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CLINICAL FEATURE
CASE REPORT

Eosinophilia as the presenting sign in pancreatic cancer: an extremely rare occurrence

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ABSTRACT

A case of pancreatic adenocarcinoma diagnosed following work up for eosinophilia is reported. A 68-year-old female was referred to our Hematology clinic for an absolute eosinophil count of 1869 per microliter. No allergic signs or symptoms were reported. Laboratory studies for parasitic infestations autoimmune disease and collagen vascular disease were negative. Computed tomography of the abdomen revealed a mass in the neck of the pancreas with fine needle aspiration biopsy consistent with adenocarcinoma. The patient received one cycle of modified FOLFIRINOX with complete resolution of the eosinophilia. There are rare case reports of tumor-associated blood eosinophilia in solid malignancies. The finding may be indicative of rapid disease progression and poor prognosis. Our case is the third in published English literature with eosinophilia being the initial finding in pancreatic cancer.

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1. Introduction

Pancreatic cancer is the fourth leading cause of cancer mortality being responsible for about 7% of all cancer-related deaths [1]. The presenting signs and symptoms are often vague and non-specific. Symptoms include weight loss, fatigue, anorexia, and nausea. In addition, signs such as obstructive jaundice and migratory thrombophlebitis may be present. Eosinophilia is an extremely rare presenting feature of the disease. We describe the third such case in English literature and the first one as eosinophilia being the sole initial presentation of the disease.

2. Case

A 68-year-old female was referred to our Hematology clinic in August 2015 for evaluation of eosinophilia on routine blood work. Her laboratory studies from June 2015 showed a total leukocyte count of $10.5 \times 10^9/L$ with an absolute eosinophil count of 1869/mL. Her hemoglobin concentration was 14.4 g/dL, hematocrit 41.3%, and platelet count was $246 \times 10^9/L$. On review of her records, she had eosinophilia dating back to 2014 when her absolute eosinophil count was 1630. She denied having fever, night sweats, or chills. She had intentional weight loss and her appetite had remained well. Over the previous two weeks, she had experienced episodes of diarrhea associated with epigastric discomfort.

The patient had a history of frequent travel outside the United States, with recent travel to the Caribbean Islands and Europe. She did swimming and snorkeling. She denied any allergic symptoms such as wheezing, pruritus, or rhinosinusitis.

However, she reported allergy to penicillin since childhood. Her past medical history was significant for diabetes mellitus, hypothyroidism, hypertension, hypercholesterolemia, and peripheral vascular disease. Her past surgical history included a carotid endarterectomy, hysterectomy, thyroidectomy for a benign tumor, and hemorrhoidectomy. The medications she was taking were clopidogrel, paroxetine, levothyroxine, valsartan, metoprolol, simvastatin, aspirin, sitagliptin, metformin, calcium, a multivitamin supplement, and omega-3 fish oil.

She smoked cigarettes with a 48-pack-year history of smoking. The patient's physical examination was normal. No jaundice, anemia, lymphadenopathy, or hepatosplenomegaly were appreciated.

The patient's repeat complete blood count showed a leukocyte count of $10.92 \times 10^9/L$, with 62% neutrophils, 6% monocytes, 20% lymphocytes, and 12.3% eosinophils with an absolute eosinophil count of 1340. We did work-up for parasitic infestations including testing for *Strongyloides*, *Trypanosoma*, *Trichinella*, and *Schistosoma*, which were all reported negative. Breakpoint Cluster Region-Abelson was not detected. Antinuclear antibody was negative. She was also found to be negative for deletion at 4q12 and for fusion of FIP1L1 and platelet-derived growth factor receptor alpha genes.

A few weeks later, the patient returned for a follow-up and an abdominal computed tomography scan was done (Figure 1) because of intermittent epigastric discomfort. The CT scan showed an ill-defined mass in the neck of the pancreas measuring $2.9 \times 2.5 \times 2.7$ cm with pancreatic ductal dilatation, subcentimeter peripancreatic lymph nodes with encasement and obstruction of the splenic and superior mesenteric arteries (SMA), and extensive varices in the upper abdomen.

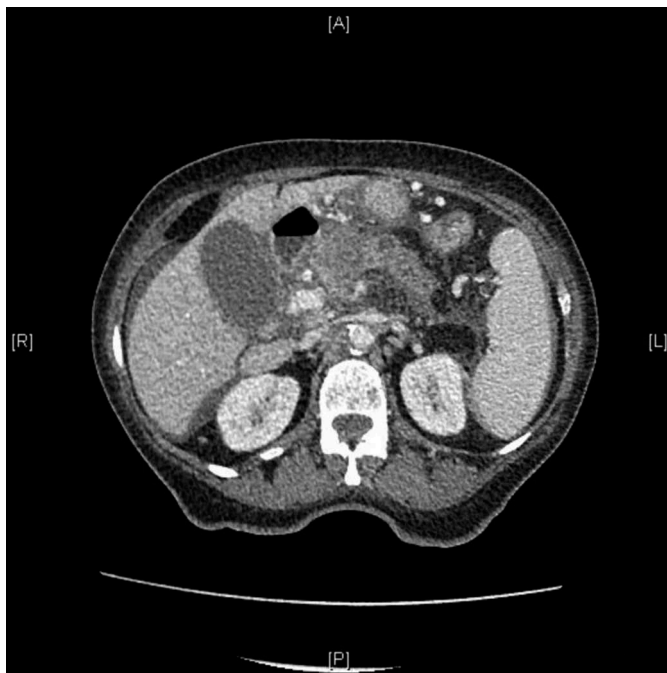


Figure 1. Abdominal CT scan.

