

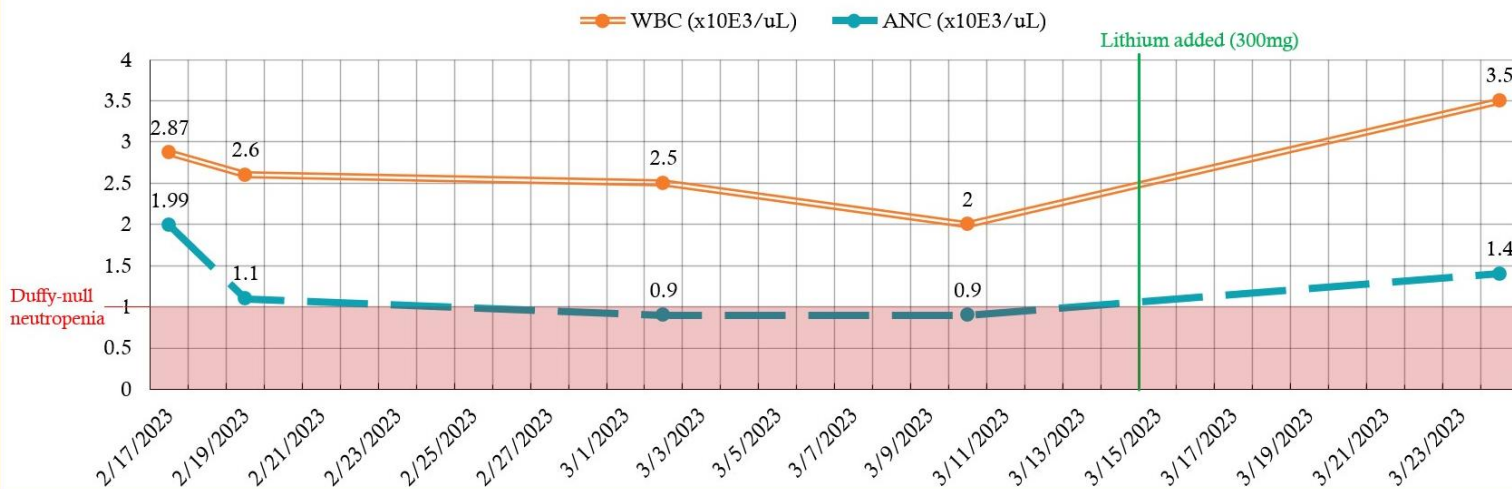
Antipsychotic Induced Neutropenia & Duffy-null status:

Ryan Atwell, OMS-III¹, BS; Veda Warriar^{1,2,3}, MD; Hadele Banna MD³, MA; Nita Bhatt MD, MPH^{3,4}

Ohio University Heritage College of Osteopathic Medicine¹(OU-HCOM), OU-HCOM Department of Psychiatry², Twin Valley Behavioral Healthcare³, Wright State University Boonshoft School of Medicine, Department of Psychiatry⁴



BD: 56y/o F on Zyprexa WBC AND ANC OVER TIME



Introductory information:

Duffy Antigen System

- Group of 6 RBC glycoprotein receptors encoded by the DARC (duffy antigen receptor cytokine) gene on chromosome 1
- These receptors bind to inflammatory cytokines, facilitating the transport of neutrophils into the periphery
- They are also the binding site for Plasmodium Vivax, which binds to them to cause malaria

Duffy-null phenotype:

- 80-100% of people in Sub-Saharan Africa have a single nucleotide polymorphism in the DARC gene that blocks transcription and results in a Duffy-null phenotype: Fy (a- b-)
 - This is thought to be due to conferred malarial resistance
- In the USA, 68% of people who identify as Black or African American are Duffy-null

Duffy-null associated Neutrophil count

- The neutrophils of duffy-null individuals cannot as readily enter the periphery.
- These individuals have decreased circulating neutrophils, but normal neutrophil maturation, function, and response
- The result is a clinically benign decrease in ANC
- 23.8% of duffy-null individuals having an ANC below $2.0E^3$
- Due to this benign decrease in ANC, a new, Duffy-null specific ANC reference range is needed: $1.0E^3$

Literature Cited

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Case Presentation: BD

- BD is 56-year-old African American female with past history of schizoaffective disorder, bipolar type, PTSD, and hypertension
- She was admitted to a state psychiatric hospital where she presented with auditory hallucinations, disorganized speech, hyperreligiosity, decreased sleep, and an inability to tend to activities of daily living.
- She had been noncompliant with medications for a month, but on admission was found to have leukopenia WBC = $2.87E^3$ without neutropenia ANC = $1.99E^3$.
- Following initiation of Zyprexa 15mg daily, her WBC + ANC declined to $2.6E^3$ and $1.1E^3$, prompting concern for neutropenia.
- Due to low WBC and ANC on admission, BD was tested for the RBC Duffy antigen, which was negative (Fya-, Fyb-). This indicated that the patient was duffy-null, and not neutropenic until ANC < $1.0E^3$
- Treatment with Zyprexa continued, and 12 days later her WBC and ANC dropped to $2.5E^3$ and $0.9E^3$, indicating mild Duffy-null neutropenia.
- Continued treatment with Zyprexa was desired, so Lithium carbonate 300mg was added for its erythropoietic effects. Repeat labs showed resolution of neutropenia

Discussion:

The Duffy-null phenotype was previously known as benign ethnic neutropenia (BEN), and this name change reflects that it is a genetic factor—not ethnicity, that is the determining factor. Studies indicate neutropenia in Asian and Caucasian populations can be due to this phenotype, and that many African Americans with neutropenia do not have this polymorphism. This case study demonstrates the need to utilize appropriate, evidence-based testing that facilitates individualized care for patients.

ANC Value	Treatment Recommendations	Frequency of ANC Monitoring
Normal Duffy-null range (established ANC baseline $\geq 1000/mm^3$)	Obtain ≥ 2 baseline ANCs before initiating treatment If treatment interrupted <30 days, continue monitoring as before If treatment interrupted ≥ 30 days, monitor as if new patient	Weekly from initiation to 6 months Every 2 weeks from 6–12 months Monthly after 12 months
Discontinuance for reasons other than neutropenia	See Discontinuance of Therapy under Dosage and Administration	
Duffy-null neutropenia (ANC 500–999/ mm^3) ^a	Recommend hematology consultation Continue treatment	3 times weekly until ANC $\geq 1000/mm^3$ or at patient's known baseline When ANC $\geq 1000/mm^3$ or at patient's known baseline, monitor weekly for 4 weeks, then return to the patient's last "normal BEN range" ANC monitoring interval (if clinically appropriate)
Duffy-null severe neutropenia (ANC <500/ mm^3) ^a	Recommend hematology consultation Interrupt treatment for suspected clozapine-induced neutropenia Do not rechallenge unless prescriber determines benefits outweigh risks	Daily until ANC $\geq 500/mm^3$ 3 times weekly until ANC is at patient's baseline or higher If patient rechallenged, once ANC $\geq 1000/mm^3$ or at patient's baseline, resume treatment as a new patient under "normal range" monitoring