Eosinophilia in a patient with lung adenocarcinoma - a case study

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Abstract

Eosinophilia, or an elevated eosinophil count in peripheral blood, is frequently seen in people with allergic reactions and parasitic infections. However, its occurrence in patients with solid tumors is relatively low. Full blood count analysis of an 86 year old patient revealed a marked eosinophilia of 42.3 x 10^9/L, who had previously been diagnosed with lung adenocarcinoma with metastasis into bone marrow and lymph nodes. It is suggested by studies that over-expression of cytokines, namely granulocyte-macrophage colony-stimulating factor (GM-CSF) and interleukin-5 (IL-5) could be involved in the process of eosinophilia development, due to their direct effects on eosinophils. Cytokine production by tumor cells, tumor necrosis and metastasis into bone marrow are considered to be the main causes of eosinophilia in patients with cancers.

Key words: eosinophilia, lung adenocarcinoma, granulocyte-macrophage colony-stimulating factor, interleukin-5.


Introduction

The eosinophil is a type of granulocyte and usually accounts for a very small proportion of total white cell count in peripheral blood. In our laboratory, an absolute eosinophil count of greater than 2.0 × 10^9/L is defined as marked eosinophilia. Eosinophilia, particularly marked eosinophilia, is a phenomenon commonly associated with allergy, parasitic infestations and drug hypersensitivities, but rarely linked to pre-existing solid tumors. We present here a case of a patient diagnosed with lung adenocarcinoma who then developed marked eosinophilia.

Case report

In July 2010, Mrs H, an 86 year old female, had her routine check-up performed at a rest home and blood samples were also taken. The full blood count analysis revealed remarkable abnormalities, including a haemoglobin (Hb) of 65 g/L (reference range: 115-155 g/L), mean cell volume (MCV) of 115 fl (reference range: 81-98 fl), platelet count of 48 x 10^9/L (reference range: 150-430 x 10^9/L) and a total white cell count of 61.3 x 10^9/L (reference range: 4.0-11.0 x 10^9/L). The DIFF scattergram from the XE2100 analyser contained a large grey-out area where the population of eosinophils normally locates (Figure 1). The analyser stated that 93% of the white cells were eosinophils. A blood film was then made to perform a manual white cell differential and examine cellular morphology. Sixty-nine percent of the white cells were identified as eosinophils, giving an absolute eosinophil count of 42.3 x 10^9/L. As shown in Figure 2, a proportion of the eosinophils appeared hypogranular. There was a left shift of neutrophils which also had features of toxic change. Moreover, occasional metamyelocytes and nucleated red blood cells were also noted.

The patient presented in the Emergency Department four hours later and similar full blood count results were obtained, where eosinophils accounted for 46% of the total white cell count. It was also found that the patient had an elevated Troponin T result and deteriorating renal function. The blood film was then reviewed by a haematologist who commented that it was consistent with secondary eosinophilia and leukamoid reaction, whilst bone marrow infiltration might also be involved. After her admission into the ward, she was transfused with two units of red cells and given prednisolone.

Further research on the patient revealed that Mrs H had pernicious anaemia since the age of 30. Since late 2007, the patient had developed mild macrocytic anaemia with a borderline low platelet count. In early 2009, she was diagnosed with malignant neoplasm of the lung, specifically adenocarcinoma of her right lung, using bronchoscopy and treated with radiotherapy. Three months later, Mrs H developed an episode of stroke. During her hospital admission, secondary neoplasm of lymph nodes, bone and bone marrow, mainly in the left pelvis, was confirmed which was then followed by another course of radiotherapy. Over the following years, she had several top-up transfusions and developed moderate thrombocytopenia of 80-100 x 10^9/L. Until the presentation of this event, an elevated white cell count (22.7-36.3 x 10^9/L) and eosinophilia ranging from 14% to 36% were frequent findings in her blood count.
Discussion
Eosinophilia in peripheral blood is often seen in individuals with allergy, parasitic infection, eosinophilic leukaemia and hyper eosinophilic syndrome (1-4). The persistence of eosinophilia for an extended period of time can cause damage to various body tissues, mainly due to release of the contents of cytoplasmic granules in eosinophils (4). As a result, some eosinophils may appear degranulated or even agranular in the blood film (5). However, the occurrence of eosinophilia in people with solid tumors is low (3).

Several studies suggest that a number of cytokines are involved in the development of blood hyper eosinophilia in cancer patients, particularly interleukin-5 (IL-5) and granulocyte-macrophage colony-stimulating factor (GM-CSF) (1-3,6,7). Both cytokines play an important role in the production, activation and survival of eosinophils in the bone marrow and peripheral blood, as well as the enhancement of cellular functions of eosinophils in peripheral circulation (6,7).

GM-CSF is a growth factor that stimulates the development of myeloid cells, or myelopoiesis, via its receptors, and is synthesized mainly by stromal cells in the bone marrow (8). As an alternative source of GM-CSF in some lung cancer patients, its secretion by tumor cells has also been detected (1, 2, 8). Subsequently, proliferation of white cells is stimulated by exogenous GM-CSF resulting in leukocytosis as well as eosinophilia (1,7). IL-5, a cytokine normally produced by T cells, acts specifically on eosinophilic cell lineage allowing its activation (3,7). Additionally, the presence of IL-5 enhances cytotoxic function of the eosinophils against tumor cells in cancer patient (3).

