

HEMOLYSIS AFTER CHEMOTHERAPY

Case Study by Jim Perkins M.D. and Leon Dragon M.D. (©2010)

History:

A 57 year old woman with ovarian cancer came to the outpatient cancer care center for infusion of carboplatin.

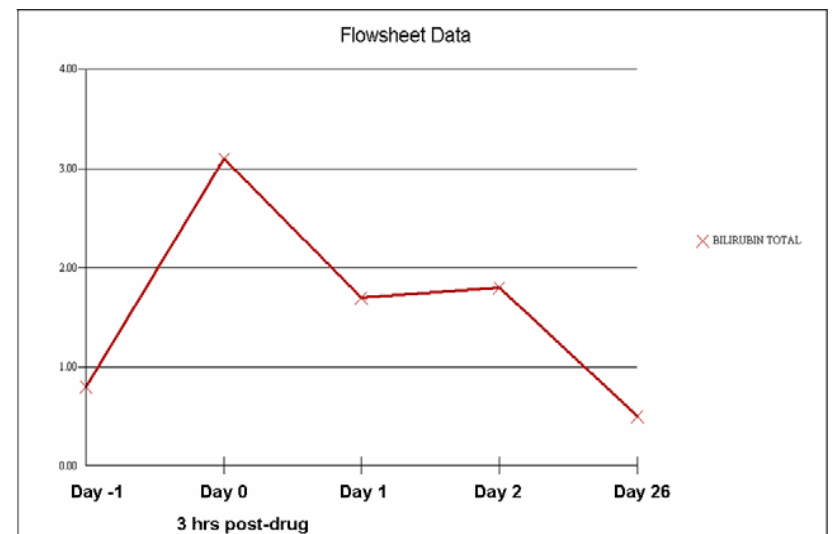
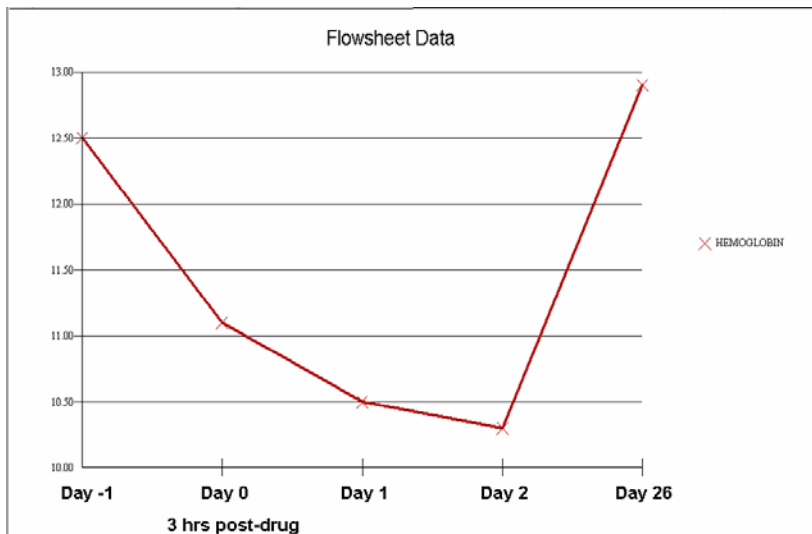
Her disease presented with inguinal lymphadenopathy 9-years earlier. She was found to have abdominal carcinomatosis and initially underwent debulking surgery. This was followed with multiple courses of chemotherapy including:

- 3 multi-cycle courses of carboplatin/Taxol 9, 7, and 5 years earlier,
- cis-platinum/Taxol 5 years earlier and cis-platinum/gemcitabine 3 years earlier,
- unsuccessful courses of doxorubicin liposomal, anastrozole (Arimidex), and vinorelbine (Navelbine).

Currently she was on a course of multiple cycles of carboplatin. The patient had never been transfused and had never had a ‘type-and-screen’ or direct antiglobulin test (DAT) performed in the 9 years she had been under our care.

