DRESS Syndrome due to Arsenic Trioxide Therapy for Acute Promyelocytic Leukemia

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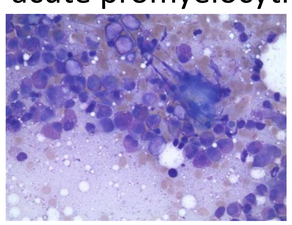
Introduction

- Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome is a rare drug-induced hypersensitivity reaction (1)
- DRESS is characterized by rash, peripheral blood eosinophilia and multiorgan dysfunction including fever, lymphadenopathy, and internal organ involvement.
- However, due to a typical latency period of 2-6 weeks between drug exposure and symptom onset, it may be difficult to determine the culprit drug.

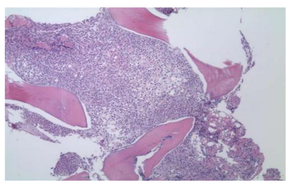
Background

A 65-year-old man presented with fatigue, pancytopenia, and coagulopathy.

Bone marrow aspiration, biopsy, and cytogenetics confirmed a diagnosis of acute promyelocytic leukemia (APL).



Core biopsy touch prep smears show a sea of atypical promyelocytes with varying nuclear shape including bilobed and overlapping forms. The cytoplasm is packed with bright red granules. Auer rods are present.



Core biopsy. The core biopsy is packed with atypical granulocyte precursors. The neoplastic infiltrate shows irregular nuclei and abundant eosinophilic cytoplasm. Background hematopoiesis is markedly reduced.

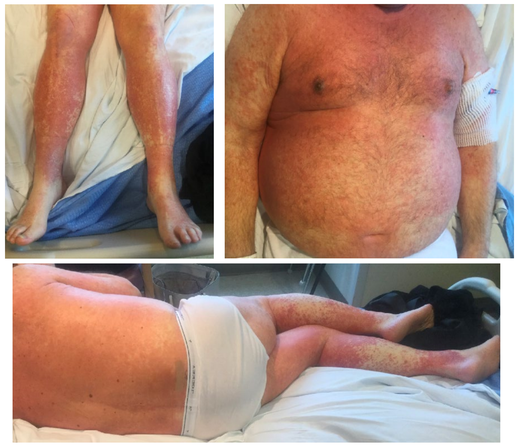
He received one month of curative-intent induction chemotherapy with all-trans retinoic acid (ATRA) and arsenic trioxide (ATO) with complete response on bone marrow biopsy (2).

Case Presentation

Two weeks after initiation of consolidation chemotherapy with ATRO and ATO for APL, a 65-year-old man presented to his hematologist/oncologist with a worsening skin rash, new onset fever, weakness, and dyspnea.

Physical Exam

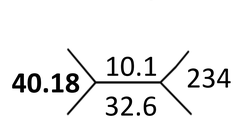
Patient with a pruritic maculopapular rash which started a on his chest and arms, but now covered 80% of his TBSA.



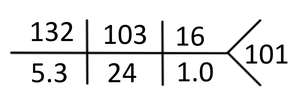
The patient's rash was extensive and covered 80% of his TBSA. Images used with patient's permission

Investigative Studies

- CBC: eosinophilia and leukocytosis



N: 16.26
L: 8.80
M: 1.13
E: 10.25
B: 1.53



- Repeat bone marrow biopsy: eosinophilia without leukemia
  - A clinical diagnosis of DRESS syndrome was made and he was admitted to the hospital
- Skin biopsy confirmed the diagnosis

Progress

He was started on corticosteroids and supportive therapy. His rash and eosinophilia improved over the next 2 weeks and he was discharged.

Initial known culprit drugs (started during induction) were removed from his future treatment plan (3)

- Levofloxacin
- Fluconazole
- Allopurinol

He restarted consolidation therapy with ATRA and ATO.

Recurrence

Two weeks later, he developed a similar rash on his upper and lower extremities with fever, edema, and weakness.

He was readmitted to the hospital and started another course of corticosteroids.

At this point, it was highly suspicious that his DRESS syndrome was due to his chemotherapy treatment.

He was advised to discontinue ATO, strengthened by a second opinion.

Outcome

He started ATRA and gemtuzumab-ozogamicin as alternative curative intent chemotherapy. (4)

He was discharged and is tolerating his new chemotherapy regimen well with ongoing remission and no recurrence of symptoms to date.

Discussion

- To our knowledge, DRESS syndrome due to arsenic trioxide has not been previously reported. Clinicians should be aware of this as a potential side effect of ATO
- This case further illustrates the necessity of a thorough evaluation of all recent medications when faced with DRESS syndrome.
  - This can be especially challenging in patients who have recently started many medications such as in cancer treatment.

References

1. Shiohara T, Kano Y. Drug reaction with eosinophilia and systemic symptoms (DRESS): incidence, pathogenesis and management. null. 2017 Feb 1;16(2):139–47.
2. Lo-Coco F, Avvisati G, Vignetti M, Thiede C, Orlando SM, Iacobelli S, et al. Retinoic acid and arsenic trioxide for acute promyelocytic leukemia. N Engl J Med. 2013 Jul 11;369(2):111–21
3. Cacoub P, Musette P, Descamps V, Meyer O, Speirs C, Finzi L, et al. The DRESS Syndrome: A Literature Review. The American Journal of Medicine. 2011 Jul 1;124(7):588–97
4. Estey EH, Thall PF, Giles FJ, Wang X-M, Cortes JE, Beran M, et al. Gemtuzumab ozogamicin with or without interleukin 11 in patients 65 years of age or older with untreated acute myeloid leukemia and high-risk myelodysplastic syndrome: comparison with idarubicin plus continuous-infusion, high-dose cytosine arabinoside. Blood. 2002 Jun 15;99(12):4343–9.