Endoscopic ultrasound with fine-needle aspiration biopsy was consistent with adenocarcinoma. Work-up for distant metastatic disease was negative. CA 19-9 was 232 units/mL. Her disease was characterized as clinic Stage III (T4, N0, M0). Based on the surgical oncologist's evaluation, the patient's tumor was deemed borderline resectable since it was encasing the SMA and a decision to administer neoadjuvant chemotherapy was made. The patient, thus far, has received one cycle of FOLFIRINOX (Leucovorin, Fluorouracil, Irinotecan, Oxaliplatin). After completion of the first cycle of chemotherapy, the patient's absolute eosinophil count trended downwards toward being zero at the time of this publication.

3. Discussion

Eosinophilia is characteristically seen with allergic diseases, parasitic infestations, collagen vascular diseases, and certain skin disorders. Tumor-associated blood eosinophilia (TABE) is rare occurring in about 0.5% of malignancies [2] with the onset usually being late when the disease is often widespread [3]. Eosinophilia has been described in cases of squamous cell carcinoma of the skin, head and neck cancer, penile cancer, lymphoma of the gastrointestinal tract, and cancer of the bladder [4–8]. Three cases of eosinophilia in patients with chromophobe renal cell carcinoma have been described by *Yong-Bao Wei et al.* [9]. Review of reported cases suggests that TABE may portend a more aggressive disease course and poor prognosis [10].

As described by *Yong-Bao Wei et al.*, in cases of renal cell carcinoma, peripheral blood eosinophilia may disappear following treatment for the malignancy. A similar finding is observed in our patient wherein only after the first cycle of chemotherapy, the absolute eosinophil count declined to zero and has remained within the normal range to date.

Several theories have been proposed as to the mechanism of tumor-associated blood eosinophilia. Colony-stimulating factors have been detected in serum and tumor extracts of patient's with malignancy and eosinophilia [11]. Other propositions include tumor necrosis promoting an increase in eosinophils as well as seeding of metastatic neoplastic cells to the bone marrow resulting in stimulation of eosinophil production [12]. Cytokines such as interleukin-3, interleukin-5, and granulocyte-macrophage colony stimulating factor (GM-CSF) also seem to play a role [13,14]. *Pandit et al.* report a case of non-small cell lung cancer with eosinophilia and excessive levels of interleukin-3 [15]. Similarly, *Vassilatou E et al.* report a case of papillary thyroid cancer with elevated levels of GM-CSF, eosinophilia, and neutrophilia [16]. *Anagnostopoulos GK et al.* report a case of metastatic colon cancer and eosinophilia with elevated levels of interleukins 2, 3, and GM-CSF [3].

As suggested in the literature cited, interplay of factors such as GM-CSF and IL-3 would potentially affect other cell lines also in addition to eosinophils. However, this was not the case in our patient. None of the other cell lines including granulocytes, lymphocytes, or monocytes were increased. This finding suggests that the driving force behind isolated eosinophilia may occur because of dysregulation of IL-5 gene expression in pancreatic cancer and manifesting itself with tissue eosinophilia as well as causing a rise of these cells in the peripheral circulation [17].

In terms of management of the disease in our patient, the tumor was deemed borderline resectable based on the imaging studies since it was encasing and obstructing the SMA. Hence, a decision for neoadjuvant chemotherapy was made. Current literature suggests that about one-third of patients who initially have borderline resectable pancreatic tumors may undergo successful resection following neoadjuvant chemotherapy [18]. In a propensity score matched analysis by *Mokdad et al.*, 8020 patients with early-stage resectable pancreatic cancer were identified and treatment strategy of neoadjuvant therapy (NAT) followed by resection (2005 patients) versus upfront resection (6015 patients) was compared. The NAT group was associated with improved survival compared with upfront resection (median survival, 26 vs. 21 months, respectively, $P < .01$) [19]. These results appear promising in patients for whom the surgeon may feel that R0 resection may not be possible upfront as was the case with our patient.

4. Conclusion

Rare cases of eosinophilia in solid malignancies have been reported. Its role in the stage and prognosis of disease needs to be further elucidated. The presence of various cytokines and stimulating factors indicates interplay between the immune system and various cancers. An in-depth study of the tumor biology and interaction of the immune system in these and future cases may lead to a better understanding of the role of this finding in terms of diagnosis, tumor aggressiveness, and prognosis of disease.

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Declaration of interest

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