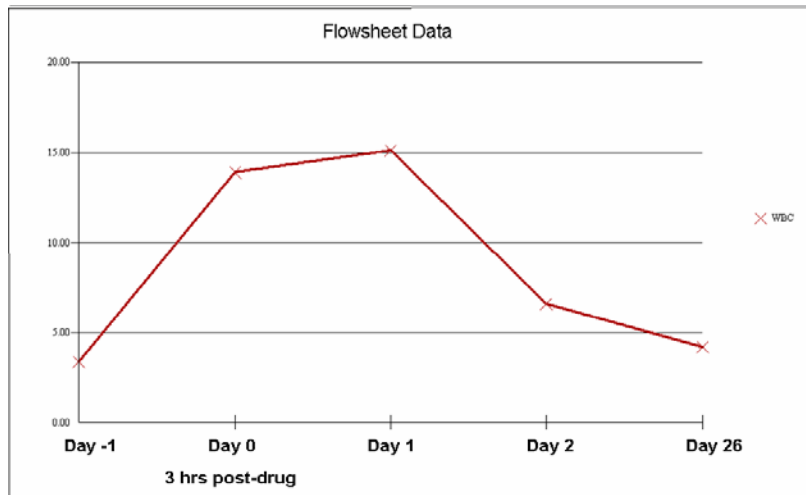
On the day of chemotherapy premedication was administered including ondansetrom (Zofran) 16 mg iv, dexamethasone 20 mg iv, famotidine (Pepsid) 20 mg iv, and loratidine (an anti-histaminic) 10 mg po. This was followed by carboplatin iv at an intended dose of 605 mg. Within 15 minutes of starting her infusion the patient developed severe lower back pain which radiated to her buttocks. She passed red urine and soon thereafter noted chest pain associated with chest tightness and mild dyspnea. The chest discomfort radiated to her right upper arm and scapula.

The patient was admitted to the hospital at which time a temperature of 100.3°F (37.9°C) was noted, soon increasing to a maximum of 102.8°F (39.3°C) and normalizing there after. Her hemoglobin level dropped 1.4 gm/dL over 3 hours and 2.2 gm/dL over 2 days, and her bilirubin rose to 3.1 mg/dL by 3 hours post-infusion as shown in the following two graphs.



HEMOLYSIS AFTER CHEMOTHERAPY: pg. 2

Also of note the patient's leukocyte count increased dramatically immediately after the event as did the platelet count (from 154,000 to 188,000/ μ L).



Other relevant lab test results included the following:

- Four hours post-infusion the urine appeared yellow and clear, the 'dipstick' demonstrated 3+ "blood", but microscopic examination revealed only 0-4 RBCs/hpf, demonstrating hemoglobinuria.
- Fourteen hours post-infusion the LDH level was 948 IU/L (normal < 200) and the haptoglobin level was 8.9 mg/dL (normal 136 - 195).

QUESTIONS:

1. What sort of reaction to chemotherapy infusion do you think is going on?

2. What testing would you like to do?

HEMOLYSIS AFTER CHEMOTHERAPY: pg. 4

Cold-antibody study (tube agglutination testing)

