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Case Report

A Case Study of Pancytopenia During the Novel 2019 Coronavirus Pandemic

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A B S T R A C T

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Patients with pancytopenia may present as either clinically stable or unstable. Although there are many common causes of pancytopenia, a new cause that has been recently documented in patient case studies is the novel 2019 coronavirus. Nurse practitioners in all practice environments need to be able to identify pancytopenia, be aware of the associated complications and emergencies, and provide appropriate intervention including a hematology consult.

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A 29-year-old well-appearing female with a past medical history of attention deficit disorder presented to a rural emergency department on the East Coast complaining of 2 weeks of vaginal bleeding with intermittent mild light-headedness. She denied any near syncope, syncope, dizziness, headache, cough, shortness of breath, chest pain, or abdominal pain. She denied any previous history of prolonged vaginal bleeding or coagulopathy disorders. Her only current medication included dexamethylphenidate. She was sexually active with a male partner and had not been using any family planning method over the past few months. Her last menstrual period was not included in the chart. Her vital signs were stable with a heart rate of 77, blood pressure of 113/75, respiratory rate of 16, pulse oximetry of 100%, and temperature of 37.3°C orally. Her orthostatic vital signs and associated symptoms of her light-headedness were not documented. The pelvic examination revealed a small amount of dark blood without clots, masses, abnormal vaginal discharge, or cervical motion tenderness. The emergency medicine clinician also noted a small amount of ecchymosis on her bilateral lower legs. Her physical examination was otherwise documented as benign. A complete blood count, comprehensive metabolic panel, prothrombin time/partial thromboplastin time/international normalized ratio, ABO Rh, chlamydia, gonorrhea, wet mount, urine human chorionic gonadotropin, and coronavirus disease 2019 (COVID-19) laboratory work were ordered. Pertinent results are listed in Tables 1, 2, and 3. In addition, ABO Rh was B positive, the comprehensive metabolic panel was within normal limits, and human chorionic gonadotropin urine was negative.

In summary, this is a generally healthy 29-year-old woman who presented with 2 weeks of increased vaginal bleeding,

mild intermittent light-headedness, and ecchymosis on her bilateral legs. Her laboratory work showed pancytopenia and a positive COVID-19 test. No previous laboratory work was available for comparison in the electronic medical record. Because the patient was hemodynamically stable, she did not require any immediate intervention within the emergency department other than a hematology consult at that time. The emergency medicine clinician spoke with the patient's primary care provider, who confirmed that the pancytopenia finding was new. On-call hematology recommended for her to be transferred to a tertiary center for acute leukemia evaluation. The patient was then transferred that evening, diagnosed with acute myeloid leukemia, and was hospitalized for over 1 month for chemotherapy initiation and bone marrow biopsies. She is currently following up with hematology/oncology, and familial acute myeloid leukemia origin biopsy results were still pending at the time of this article.

Discussion

Pancytopenia is the simultaneous presence of leukopenia, thrombocytopenia, and anemia.¹ The most common causes of pancytopenia include leukemias; multiple myeloma; metastatic cancer; tuberculosis; medication side effects; autoimmune disorders including systemic lupus erythematosus, rheumatoid arthritis, and sarcoidosis; viral infections including Epstein-Barr virus, hepatitis C, and human immunodeficiency virus; nutritional causes including vitamin B₁₂ or folate deficiency and excessive alcohol intake; and disseminated intravascular coagulation (Table 4).¹⁻³ Emergencies associated with pancytopenia include neutropenia with evidence of infection; symptomatic anemia; thrombocytopenia with platelets < 10,000/ μ L or less

