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Case Report

Epinephrine induced leucocytosis in a non-infective exacerbation of asthma

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Key Learning Points
- A marked leucocytosis can occur in response to iatrogenic epinephrine.
- In the absence of clinical findings to suggest an infective process, consider other causes for leucocytosis.

Abstract
In life-threatening cases of Acute Asthma the administration of epinephrine may be given as part of the initial management by paramedics. Concurrent infection is a frequent precipitant of an asthma exacerbation and consequently a leucocytosis is often found in such a situation. This case illustrates that marked leucocytosis can occur without an underlying infective process following epinphrine use.

Keywords
Asthma; Epinephrine; Iatrogenic; Leucocytosis; Neutrophilia.

Case study
A 41 year old Caucasian woman with a history of asthma presented via blue-light ambulance to the Medical Assessment Unit (MAU), following an episode of severe acute dyspnoea, wheeze and chest tightness. She had no recent history of cough, sputum production, fevers or rigors.

The paramedic team made a diagnosis of life threatening asthma. She was given oxygen, salbutamol and ipratropium bromide nebulisers and 0.5mg intramuscular epinephrine, in line with UK Resuscitation Council guidelines.[1]

Her usual medication included montelukast, symbicort 100/6 and salbutamol inhalers. There was no other significant past medical history. She smoked 15 to 20 cigarettes per day. She had not received any recent corticosteroids or antibiotics.

On arrival in MAU, she was comfortable and not dyspnoeic. On examination she was afebrile with a blood pressure of 128/58, heart rate of 84, respiratory rate of 20 and oxygen saturation of 98% while breathing room air. Chest auscultation revealed good air entry bilaterally and no wheeze. Specifically there were no clinical signs of anaphylaxis and no evidence of infection.

Initial blood tests revealed a total white cell count of 35.5, neutrophil count of 27.8, lymphocyte count of 5.8 and eosinophil count of 0.1 (Figure 1) The results were confirmed as genuine by the Haematologists and blood films were unremarkable. Her C-reactive protein (CRP) was <5. Renal and liver function was normal. Chest radiograph was entirely normal, other than ECG electrode stickers and a cosmetic piercing (Figure 2).

In view of the apparent severity of her initial presentation she was observed in hospital overnight so that further bronchodilator treatment could be given if required; however given the resolution of her symptoms no antibiotics, anti-inflammatory drugs or steroids were given, despite the marked neutrophilia.

She remained entirely well overnight and did not develop any further dyspnoea or wheeze. A repeat blood test the following morning (18 hours after admission) showed normalisation with a white cell count of 8.0, neutrophils of 4.0, lymphocytes of 3.3 and eosinophils of 0.2.

She was discharged home with a diagnosis of acute non-infective exacerbation of asthma with epinephrine induced leucocytosis.

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	On admission	Prior to discharge (18hrs later)	Normal values
White cell count ($\times 10^9$/L)	35.5	8.0	4 – 11
Neutrophils ($\times 10^9$/L)	27.8	4.0	2.0 - 7.5
Lymphocytes ($\times 10^9$/L)	5.8	3.3	1.3 – 3.5
Eosinophils ($\times 10^9$/L)	0.1	0.2	0.04-0.44

Figure 1. Differential white cell count on admission and 18 hours later at discharge.

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Figure 2. Chest radiograph of the patient on admission.

Discussion

Epinephrine is known to produce an acute neutrophilia. Studies on humans have demonstrated a leucocytosis following intramuscular administration of epinephrine.[2-3] A biphasic leukocyte response has been described, characterised by an initial rise in neutrophils, lymphocytes and eosinophils.[4] The neutrophilia then persists for several hours, while lymphocyte and eosinophil numbers rapidly normalise.[4]

Under normal physiological conditions, a marginal pool of leucocytes exists which adheres to vascular endothelium.[5] These leucocytes can be rapidly released into the circulating pool by a range of stimuli, including epinephrine.[6] There are several hypotheses regarding how epinephrine produces this effect. One suggestion is that the increased blood flow caused by activation of the sympathetic nervous system, especially in the pulmonary vasculature, leads to the mechanical demargination of these intravascular, non-circulating leucocytes.[7-9] Alternatively, this mobilisation could be explained by a humoral event which reduces the adherence of leucocytes to endothelial walls.[10] Lymph glands are also known to contract in response to epinephrine, which is likely to increase the circulating number of lymphocytes.[9]

This case should remind physicians of the need to consider causes other than infection when a marked neutrophilia is identified on initial blood testing. Although bacterial infection is the most common cause of this abnormality, the absence of clinical or radiological signs of pneumonia in this case, combined with the normal CRP led the clinical team to suspect that adrenaline administration was the likely cause.. The rapid resolution of the neutrophilia without the administration of any specific treatment re-inforces this view. Although antibiotics should not be withheld in cases where severe sepsis is considered likely, this decision should never be based entirely on the results of the full blood count.

References

1. Resuscitation Council UK. Medical Emergencies and Resuscitation. 2006 (revised may 2008), appendix ii
2. Steel CM, French EB, Aitchison WRC. Studies on adrenaline-induced leucocytosis in normal man. I. The role of the spleen and of the thoracic duct. *Br J Haematol*. 1971; **21**: 413–422.
3. Burns AM, Keogan M, Donaldson M *et al*. Effects of inotropes on human leukocyte numbers, neutrophil function and lymphocyte subtypes. *Br J Anaesth*. 1997; **78**: 530–535.
4. Samuels AJ. Primary and secondary leukocyte changes following the intramuscular injection of epinephrine hydrochloride. *J Clin Invest*. 1951; **30**: 941.
5. Harlan JM. Leukocyte-endothelial interactions. *Blood*. 1985 Mar; **65(3)**: 513–525.
6. Davis JM, Albert JD, Tracy KJ *et al*. Increased neutrophil mobilization and decreased chemotaxis during cortisol and epinephrine infusions. *J Trauma*. 1991 Jun; **31(6)**: 725–31.
7. Sturgis CC, Bethell FH. Quantitative and qualitative variations in normal leukocytes. *Physiol Rev* 1943; **23**: 279–303.
8. Athens JW. Blood: leukocytes. *Annu Rev Physiol*. 1963; **25**: 195–212.
9. Foster NK, Martyn JB, Rangno RE *et al*. Leukocytosis of exercise: role of cardiac output and catecholamines. *J Appl Physiol*. 1986 Dec; **61(6)**: 2218–23.
10. White C, Ling TH, Klein AM. The effect of administration of epinephrine on the leukocyte counts of normal subjects. *Blood*. 1950; **5**: 723–31.

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