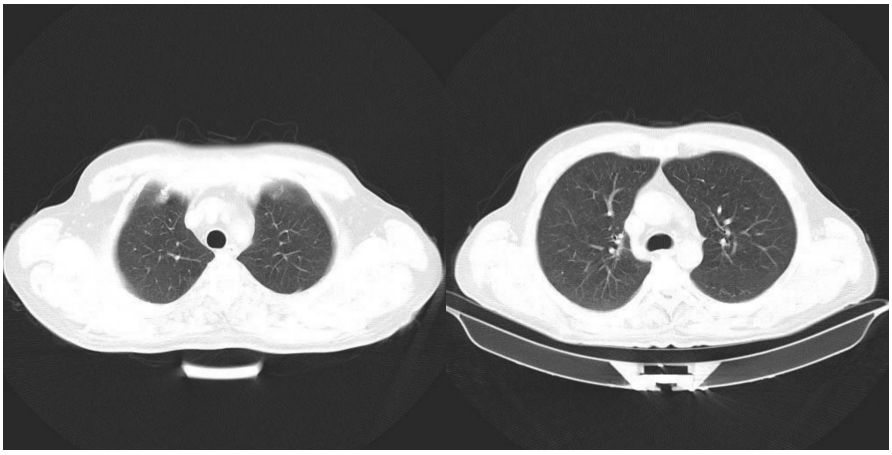

FIGURE 2 Chest CT scan after the prescription of methylprednisolone.

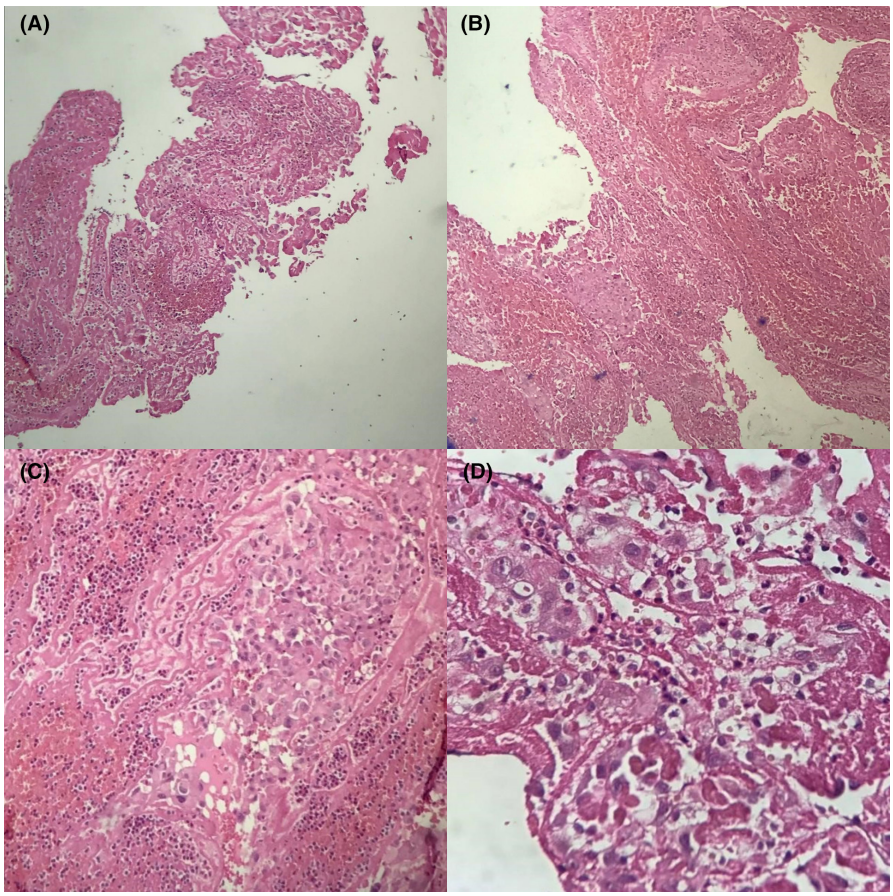

FIGURE 3 Sections of right shoulder soft tissues in magnification order (a = 4x, b = 40x, c = 400x, d = 1000x). Slides and sections show mainly blood clots with scattered clusters of atypical plump round to polygonal cells having large vesicular or hyperchoromatic nuclei, prominent nucleoli, and eosinophilic cytoplasm, focal intracytoplasmic lumen formation, and irregular vascular channels lined by atypical cells.