Table 1
Complete Blood Count

Laboratory Test	Laboratory Result	Normal Range
WBCs	0.5 K/ μ L	4.0–10.8 K/ μ L
Hemoglobin	8.5 g/dL	12.0–16.0 g/dL
Hematocrit	24.4%	35%–45%
Platelets	48 K/ μ L	160–450 K/ μ L
Neutrophils (absolute)	0.0 K/ μ L	2.4–8.0 K/ μ L
Neutrophils %	7%	40%–75%
Bands	2 %	0%–3%
Lymphocytes (absolute)	0.4 K/ μ L	1.0–5.0 K/ μ L
Monocytes (absolute)	0.0 K/ μ L	0.1–1.5 K/ μ L
RBCs	2.54 million/ μ L	4.20–5.40 million/ μ L
MCH	33.4 pg	27.5–33.2 pg
MCHC	34.8 g/dL	33.4–35.5 g/dL
MCV	96.0 fL	81.6–98.3 fL
Mean platelet volume	6.9 fL	7.4–10.4 fL

MCH = mean corpuscular hemoglobin; MCHC = mean cell hemoglobin concentration; MCV = mean cell volume; MPV = ; RBCs = red blood cells; WBCs = white blood cells.

than 50,000/ μ L with associated bleeding; disseminated intravascular coagulation; and metabolic emergencies including hypercalcemia, hyperkalemia, and tumor lysis syndrome.² This patient did have ecchymosis on her bilateral lower legs and increased vaginal bleeding with a platelet count < 50,000/ μ L. Although this patient presented in no acute distress with stable vital signs, her physical examination and pancytopenia warranted an emergent hematology consult and hospital admission for further evaluation.

Lymphopenia is a common finding in active COVID-19 infections and has even been declared a “cardinal” laboratory finding.⁴ Many research studies are finding that 82% to 85% of admitted patients develop lymphopenia.⁴ Furthermore, the degree of lymphopenia has been shown to be able to predict disease severity.⁵ Patients who had a lymphocyte percentage of less than 5% were often found to need intensive care unit admission and deemed critically ill with a high mortality rate.⁵

Although many patients diagnosed with COVID-19 have lymphopenia and/or thrombocytopenia, pancytopenia is less common.^{6,7} However, viral infections are known causes of pancytopenia, and severe cases of COVID-19 have been found to cause pancytopenia due to generalized bone marrow suppression.^{8,9} There are 2 current theories as to how COVID-19 infections can cause bone marrow suppression. The first theory involves COVID-19 directly infecting myelocytes, which thereby causes suppression of bone marrow formation and pancytopenia.⁹ The second theory involves the elevated proinflammatory cytokines associated with COVID-19 affecting hematopoietic stem cells and impairing hematopoiesis.^{9,10} Despite this patient not having any typical respiratory symptoms of COVID-19 and not recalling any recent known exposure, she had a positive rapid COVID-19 polymerase chain reaction test at the rural emergency department upon initial

Table 2
Coagulation

Laboratory Test	Laboratory Result	Normal Range
PT	10.4 s	9.0–13.0 s
INR	1.00	0.90–1.30
PTT	27.1 s	23.0–36.0 s
Fibrinogen	320.9 mg/dL	180.0–460.0 mg/dL

INR = international normalized ratio; PT = prothrombin time; PTT = partial thromboplastin time.

Table 3
Microbiology/Infectious Disease

Laboratory Test	Laboratory Result	Normal Range
COVID-19	Positive	Negative
Chlamydia	Negative	Negative
Gonorrhea	Negative	Negative
Trichomonas	Absent	Absent
Yeast	Absent	Absent
Clue cells	Absent	Absent
WBCs	Rare	Absent

COVID-19 = coronavirus disease 2019; WBCs = white blood cells.

evaluation. During the first week of her hospital stay, she tested positive for COVID-19 immunoglobulin G and immunoglobulin A antibodies, indicating she had a previous COVID-19 infection and not a current active infection. The clinicians determined that because of these antigen results, the patient’s pancytopenia was not caused by COVID-19. However, recently the Centers for Disease Control and Prevention published an article that found that antigen tests have a 41.2% sensitivity rate when used to screen asymptomatic patients.¹¹ This new data suggest that COVID-19 cannot be ruled out as a compounding factor of her pancytopenia.

