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Case report

Marked hypereosinophilia secondary to endometrioid ovarian cancer presenting with asthma symptoms, a case report

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ABSTRACT

Background: Hypereosinophilia (HE) is defined by the presence of >1.5 × 10^9/L eosinophils in the peripheral blood. Paraneoplastic HE has been reported in a number of solid and hematologic malignancies including ovarian cancer. We present a case with paraneoplastic HE in the setting of underlying endometrioid ovarian carcinoma.
Case presentation: An 88-year-old woman presented with cough, dyspnea and 20-pound unintentional weight loss of one month duration. Evaluation revealed peripheral hypereosinophilia (HE) with absolute eosinophil count of 15.38 × 10^9/L (53.8%) and an elevated exhaled nitric oxide at 172 parts per billion (normal < 39 PPB). Given the HE and unintentional weight loss, computed tomography (CT) scan was obtained and showed a pelvic mass. The patient underwent bilateral salpingo-ophorectomy with pathology consistent with endometrioid ovarian carcinoma. The patient experienced complete resolution of her cough, dyspnea, and peripheral eosinophilia following surgical resection.
Conclusion: This case highlights that solid malignancy should be considered in patients with marked HE.

1. Background

Peripheral eosinophilia and hypereosinophilia (HE) are defined by the presence of >0.5 × 10^9/L and >1.5 × 10^9/L eosinophils in the peripheral blood, respectively [1]. HE can occur in a variety of disorders ranging in severity from mild to life-threatening including allergic conditions; infections; autoimmune diseases; hematologic malignancies; and solid malignancies. It may also be idiopathic [1]. Paraneoplastic HE may occur in approximately 0.6–5% of all malignant tumors [2]. We present an 88-year-old woman with paraneoplastic HE presenting initially with cough and dyspnea who was ultimately found to have endometrioid ovarian carcinoma.

2. Case Presentation

An 88-year-old woman with history of hypertension and hyperlipidemia presented to our pulmonary outpatient clinic with a 1 month history of nonproductive cough and dyspnea. The patient's symptoms were associated with fatigue and unintentional weight loss of 20 pounds over the one-month period. She had been previously diagnosed with cough-variant asthma and had been treated with inhaled corticosteroids. Physical examination revealed widespread, high-pitched, expiratory wheezes. Laboratory evaluation revealed eosinophil-predominant leukocytosis with leukocyte count of 28.6 × 10^9/L (3.4–9.6 × 10^9/L) and eosinophil count of 15.38 × 10^9/L (0.01–0.08 × 10^9/L) which was a remarkable change from a normal complete blood count obtained one year prior. Pulmonary function testing showed normal baseline spirometry, lung volumes, diffusion capacity, and oxygen saturation at rest and during exercise. Methacholine challenge was negative. However, exhaled nitric oxide (eNO) was significantly elevated at 172 parts per billion (ppb) (normal < 39 ppb).

Further workup for eosinophilia showed negative anti-myeloperoxidase and anti-proteinase 3 antibody titers of <0.2U (<0.2U); normal immunoglobulin E titer of 18.9 kU/L (<213 kU/L); and tryptase level of 7.2 ng/mL (<11.5 ng/mL). Strongyloides serum IgG was undetectable. Bone marrow biopsy showed hypercellular bone marrow (80%) with marked bone marrow eosinophilia. Genetic studies including BCR/ABL1, KIT Asp816Val & JAK2 V617F gene mutation

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analysis, florescent in situ hybridization (FISH) for CHIC2 (4q12) deletion, FGFR1 (8p11.2) rearrangement and PDGFRB/TEL translocation [5, 12] were all negative.

Contrast-enhanced computed tomography scan of the chest, abdomen, and pelvis showed a large necrotic pelvic mass with coarse calcification measuring 11.5x13.3 × 10.4 cm with associated right pyelocaliectasis (Fig. 1).

Ultimately, the patient underwent hysterectomy with bilateral salpingo-ophorectomy. Pathology showed ovarian endometrioid carcinoma with negative surgical margins and no involvement of other pelvic organs consistent with stage II disease (Fig. 2).

Twenty 4 h following the surgery, her eosinophil count normalized. On subsequent follow-up, she also reported resolution of her cough and dyspnea and continued to have normal eosinophil counts.

3. Discussion and conclusions

Hypereosinophilia (HE) is defined as an absolute eosinophil count of $\geq 1.5 \times 10^9$/L confirmed on two occasions one month apart and/or histologically proven tissue involvement by HE [1]. Definition of tissue HE includes bone marrow involvement with greater than 20% eosinophils of all nucleated cells; extensive tissue infiltration by eosinophils reviewed by an expert pathologist; or extensive deposition of eosinophil-derived proteins even in the absence of eosinophilic infiltration [1]. When HE is associated with eosinophil-mediated organ damage, the term hypereosinophilic syndrome is used.

