

Anti-inflammatories, Antibiotics, Agranulocytosis: A Case of Ibuprofen and Cephalexin Associated Agranulocytosis

Abigail Arrigo, DO,¹ Brianna Rosa, DO,¹ Mehak Laharwal, MD,² Deep Shah, MD²

Medicine Institute¹; Division of Hematology and Cellular Therapy², Allegheny Health Network, Pittsburgh, PA, USA

Introduction

Acquired neutropenia can be seen after infection or exposure to certain medications by causing direct toxic effects on the bone marrow, or immune mediated destruction of circulating neutrophils.^{1,2} Agranulocytosis is often used to describe severe degrees of neutropenia, typically $<500/\mu\text{L}$.¹ We describe the rare occurrence of drug-induced agranulocytosis to not one, but two different medications in a young male patient.

Case

36-year-old male with no medical history presented with worsening sore throat and dysphagia despite ibuprofen and prednisone he received from an urgent care.

First Admission

Initial work up

- WBC count of $530/\mu\text{L}$, ANC 0
- Rapid strep A test was positive
- CT soft tissue of the neck (image 1)
- CT TAP showed no other sites of lymphadenopathy but did show hepatomegaly with top-normal spleen size.
- Negative testing - Parvovirus antibodies, HIV antigen, CMV PCR, EBV PCR, Lyme and syphilis serologies
- Peripheral smear - no neutrophils
- Flow cytometry - no evidence of increased blasts or lymphoproliferative disorder
- Bone marrow biopsy - hypocellular marrow with decreased myeloid series and maturation arrest at promyelocyte stage raising the suspicion of drug induced agranulocytosis

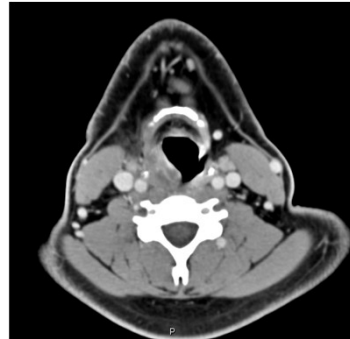


Image 1: CT soft tissue of the neck with bilateral cervical lymphadenopathy and palatine tonsil edema.

Hospital Day	ANC (k/mcL)
1-4	0.00
5*	0.00
6*	0.02
7*	3.15
8	8.07
9	23.73

Table 1: First hospitalization and corresponding ANC trend
* Days of Filgrastim administration

Treatment

- Filgrastim started on hospital day 5
- Discharged home with Cephalexin

Second Admission

Three months later he presented with similar symptoms after having completed a course of cephalexin for right leg cellulitis.

- Work up was unremarkable
- ELANE gene testing for cyclical neutropenia was negative.

Outcome:

- ANC improved without any filgrastim
- Discharged on day 5 with 5-day course of Prednisone.
- He was advised to stop cephalexin and on follow up, his ANC remained > 1000 without any interventions.

Hospital Day	ANC (k/mcL)
1	0.00
2	0.01
3	0.04
4	0.021
4 days post discharge	2.31

Table 2: Second hospitalization and corresponding ANC trend during second hospital admission.

Discussion

- This case describes a patient who developed neutropenia with an ANC of zero despite no re-exposures to the initial inciting drug, ibuprofen and again to Cephalexin.
- We hypothesize that after his initial admission, he developed drug-dependent neutrophil antibodies secondary to cephalexin that was prescribed for tonsillitis.
- Upon re-exposure to Cephalexin for treatment of his cellulitis, he then developed neutropenia prompting his second admission.
- Anti-inflammatories and antibiotics are classes of medications with a known association with agranulocytosis.³
- This case prompts us to do a thorough medication review in patients with agranulocytosis and take caution when prescribing medications

References

1. Alexander Johnston & Jack Utrecht (2015) Current understanding of the mechanisms of idiosyncratic drug-induced agranulocytosis, Expert Opinion on Drug Metabolism & Toxicology, 11:2, 243-257, DOI: 10.1517/17425255.2015.985649
2. Rattay B, Benndorf RA. Drug-induced idiosyncratic agranulocytosis - infrequent but dangerous. Frontiers in Pharmacology. 2021;12. doi:10.3389/fphar.2021.727717
3. Lorenzo-Villalba N, Alonso-Ortiz MB, Maoche Y, Zulfiqar AA, Andrés E. Idiosyncratic Drug-Induced Neutropenia and Agranulocytosis in Elderly Patients. J Clin Med. 2020;9(6):1808. Published 2020 Jun 10. doi:10.3390/jcm9061808