



## Case Report

# A 67-Year-Old Man with a New Neutropenic Fever of Unknown Origin

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A 67-year-old man was admitted to the hospital for a new neutropenic fever of unknown origin. After 12 days of evaluation, a long list of laboratory tests and a bone marrow examination, a diagnosis was made.

**Introduction**

Assessing a patient presenting with a new onset of neutropenia is a multifaceted and complex topic. Neutropenia can arise due to different etiologies, ranging from benign and transient causes to severe and life-threatening conditions. The evaluation process demands a meticulous approach, starting with a comprehensive medical history and physical examination to unearth potential triggers such as recent infections, medication use, or underlying systemic illnesses [1].

Unravelling the underlying cause often necessitates a cascade of investigations, including serological assays, bone marrow biopsy, and genetic testing, each adding layers of complexity to the diagnostic puzzle. Moreover, the management of neutropenia must navigate a delicate balance between addressing the primary pathology, mitigating infection risk, and minimizing treatment-related adverse effects. Collaborative efforts among healthcare professionals, including hematologists, infectious disease specialists, and primary care providers, are imperative to provide optimal care tailored to the individual patient's needs [1].

In our case, a 67-year-old man presented with a new onset neutropenic fever of unknown origin after 6 days of persistent daily fever and sore throat.

**Case**

A 67-year-old man presented to the hospital with neutropenia discovered through blood workup done by his primary care physician after 6 days of fever and sore throat.

The patient is MSM, married to an HIV positive husband who is well treated with anti-retroviral treatment and recent tests showing viral load undetectable 1 month prior to the patient's presentation. His past medical history consists of GERD treated with omeprazole. He also uses PREP. He is a non-smoker and drinks alcohol occasionally.

For the last 6 days prior to his admission, he suffered from sore throat and oral lesions, pain that radiates to his ears and daily fever up to 39 degrees Celsius. He was evaluated by his primary care physician who diagnosed him with pharyngitis and started him on penicillin regimen. Two days later, throat swab came back negative for GAS and penicillin was stopped. Due to the lack of improvement, he was referred to perform blood workup that revealed neutropenia of 0 cell/microL.

He was immediately admitted to this hospital on the same day. Upon his arrival he denies any other complaint. His vital signs are normal, and he is hemodynamically stable. On physical exam his tongue is covered with a white material that is easily scraped off, his buccal mucosa is erythematous and a few aphthous lesions were located on the hard palate, a small left submandibular lymph node was palpated on examination, measuring about 1.5cm and is painful to touch. Liver and spleen were not enlarged. There was no evidence of endocarditis findings. Lungs were clear to auscultation and the heart rate was normal with no murmurs.

On blood work taken on his arrival his neutrophil count was 0 cells/microL with normal hemoglobin and platelets levels. His electrolytes, liver enzymes and creatinine are within normal

limits. CRP was elevated to 400 mg/L. Chest x-ray showed no abnormalities and ECG showed normal sinus rhythm. Urinalysis was normal.

A diagnosis of neutropenic fever was made while there was no clear explanation for why he was neutropenic from the beginning. Was the fever and sore throat the reason for his neutropenia or was the neutropenia the cause of his infectious presentation.

Differential diagnosis for unexplained neutropenia: [2]

- Duffy-null associated neutrophil count (DANC; formerly called benign ethnic neutropenia) – an inherited disease that is not associated with recurrent infections and it and there should be persistent neutropenia while our patient had normal neutrophil count before this presentation.
- Familial neutropenia – refers to unexplained mild neutropenia in families from specific ethnic groups. Our patient had severe neutropenia.
- Congenital neutropenia syndromes usually detected in childhood and are associated with recurrent infections. Our patient had never had neutropenia before.
- Infections Neutropenia can be seen with different viral infections, parasitic and rickettsial infections.
- Medications can be seen as a side effect of cytotoxic or immunosuppressive agents. It is usually associated with pancytopenia. Many other medications have been associated with severe idiosyncratic isolated neutropenia.
- Dietary deficiencies usually cause pancytopenia.
- Hematologic malignancies – different types of leukemias, MDS and lymphoproliferative disorders can occasionally present with isolated neutropenia but commonly typically manifest as pancytopenia.

– Rheumatologic – Rheumatoid arthritis, systemic lupus erythematosus, and other rheumatologic disorders may be associated with neutropenia.

As the patient was admitted to our department we started him on piperacillin-tazobactam coverage as we act in most neutropenic fever patients.

Blood cultures, wide serology panel, urine culture, rheumatology panel and total body CT were performed. Blood cultures showed no growth, so as the urine culture, serologies were negative to a wide range of bacterial and viral infections. Total body CT showed no abnormalities that could have explained this presentation.

In this case there were many possible causes according to the differential diagnosis suggested above husband who is HIV positive, the use of antibiotics and other antipyretics before his admission, a possible throat infection etc.

After one week of hospitalization, we proceeded to hematological consultation and performed bone marrow biopsy. The biopsy showed a picture that can match neutropenia that is related to a viral infection with reactive plasmacytosis with very little myelopoiesis. The biopsy was also sent to PCR for viruses and cultures.

A few days later a positive PCR of Parvovirus B19 came back positive. While being treated with GCSF, after 3 days of treatment neutrophil count started raising. A week later normal neutrophil count was reached and the patient was discharged and continued follow up in the hematology clinic ambulatory. This case was eventually considered as Parvovirus induced agranulocytosis.

## References

1. Hoffman R, Benz EJ, Shattil SJ, Heslop HE, Weitz JI, et al. (2018) Hematology: Basic Principles and Practice (4th ed.). Elsevier.
2. Neutropenia in Adults: Diagnostic Approach and Evaluation. UpToDate,