The underlying etiology of hypereosinophilia (HE) can be broadly placed into 3 categories: reactive or "secondary"; clonal and idiopathic. Reactive or "secondary" eosinophilia results in polyclonal expansion of eosinophils from overproduction of eosinophilopoietic cytokines such as interleukin-5 [3,4].

Paraneoplastic reactive eosinophilia has been reported in both hematologic and solid malignancies including ovarian [5,6], bronchial [3, 7], gastrointestinal [2,8], hepatic [9], renal [10] and thyroid [11] cancers, in addition to sarcoma [12]. Although pulmonary involvement can be seen in up to 25% of patients with HE and hypereosinophilic syndrome, asthma symptoms are uncommon [13–16]. In their study, Dulohery et al. reported that only 12% of patients with pulmonary involvement had a new diagnosis of asthma at presentation with HE [16].

Although reported before, the paraneoplastic eosinophilia in this case is unique in multiple aspects. First, our patient had underlying endometrioid ovarian cancer which has not been previously reported to cause paraneoplastic HE. Moreover, this case also serves as a reminder that although eosinophilia can be seen in asthma, persistent eosinophilia and HE should prompt the search for causes of reactive HE including underlying malignancy in appropriate patients. Lastly, this case highlights the fact that management of the underlying etiology of HE can lead to rapid resolution of eosinophilia, and potentially, resolution of asthma symptoms.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Included.

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to patient's privacy concerns but are available from the corresponding author on reasonable request.

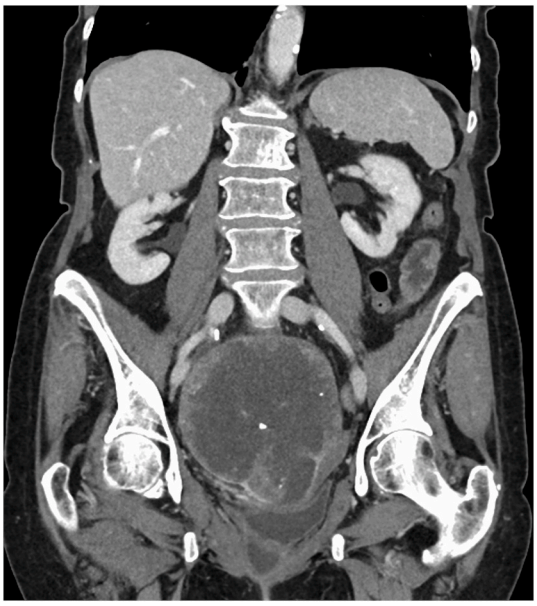

Fig. 1. Contrast-enhanced pelvic computed tomography scan showing a large necrotic pelvic mass with coarse calcifications.

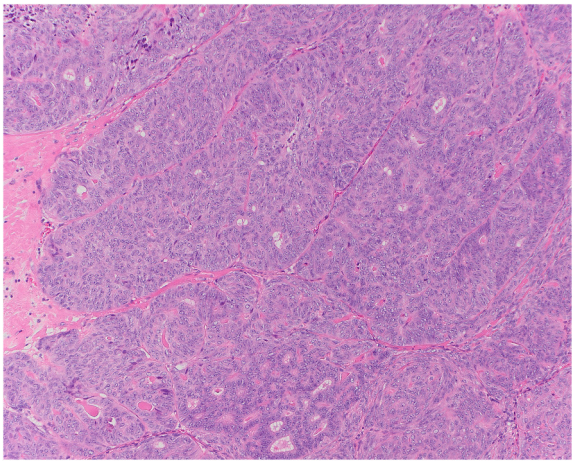

Fig. 2. Microscopic examination of the surgically excised mass showing findings consistent with low-grade endometrioid ovarian carcinoma.

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Authors' contributions

Conception and design: HA, AM, HA, VI; acquisition and analysis of data: HA, AM, HA, YA, VI; interpretation of data: HA, AM, HA, VI; drafting the manuscript: HA, AM, HA, YA, VI; substantial revision: HA, AM, HA, YA, VI.

Declaration of competing interest

The authors declare that they have no competing or conflicting interests.

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none.

List of abbreviations

HE	Hypereosinophilia
CT	computed tomography
eNO	exhaled nitric oxide
ppb	parts per billion
FISH	florescent in situ hybridization

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