Conclusion

Nurse practitioners in any practice environment need to assess for common symptoms associated with cytopenias including recurrent or unusual infections; fatigue, chest pain, or dyspnea, which may be due to anemia; bleeding and easy bruising from thrombocytopenia, constitutional, or “B” symptoms associated with cancers including fevers, night sweats, and weight loss; and jaundice, nausea, and vomiting, which may be secondary to liver disease.² The history should also include any comorbid illnesses, medications that can potentially cause pancytopenia, nutritional and alcohol-intake history, and any recent toxic exposures. Laboratory tests should include a complete blood count, peripheral blood smear, reticulocyte count, prothrombin time, and partial thromboplastin. COVID-19 needs to be added to the differential of any patient who presents with pancytopenia. If a stable patient with pancytopenia presents to an outpatient primary care office, hematology referral can be arranged on an outpatient basis within a few days. If any of the previously listed emergencies associated with pancytopenia are present, the patient needs emergent transfer to an emergency department for stabilization and hematology consult.

Table 4
Common Causes of Pancytopenia

Leukemia
Multiple myeloma
Metastatic cancer
Tuberculosis
Side effect of the following medications: chloramphenicol, phenylbutazone, quinidine, trimethoprim/sulfadiazine, albendazole, and fenbendazole
Autoimmune disorders: systemic lupus erythematosus, rheumatoid arthritis, and sarcoidosis
Viral infections: Epstein-Barr virus, hepatitis C, and human immunodeficiency virus
Nutritional deficiencies: vitamin B ₁₂ and folate
Excessive alcohol intake
Disseminated intravascular coagulation

References

1. Jain A, Naniwadekar M. An etiological reappraisal of pancytopenia – largest series reported to date from a single tertiary care teaching hospital. *BMC Hematol.* 2020;13:10. <https://doi.org/10.1186/2052-1839-13-10>.
2. Berliner N. Approach to the adult with pancytopenia. *Uptodate.* 2020; Accessed January 27, 2021, <https://www.uptodate.com/contents/approach-to-the-adult-with-pancytopenia>.
3. Pascutti M, Erkelens M, Nolte. Impact of viral infections on hematopoiesis: from beneficial to detrimental effects on bone marrow output. *Front Immunol.* 2016;7:364. <https://doi.org/10.3389/fimmu.2016.00364>.
4. Terpos E, Ntanasis-Stathopoulos I, Elalamy I, et al. Hematological findings and complications of COVID-19. *Am J Hematol.* 2020;95(7):834-847. <https://doi.org/10.1002/ajh.25829>.
5. Tan L, Wang Q, Zhang D, et al. Lymphopenia predicts disease severity of COVID-19: a descriptive and predictive study. *Signal Transduct Target Ther.* 2020;5(1):33. <https://doi.org/10.1038/s41392-020-0148-4>.
6. Fu J, Kong J, Wang W, et al. The clinical implication of dynamic neutrophil to lymphocyte ratio and d-dimer in COVID-19: a retrospective study in Suzhou China. *Thromb Res.* 2020;192:3-8. <https://doi.org/10.1016/j.thromres.2020.05.006>.
7. Yang W, Cao Q, Qin L, et al. Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19): a multi-center study in Wenzhou city, Zhejiang, China. *J Infect.* 2020;90:388-393. <https://doi.org/10.1016/j.jinf.2020.02.016>.
8. Al-Samkari H, Karp L, Dzik W, et al. COVID-19 and coagulation: bleeding and thrombotic manifestations of SARS-CoV-2 infection. *Blood.* 2020;136(4):489-500.
9. Zhao Y, Wang J, Li W, et al. Development of pancytopenia in a patient with COVID-19. *J Med Virol.* 2021;93(3):1219-1220. <https://doi.org/10.1002/jmv.26566>.
10. Clapes T, Lefkopoulou S, Trompouki E. Stress and non-stress roles of inflammatory signals during HSC emergence and maintenance. *Front Immunol.* 2020;7:487. <https://doi.org/10.3389/fimmu.2016.00487>.
11. Pray I, Ford L, Cole D, et al. Performance of an antigen-based test for asymptomatic and symptomatic SARS-CoV-2 testing at two university campuses. *MMWR Morb Mortal Wkly Rep.* 2021;69(5152):1642-1647.

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