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# IVIG Induced Hemolytic Anemia

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## Abstract

Intravenous immunoglobulin (IVIG) is derived from donated plasma used to treat immune deficiency, autoimmune, and inflammatory disorders. Adverse effects occur in 5-15% of patients with hemolytic anemia being a delayed reaction. Risk factors for hemolysis are high-dose infusions (1-2g/kg/day or >100g/day), female sex, and non-O blood group. Our case involves a 69-year old male presenting with bilateral lower extremity weakness for 1 year after sustaining a fall, affecting his ability to ambulate with no bowel or urinary incontinence. MRI revealed spondylotic changes of the lumbar spine. EMG showed severe bilateral lumbosacral polyradiculopathy with ongoing denervation and severe sensorimotor peripheral polyneuropathy with axonal loss. He was diagnosed with chronic inflammatory demyelinating polyneuropathy (CIDP) and started on high-dose IVIG (0.4mg/kg; 77.6mg) therapy for 5 days. 48 hours after IVIG completion, patient developed acute drop in hemoglobin (9.1 g/dL to 7.0 g/dL) that continued to down-trend (5.7 g/dL). Type and screen was AB positive. Labs were significant for elevated absolute reticulocyte count (141.5 K/uL), reticulocyte percentage (6.1%), and LDH (321 IU/L) while haptoglobin was low (<30.0 mg/dL), consistent with hemolytic anemia. Direct antiglobulin anti-IgG coombs test was positive and anti-complement negative, consistent with immunohemolytic anemia. He was supported with blood transfusion and continued on high-dose Prednisone (1mg/kg/day) for 3 months. Antibodies present in IVIG product react with RBC antigens predominantly of the ABO blood group, causing intravascular hemolysis. Although IVIG induced hemolysis is typically mild and self-limiting, it can often go undetected and prescribers should be aware.

## Patient Presentation

- 69-year old male admitted to the neurology unit from clinic for worsening lower extremity weakness
- MRI, EMG, and LP were performed, and the patient diagnosed with CIDP
- Patient initiated on IVIG therapy, received doses on hospital day 3-8
- Patient was planned for discharge to inpatient rehabilitation following IVIG

## About IVIG

- Intravenous immunoglobulin (IVIG) is derived from donated plasma used to treat immune deficiency, autoimmune, and inflammatory disorders.
- Adverse effects are typically mild and include malaise, headache, fever, chills, and flushing
- More serious complications are rare and include renal failure, transfusion reactions, and thrombosis
- Adverse effects can be mitigated by slow infusion, premedicating with NSAIDs or steroids, and using subcutaneous formulations of IVIG

## Clinical Course

- On hospital day 8, Hgb noted to fall from 9.1 to 7.0 g/dl
- No signs of bleeding was noted, and patient had been tolerating physical therapy well
- Internal Medicine and Hematology were consulted
- Laboratory work-up was consistent with an IgG mediated hemolytic process with component of iron deficiency
- Reticulocyte studies showed hypoproliferation –Reticulocyte index 0.95
- Pathology review of the peripheral blood showed no abnormal cells
- Patient received 2 units pRBC on hospital day 11 for Hgb 5.7 g/dl
- Patient started on Prednisone 80 mg daily for 3-month course

## Hematologic Lab Values

CBC	5.4	2.9	2.8	2.3	4.9	5.4	5.3	5.8
WBC Count	5.4	2.9	2.8	2.3	4.9	5.4	5.3	5.8
RBC Count	4.82	4.41	3.78	3.68	2.74	2.70	2.54	2.31
HEMOGLOBIN	11.2	10.7	9.1	9.1	7.0	7.2	6.3	5.7*
HEMATOCRIT	34.4	31.3	27.7	25.9	19.5	20.3	18.4	16.7
MCV	71.2	71.0	73.4	70.3	71.1	75.2	72.6	72.0
MCH	23.1	24.4	23.9	24.8	25.6	26.5	24.8	24.6
MCHC	32.5	34.4	32.6	35.3	36.0	35.2	34.2	34.1
RDW	16.1	15.9	16.0	15.4	15.9	16.4	16.2	16.0
PLATELET COUNT	319	250	216	221	272	311	311	287

Figure 1. CBC data. Column 1- on admission. Column 2-4 During IVIg treatment. Columns 5-8 Days following IVIg. All hemoglobin values are in g/dl.

## Direct Antiglobulin Test

Status: Final result Visible to patient:

Component	4mo ago
DAT, Broad Spectrum	POSITIVE
DAT, Anti-IgG Coombs Serum	POSITIVE
DAT, Anti-Complement	NEGATIVE

Figure 2. Direct Antiglobulin test results

ROUTINE CHEMISTRY	
LDH, Total	281
HEPATITIS / LIVER ...	
Haptoglobin	<30.0
Bilirubin, Total	1.2
Bilirubin, Direct	0.3

Figure 3. Hemolysis testing results

LDH values in IU/L. Haptoglobin, Bilirubin in mg/dl.

## Patient Outcome

- Required 2 units packed RBC inpatient, with appropriate recovery and stability following
- IV iron infusion provided inpatient
- Patient discharged to subacute rehabilitation on hospital day 14
- Discharged on prednisone for bone marrow support, CIDP management
- Hemoglobin had recovered to 9.5 g/dL on day of discharge

## Discussion

- Adverse effects with IVIG occur in 5-15% of patients with hemolytic anemia being a delayed reaction. Risk factors for hemolysis are high-dose infusions (1-2g/kg/day or >100g/day), female sex, and non-O blood group
- Antibodies present in IVIG product react with RBC antigens predominantly of the ABO blood group, causing intravascular hemolysis.
- Although IVIG induced hemolysis is typically mild and self-limiting, it can often go undetected and prescribers should be aware.
- onset of hemolysis ranged from 12 hours to 10 days, and the mean decrease in hemoglobin was 3.2 g/dL

## Conclusion

- IVIG induced hemolytic anemia is an uncommon event and often clinically mild
- Providers should maintain a higher index of suspicion in patients with new anemia on IVIG therapy, especially in those receiving higher doses
- IVIG induced hemolytic anemia is managed supportively and has a good prognosis

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