Case Report

Case Report: Metastatic Dedifferentiated Liposarcoma Presenting as Hypereosinophilia in an Adolescent

Sadhana Balasubramanyam,1 Joud Hajjar1–3

1Baylor College of Medicine, Houston, TX, USA
2Texas Children’s Hospital, Houston, TX, USA
3William T. Shearer Center for Human Immunobiology, Houston, TX, USA

Address correspondence to Sadhana Balasubramanyam (sadhana.balasubramanyam@bcm.edu)

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ABSTRACT

Soft-tissue sarcomas associated with eosinophilia are rare, with limited cases reported in adults, and even fewer in the pediatric population. In this report, we highlight the importance of malignancy in the differential of hypereosinophilia in an adolescent. A 17-year-old boy presented with incidental findings of multiple bilateral pulmonary nodules on chest computed tomography (CT), and hypereosinophilia (absolute eosinophilic count [AEC] 7029 cells/mm³, hypereosinophilia defined as AEC >1500 cells/mm³). Lung biopsy showed high-grade metastatic sarcoma. A positron emission tomography–computed tomography (PET-CT) demonstrated a 7.9-cm mass in the left thigh, with biopsy revealing dedifferentiated liposarcoma. Subsequently, the patient was diagnosed with liposarcoma, with lung, mediastinal, and brain metastases. He completed six cycles of ifosfamide/doxorubicin, followed by surgical resection of primary thigh tumor and brain lesion. Given widely metastatic disease, he received palliative chemotherapy, and later transitioned to hospice. The patient died of respiratory failure from malignant pleural effusions. In conclusion, this case demonstrates the importance of having a broad differential for hypereosinophilia, including malignancy, to expedite the diagnosis and initiate appropriate management promptly.

Keywords: hypereosinophilia, sarcoma, paraneoplastic, pediatric

INTRODUCTION

Soft-tissue sarcomas associated with eosinophilia are rare, with limited cases reported in adults, and even fewer in the pediatric population. In this report, we highlight the importance of including malignancy in the differential of hypereosinophilia in children as well as adults.

CASE DESCRIPTION

A 17-year-old male with mild persistent asthma initially presented to the emergency room following a head trauma. His head imaging was normal. However, owing to intermittent cough, a chest X-ray was obtained, and he was found to have a 1.8-cm nodule in his left middle lung and a 1-cm nodule in the right lung base. Complete blood count (CBC) was notable for total white blood cell (WBC) of 22,000 cells/mm³ with 33% eosinophils, and absolute eosinophil count (AEC) 7029 cells/mm³ (Fig. 1). This laboratory abnormality prompted further work-up to characterize the incidental lung nodules. A computer tomography (CT) scan of the chest was obtained at an outside facility, showing multiple bilateral pulmonary nodules (largest 2.1 cm). Per Fleischner Society’s guidelines for evaluating small pulmonary nodules,[1] patient had follow-up imaging at 6 months (ideally should have been around 3 months per guidelines), showing enlargement of previous nodules by few millimeters, and appearance of new nodules as large as 3.3 cm in the left upper lobe (Fig. 2). At initial encounter, patient did not endorse any respiratory symptoms, weight loss, night sweats, fatigue, fever, or chills. He denied tuberculosis risk factors, sick contacts, recent travel, or smoking exposure. He denied family history of malignancy and other atopic diseases.

The patient was followed in our allergy and immunology clinic as a clinical patient, and not research subject, and all testing reported was performed on clinical basis, and consent form to obtain clinical testing was done when indicated.
RESULTS

Given findings of pulmonary nodules and eosinophilia, investigation of hypereosinophilia was initiated. An infectious workup was essentially unremarkable, including fungal serologies of Aspergillus antibody (Ab) and antigen (Ag), Blastomyces Ab, Cryptococcus Ag, Coccioidoides Ab, Histoplasmosis Ab and Ag and Toxoplasmosis Ab, parasitic serologies of Toxocara Ab, Strongyloides Ab, and Trichinella Ab, and stool ova and parasites. Bone marrow biopsy was negative for any evidence of malignancy, and flow cytometry of bone marrow aspirate did not have evidence of CD3+CD4+ T cells. Peripheral blood flow cytometry showed normal CD3, CD4, CD8, CD19, and CD56 subsets. Additional testing to evaluate for an underlying rheumatologic condition also came back negative, including normal antineutrophil cytoplasmic antibodies, antinuclear antibody, erythrocyte sedimentation rate, and C-reactive protein (Table 1). Bronchoscopy with bronchoalveolar lavage was performed showed no eosinophilia. Lung nodule biopsy revealed high-grade metastatic sarcoma with overexpression of murine double minute 2 homolog (MDM2). Positron emission tomography–computed tomography (PET-CT), demonstrated a 7.9-cm mass in the left posterior thigh with metastases to the brain, lungs, and mediastinum (Fig. 3). Biopsy of the thigh mass revealed dedifferentiated liposarcoma, confirming the primary tumor. Both biopsies were performed at Texas Children’s Hospital.

He underwent four cycles of ifosfamide/doxorubicin, followed by resection of the primary thigh tumor. In addition, he underwent craniotomy for resection of brain metastatic lesion, followed by gamma knife therapy. He completed two more cycles of ifosfamide/doxorubicin postsurgery to complete a six-cycle course, but unfortunately, he had persistent lung nodules on repeat imaging. Repeat wedge resection of the lung for diagnostic purposes, continued to show persistent disease, and he was started on pazopanib. Given MDM2 amplification of tumor, he was enrolled in a clinical trial with palbociclib with no response, so he was...