biopsy is rarely indicated. Histologically, AEP's interstitium and alveolar space have dense eosinophil accumulations.[11] Airway epithelial structures usually remain intact despite fibrin deposits, interstitial edema, and detached type II epithelial cells. However, diffuse alveolar destruction was reported in severe cases.[12] AEP patients typically have bilateral ground grass attenuations with consolidations on chest radiography. AEP can be diagnosed with the aid of high-resolution CT examinations. Previous HRCT studies of AEP patients reported that 70%–90% had interlobular septal thickening and almost all had bilateral ground glass attenuation in addition to bilateral pleural effusion in more than 90% of cases.[13] There are no official diagnostic criteria; however, the modified Philit criteria has been used for AEP diagnosis, which includes some clinical factors (length of fever and hypoxemia), radiologic findings (bilateral diffuse pulmonary infiltrates on chest radiography), paraclinical results (BAL fluid eosinophilia and/or infiltrations of eosinophils in the lung parenchyma on lung biopsy), and a lack of known causes of eosinophilic lung disease such as infection and drugs.[14,15] AEP patients often experience progressive respiratory failure or severe hypoxia; however, intravenous high-dose systemic corticosteroid therapy dramatically improves their condition within days.[14] Two weeks of steroid medication is usually enough, although no clinical trial has investigated this. However, Rhee et al.[9] retrospectively examined the effectiveness of 2 week and 4 week steroid treatments and identified no obvious differences in terms of clinical and radiographic remission.

Our patient was struggling with two rare and acute diseases at the same time; angiosarcoma and eosinophilic pneumonia. The initial pattern of eosinophilic pneumonia in our patient's lung led us to suspect that the cause of this pattern might be metastasis, but the history and clinical course of the patient, laboratory tests, biopsies, imaging, and the patient's remarkable response to corticosteroids eventually led us to the correct diagnosis, which was AEP. This emphasizes that we should analyze a patient's signs and symptoms as a whole rather than relying exclusively on a common pattern to diagnose the condition. This patient's rare carotid artery tumor was treated after a quick and accurate identification of angiosarcoma, a rare and severe disease. This instance indicates that thorough histological investigation and sample collection are needed to accurately diagnose this malignancy.

AUTHOR CONTRIBUTIONS

Elham Paraandavaji: Data curation; validation. **Homa Hadidi:** Writing – original draft. **Mahtab Norouzi:** Writing – original draft. **Mryam Azaddehghan:** Writing – original draft. **Mohadeseh Khodaparasti:** Data

curation; resources. **Sasan Shafiei:** Project administration; writing – review and editing. **Erfan Ghadirzadeh:** Conceptualization; writing – review and editing. **Seyyed Mojtaba Nekooghadam:** Investigation; project administration; resources; supervision. **Hanie Karimi:** Validation; writing – review and editing.

ACKNOWLEDGMENTS

None.

FUNDING INFORMATION

None.

CONFLICT OF INTEREST STATEMENT

None.

DATA AVAILABILITY STATEMENT

Availability of Data and Materials: The data are available with the correspondence author and can be reached on request.

CONSENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

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How to cite this article: Paraandavaji E, Hadidi H, Norouzi M, et al. Paraneoplastic acute eosinophilic pneumonia due to carotid angiosarcoma: A rare case. *Clin Case Rep*. 2023;11:e7348. doi:10.1002/ccr3.7348