Three major factors are thought to be responsible for the development of eosinophilia in patients with known cancers with or without metastasis (3). Locally produced active cytokines by tumor cells have direct effects on eosinophils and their functions (1,3). Tumor necrosis, as a result of treatment for cancers, such as radiotherapy, can lead to eosinophilia (3). It is usually a poor prognosis indicating possible persistence of tumor after treatment (9). Metastasis from the primary tumor, especially into bone marrow, results in bone marrow stimulation mediated by various cytokines and thus, eosinophilia in the peripheral circulation (3). For our patient, all theories above could be accountable.

Bone marrow aspirate is of limited use for differentiating between eosinophilia due to chronic eosinophilic leukaemia and paraneoplastic syndrome, relating to the underlying malignancy, since the hypercellular feature is common to both conditions. However, a measurement of GM-CSF level by immunoassay in pleural fluid in patients with lung cancer is valuable (1). Intracellular IL-5 in tumor cells determined by immunohistochemistry may also be used as a supplementary test (3). On the other hand, a chromosomal abnormality or molecular mutation is often one of the major findings in cases of chronic eosinophilic leukaemia (4). Unfortunately, our patient passed away two days after admission and no further analysis was carried out.

Conclusion
Besides the common eosinophilia occurring during allergic reactions and parasitic manifestations, it is likely that some patients with solid tumors will develop eosinophilia as one of the paraneoplastic syndromes, which is mediated by the actions of cytokines, especially when treatment-related tumor necrosis and/or metastasis into bone marrow have also been confirmed.

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References

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TWENTY FOURTH ANNUAL NICE WEEKEND
17—19 May 2013
Bayview Wairakei Resort

The 24th National Immunohaematology Continuing Education (NICE) weekend was held 17th to 19th of May at the Bayview Wairakei Resort in Taupo. All attendees at NICE are required to give a two – five minute presentation or prepare a poster. NICE provides a supportive atmosphere for those who are not so familiar or comfortable with presenting to “give it a go”, while being able to learn from the more seasoned presenters amongst us. It is also a great way to network and catch up with our fellow transfusion science colleagues.

Over the weekend we were treated to 47 fantastic presentations and were able to view and discuss 11 poster presentations. All presenters did a fantastic job. The general consensus was that the standard of presentations delivered over the weekend was very high and a wide variety of presentation topics were covered.

Congratulations to all our attendees who took away awards for their presentations/poster:

- The Abbot Award for Best Overall Presenter went to Jared Pratt (Pathlab BOP) for his talk — I can feel it in my bones
- The Ortho Clinical Diagnostics Award for Most Promising Transfusion Scientist went to Abby Clayton (NZBS Wellington) for her talk on her MSc Research Project — Comparison of Methods to Assess Postpartum Haemorrhage in Rh (D) Negative Women
- The Pharmaco Award for Best Poster went to Alexandra Shafer (NZBS Auckland) for her poster Transfusion Support of a Malaria Patient
- The bioCSL award for a New Zealand attendee to attend NICE Australia was this year won by Eamon Karalus (T-Lab Ltd Gisborne)
- The NZIMLS Award for the Best First Time Speaker — a presenter who has never attended NICE weekend before, giving them the title of NICEst Virgin. This went to Sandya Arunachalam (AUT Student) for her talk explaining the relationship between Blood Group Antigens and Infectious Disease

A huge thank you on behalf of all must be extended to our amazing NICE Convenors – Grace Agustin and Raewyn Cameron. These ladies delivered another spectacular educational weekend. So on behalf of the TSSIG and the wider NICE group I would like to extend a huge Thank You. We look forward to celebrating our 25th Weekend with a silver birthday bash on the 23-25th May 2014.

Prizewinners: Eamon Karalus (NICE Australia winner), Jared Pratt (Best Presentation), Alex Shafer (Best Poster), Sandya Arunachalam (NICEst Virgin)

Absent: Abby Clayton (Most Promising Transfusion Scientist)

Melissa May
The Haematology SIG meeting was held 2nd March 2013 in the Napier War Memorial Conference Centre. There were 49 registered delegates with 26 attending the dinner at the Scenic Hotel Te Pania following the meeting.

There was a full and varied scientific programme incorporating all aspects of haematology, coagulation and transfusion medicine. Topics ranged from case studies through to method reviews and in-house studies. Dr Elayne Knottenbelt (Consultant Haematologist, Midcentral DHB) also presented a comprehensive morphology review of haematological emergencies.

The Best Overall Presenter award was won by Jacquie Case (Middlemore Hospital) who presented an interesting case study about malaria and the use of ICT cards.

There has been an amendment to the Best First Time Presenter award initially announced on the day. This has now been awarded to Joanna Mucznik (Pathlab Hamilton) who presented on the problems associated with platelet clumping and estimation.

It was challenging to be able to fill the programme with enough advance notice to enable the programme to appear on the NZIMLS website. Many laboratories were unable to attend and/or present for a variety of reasons. However, the feedback has been positive and the facilities provided by the Napier War Memorial Conference Centre were to a high standard. The dinner went well and the food was excellent.

I would like to again thank the sponsors – Bio-Rad Laboratories, Stago, Siemens, Beckman Coulter, Roche and the NZIMLS.

The convener for the next Haematology SIG meeting is to be decided.

Sarah Hardingham
Haematology SIG Convener 2013