Figure 1.—Complete blood count trend from initial diagnosis through course of treatment. Abs, absolute; mets, metastases; WBC, white blood cells.

Figure 2.—Computed tomography chest scan showing multiple bilateral centrilobular pulmonary nodules with an elongated lesion in the left upper lobe suggesting mucoid impaction, measuring 3.3 cm (arrow).
switched to gemcitabine/docetaxel, and later switched back to pazopanib. Unfortunately, his disease continued to progress, and he developed malignant pleural effusions, requiring several hospitalizations. Patient and family eventually opted for home hospice. Patient met his demise secondary to increased tumor burden causing respiratory distress 18 months after diagnosis. See Table 2 for timeline of events.

DISCUSSION

Mild eosinophilia (defined as absolute eosinophil count AEC 500–1000 cells/mm³) is common and is caused by variety of conditions, including allergic disease, drug hypersensitivity, or parasitic infections. On the other hand, hypereosinophilia (AEC >1500 cells/mm³) is uncommon, which when present should prompt a thorough evaluation to identify the underlying cause, and to assess if there is evidence of eosinophil-induced end-organ damage.[2] Differential diagnoses for hypereosinophilia include myelodysplastic syndromes, leukemias, lymphomas, other hematologic or solid malignancies, immune disorders, and systemic mastocytosis, to name a few. In this particular patient, the mild persistent asthma alone does not sufficiently explain the extent of hypereosinophilia. Therefore, it was crucial to further investigate other causes that could contribute to this abnormal lab value. Malignancy workup should be initiated when initial history is not necessarily sufficient to point toward an obvious etiology of hypereosinophilia.

Paraneoplastic hypereosinophilia (hypereosinophilia associated with malignancy), is generally more common in hematologic malignancies, including Hodgkin’s lymphoma and leukemia,[3] and is rarely found in solid tumors and is usually associated with poor prognosis.[4] Some cases of hypereosinophilia have been noted in solid tumors through few case reports, including renal cell carcinoma, lung adenocarcinoma, and so on. Paraneoplastic syndromes themselves are very rare in patients with soft tissue sarcomas. Previous case reports review soft tissue sarcomas and its association with peripheral eosinophilia in adults, including 1 case report

| Test | Result |
|------|--------|
| Absolute eosinophilic count, cells/mm³ | 7029 ↑ |
| Total IgE, kU/L | 147 |
| CMP | Normal |
| ESR | Normal |
| FIP1L1/PDGFRα mutation | Normal |
| T-cell clonality test | Normal |
| B-cell clonality test | Normal |
| Tryptase level | Normal |
| Fungal serology | Normal |
| B12 level | Normal |
| Stool ova and parasites | Normal |
| Trichinella serology | Normal |
| Toxocara serology | Normal |
| Strongyloides serology | Normal |
| Troponin | < 0.01 |
| Bone marrow biopsy | Unremarkable |
| Cardiac echo | Normal |
| EKG | Sinus rhythm |
| PFTs | No obstructive/restrictive pattern |
| CT chest | Bilateral pulmonary nodules |
| CT abdomen/pelvis | 2 small splenic calcifications |
| Tissue biopsy | Left thigh: dedifferentiated high-grade sarcoma with overexpression of MDM2 |
| T cell CD3⁺CD4⁺, CD3⁺CD4⁻CD8⁻, and CD4⁺CD7⁻ | Normal |

↑, indicates critically high level; CMP, complete metabolic panel; ESR, erythrocyte sedimentation rate; FIP1L1 (factor interacting with PAPOLA and CPSF1); PDGFRA, platelet-derived growth factor receptor A; EKG, electrocardiogram; PFT, pulmonary function test; CT, computed tomography; MDM2, murine double minute 2 homolog

Figure 3.—Whole-body positron emission tomography demonstrating diffuse metastatic disease in the lungs, mediastinum, brain, and left femoral lymph nodes, with left popliteal mass.
describing eosinophilia that is present in an adult patient with spindle cell sarcoma, and another case describing eosinophilia in an adult with pleomorphic soft tissue sarcoma of the elbow.

The role of eosinophils in solid tumor progression remains yet to be well defined. Tumor cells themselves secrete cytokines that recruit eosinophils. These commonly tend to occur in areas of necrosis. Once eosinophils infiltrate the tumor tissue, their effector mechanism is not completely established. In some malignancies, such as colon cancer, there is evidence for a synergistic cytotoxic effect with eosinophils and tumor cells, through release of toxic cationic proteins, such as MBP, or increase in the release of chemotactic factors that leads to further recruitment of eosinophils.

Through this case, we display the finding of hyper-eosinophilia in an adolescent found to have metastatic dedifferentiated liposarcoma, initially presenting with multiple lung nodules. To the best of our knowledge, there are no reported cases of paraneoplastic eosinophilia in the pediatric population, especially in the context of soft tissue sarcomas. Given this is a clinical case description, one of our limitations of this study is elucidating the mechanism of eosinophilia in solid tumor progression. Although there are proposed ideas, as mentioned above, future experimental studies should be conducted to further explore the role of eosinophils in the tumor microenvironment. Defining the effector functions of eosinophils can potentially provide novel therapeutic options for cancers associated with eosinophilia.
Though rare in children, eosinophilia should always prompt a thorough evaluation of the underlying cause and assessment of end-organ damage. Without appropriate assessment, the root cause of hypereosinophilia might be missed, leading to adverse outcomes. Therefore, it is important to maintain a broad differential and investigate all causes of eosinophilia, including malignancy.

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