| Cell | Rh system | | | | | Kell | | | | Duffy | | Kidd | | Xg | Lewis | | MNSs | | | | P | Lu | Other | Cell | RT | 15°C | 4°C |
|---------|-----------|---|---|---|---|------|---|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|------|---|---|---|----|-----------------|-------------|------|----|------|-----|
| | D | C | E | c | e | K | k | Kp ^a | Js ^a | Fy ^a | Fy ^b | Jk ^a | Jk ^b | Xg ^a | Le ^a | Le ^b | S | s | M | N | P1 | Lu ^a | | | | | |
| 1* | + | + | 0 | 0 | + | 0 | + | 0 | 0 | + | 0 | + | + | + | 0 | + | 0 | + | + | + | + | + | 0 | 1 | w+ | w+ | 2+ |
| 2* | + | 0 | + | + | 0 | 0 | + | 0 | 0 | + | 0 | 0 | + | + | 0 | + | 0 | + | 0 | + | 0 | + | 0 | 2 | w+ | w+ | 2+ |
| 3* | 0 | 0 | 0 | + | + | 0 | + | 0 | 0 | 0 | + | + | + | + | 0 | + | + | + | + | + | + | + | 0 | 3 | w+ | 1+ | 2+ |
| 4** | | | | | | | | | | | | | | | | | | | | | | | Cord cell 1 | 4 | w+ | w+ | 2+ |
| 5** | | | | | | | | | | | | | | | | | | | | | | | Cord cell 2 | 5 | w+ | w+ | 2+ |
| 6** | | | | | | | | | | | | | | | | | | | | | | | Cord cell 3 | 6 | w+ | w+ | 2+ |
| 7* | | | | | | | | | | | | | | | | | | | | | | | A1 cell | 7 | w+ | w+ | 2+ |
| 8* | | | | | | | | | | | | | | | | | | | | | | | A2 cells | 8 | w+ | w+ | 2+ |
| Patient | | | | | | | | | | | | | | | | | | | | | | | | AC | w+ | w+ | 2+ |

* Commercially prepared cells, **Fresh, DAT negative umbilical cord RBCs

Specimens and a sample of carboplatin were sent to the Blood Center of Wisconsin for a drug study with the following results:

| Reactants: (all reactions with screening cell I) | 30', RT | 60', 37°C | AHG** |
|--|---------|-----------|-------|
| Pt. serum + drug | 3+ | 4+ | 4+ |
| Pt. serum + 6% albumin | 0 | 0 | 0 |
| Normal serum + drug | 0 | 0 | 0 |
| Normal serum +6% albumin | 0 | 0 | 0 |
| 6% albumin + drug | 0 | 0 | 0 |
| Eluate + drug | NT* | NT | NT |
| Pos control (anti-carboplatin) + drug | 4+ | 4+ | 4+ |

"NT" = not tested, *"AHG" = Anti-human globulin or "indirect antiglobulin test" phase

Drug + RBCs + serum diluted as shown with 6% albumin

| | 1:2 | 1:4 | 1:8 | 1:16 | 1:32 | 1:64 | 1:128 | 1:256 | 1:512 | 1:1024 | 1:248 | 1:4096 |
|-----------|-----|-----|-----|------|------|------|-------|-------|-------|--------|-------|--------|
| 30', RT | 3+ | 3+ | 2+ | 1+ | 1+ | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 60', 37°C | 4+ | 4+ | 3+ | 2+ | 2+ | 1+ | 0 | 0 | 0 | 0 | 0 | 0 |
| AHG | 4+ | 4+ | 4+ | 4+ | 4+ | 4+ | 4+ | 4+ | 4+ | 3+ | 1+ | 0 |

HEMOLYSIS AFTER CHEMOTHERAPY: pg. 5

QUESTIONS:

3. What antibodies are present? What is the immunohematologic diagnosis?
4. How might the positive DAT and the antibody in the eluate be related to the process?

Three months after the event a blood sample was received and the following results were obtained:

ABO and Rh Typing

| <A | <B | A1 cells | B cells | 6% alb | <D | <D/AHG | CCC | Interp |
|----|----|----------|---------|--------|----|--------|-----|--------|
| 4+ | 0 | 0 | 4+ | | 0 | 0 | 2+ | A, neg |

Antibody Detection Test (Ab Screen)

| | Gel, initial |
|-----|--------------|
| OI | 0 |
| OII | 0 |

Direct Antiglobulin Test

| | Poly | IgG | <C3 |
|-----------|------|-----|-----|
| AHG | 0 | | |
| 5' incub. | 0 | | |
| CCC | 2+ | | |

A repeat cold-reactive antibody study yielded results essentially identical to those obtained 3 months earlier.

QUESTIONS:

5. What is the implication of the new results?