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

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1. Background

Peripheral eosinophilia and hypereosinophilia (HE) are defined by the presence of $>0.5 \times 10^9/L$ and $>1.5 \times 10^9/L$ 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 eosinophilic count of 15.38 $\times 10^9/L$ (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-oophorectomy 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.
analysis, fluorescent 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 11.5×13.3 × 10.4 cm with associated right pyelocaliectasis (Fig. 1).

Ultimately, the patient underwent hysterectomy with bilateral salpingo-oophorectomy. 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 eosinophil 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.

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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

| Abbreviation | Description |
|--------------|-------------|
| HE           | Hypereosinophilia |
| CT           | computed tomography |
| eNO          | exhaled nitric oxide |
| ppb          | parts per billion |
| FISH         | fluorescent in situ hybridization |

References

[1] P. Valent, A.D. Klion, H.-P. Horny, F. Roufosse, J. Geiß, P.F. Weller, et al., Contemporary consensus proposal on criteria and classification of eosinophilic disorders and related syndromes, J. Allergy Clin. Immunol. 130 (3) (2012), 607-612 e9.
[2] Z.G. Fridlender, M. Shalit, H.-U. Simon, Metastatic carcinoma presenting with concomitant eosinophilia and thromboembolism, Am. J. Med. Sci. 326 (2) (2003) 98–101.
[3] M. Watanebe, K. Ono, Y. Ozeki, S. Tanaka, S. Aida, Y. Okuno, Production of granulocyte—macrophage colony-stimulating factor in a patient with metastatic chest wall large cell carcinoma, Jpn. J. Clin. Oncol. 28 (9) (1998) 559–562.
[4] A. Tefferi, M.M. Patnaik, A. Pardanani, Eosinophilia: secondary, clonal and idiopathic, Br. J. Haematol. 133 (5) (2006) 468–492.
[5] R.I. Larsen, N.M. Savage, How I investigate eosinophilia, Int. J. Lit. Humanit. 41 (2) (2019) 153–161.
[6] S. Sakkal, S. Miller, V. Apostolopoulos, K. Nurgali, Eosinophils in cancer: favourable or unfavourable? Curr. Med. Chem. 23 (7) (2016) 650–666.
[7] G. Manelis, D. Aderka, [Eosinophilia associated with malignant tumors of the bronchus and stomach], Harefuah 90 (5) (1976) 213–215.
[8] G.K. Anagnostopoulos, G.H. Sakorafas, P. Kostopoulos, G. Marganitinis, S. Tsikos, E. Terpas, et al., Disseminated colon cancer with severe peripheral blood eosinophilia and elevated serum levels of interleukine-2, interleukine-3, interleukine-5, and GM-CSF, J. Surg. Oncol. 89 (4) (2005) 273–275.
[9] A. Balian, E. Bonte, S. Naveau, A. Foussat, L. Bouchet-Delbos, D. Berrebi, et al., Intratumoral production of interleukin-5 leading to paraneoplastic peripheral eosinophilia in hepatocellular carcinoma, J. Hepatol. 34 (2) (2001) 355–356.
[10] D.A. Kruse, K.L. Bailey, Paraneoplastic Hypereosinophilia Presenting with Non-allergic Asthma and Rhinitis. B45 OBSTRUCTIVE LUNG DISEASE: INTERESTING CASES, American Thoracic Society, 2016 p. A3590-A.
[11] J. Feffer, M. Aziz, R. Schulman, Paraneoplastic hypereosinophilia and neutrophilia due to anaplastic thyroid carcinoma, Endocr. Pract. 22 (2016) 294.
[12] J. Ando, K. Sugimoto, K. Tamayose, M. Ando, Y. Kojima, K. Oshimi, Cytokine-producing sarcoma mimics eosinophilic leukaemia, Eur. J. Haematol. 78 (2) (2007) 169–170.
[13] C.J. Spry, The hypereosinophilic syndrome: clinical features, laboratory findings and treatment, Allergy 37 (8) (1982) 539–551.
[14] C.J. Spry, J. Davies, P.C. Tai, E.G. Olsen, C.M. Oakley, J.F. Goodwin, Clinical features of fifteen patients with the hypereosinophilic syndrome, Q. J. Med. 52 (205) (1983) 1–22.
[15] P.U. Ogbogu, B.S. Bochner, J.H. Butterfield, G.J. Gleich, J. Huss-Marp, J.E. Kahn, et al., Hypereosinophilic syndrome: a multicenter, retrospective analysis of clinical characteristics and response to therapy, J. Allergy Clin. Immunol. 124 (6) (2009) 1319–1325 e3.
[16] M.M. Dulohery, R.R. Patel, F. Schneider, J.H. Ryu, Lung involvement in hypereosinophilic syndromes, Respir. Med. 105 (1) (2011) 114–121.