

Fournier's Gangrene in a Case of Acute Promyelocytic Leukemia during ATRA Therapy

Nasim Valizadeh¹

Hematology-Oncology Department, Emam Khomeini Hospital, Urmia University Of Medical Sciences, Urmia, Iran

Corresponding author: Nasim Valizadeh, MD, Assistant professor of Hematology/Medical Oncology
Department of Internal Medicine, Urmia University Of Medical Sciences, Emam Khomeini Hospital, Urmia, Iran.
Tel: +989125474755
Email: Nsedaha0@gmail.com

Abstract

Introduction: Fournier's gangrene or necrotizing fasciitis of external genitalia is a medical emergency. It was reported in cases of acute promyelocytic leukemia (APL) before and during induction therapy with all-*trans* retinoic acid (ATRA). We present a case of APL that developed Fournier's gangrene during ATRA therapy.

Key Words: Fournier's gangrene, Acute promyelocytic leukemia, ATRA

Introduction: Combination of all-*trans* retinoic acid (ATRA) with systemic chemotherapy leads to induction of complete remission in 90% of APL cases. The side effects of ATRA in most patients are included: fever, fatigue, skin dryness, rash, nausea, vomiting, abdominal pain and headache. These are seldom permanent and irreversible. (1) Scrotal ulceration is reported as a rare adverse effect of ATRA therapy in literature. (2, 3, 4, 5) These ulcers improve after discontinuing of ATRA. Genital ulcers during ATRA therapy may be progressed to Fournier's gangrene. (5, 6, 7)

Case Report

A 36 y/o male came with prolonged bleeding after tooth extraction. On admission he had pancytopenia (WBC= 2000/ μ L, Plt count= 7000/ μ l, Hb= 8 gr/dl). Bone marrow aspiration and biopsy revealed AML (M3). We administered induction of remission therapy with all-*trans* retinoic acid (ATRA) followed by 3-7 regimen (daunorubicin and cytarabine). About 2 week after starting chemotherapy and during treatment with ATRA he developed fever, oral and genital ulcers with scrotal swelling and erythema, then broad-spectrum antibiotics was started. Testicular sonography was showed only scrotal edema and without subcutaneous emphysema. We consulted with urologist and infectious disease specialist; they recommended continuing antibiotic therapy. At first, they said that there is no evidence of Fournier's gangrene, but fever and perineal edema

and pain did not resolve and in repeated examination we found overt gangrene and subcutaneous emphysema in external genitalia of the patient and the diagnosis of Fournier's gangrene was made. Again, we consulted with urologists; they recommended surgery for debridement of the diseased tissue and continuing of appropriate antibiotics.

Results

This 36 y/o male with AML (M3) during induction therapy with ATRA developed initially scrotal swelling and ulcers that finally progressed to Fournier's gangrene.

Discussion

Scrotal ulceration is a rare side effect of ATRA therapy; it may progress to Fournier's gangrene which is a urologic emergency. (2, 3, 4, 5, 6, 7) If corticosteroids cannot control progression of genital ulcers, ATRA should be stopped temporarily. Clinicians should consider Fournier's gangrene in any patient with acute leukemia and fever especially in patients with APL during ATRA therapy. We should repeat perineal examination in APL patients with fever and perineal pain, edema or ulceration, because any ulceration can progress to Fournier's gangrene. Wide spectrum antibiotic therapy and surgical debridement would be necessary in this situation. ATRA combined with systemic chemotherapy is most effective therapy in patients with APL. The exact mechanism of ATRA

induced genital ulceration is not understood but possible pathogenesis is cytokine release and superoxide production and leukocyte activation and tissue damage.(8, 9) Our patient developed genital ulceration two weeks after starting ATRA and chemotherapy that progressed to Fournier's gangrene. ATRA induced genital ulceration with progression to Fournier's gangrene can not preclude using of this effective therapy in APL patients.

Conflicts of Interest: The author indicated no potential conflicts of interest.

References

1. Drug information: ATRA. Up to date. Version: 17.3.
2. Pavithran K, Arjun R, Aruna R, Thomas M. Scrotal Ulceration during Induction Therapy of Acute Promyelocytic Leukemia with ATRA. *Am J Hematol.* 2004; 75: 260- 1.
3. Charles KS, Kanaa M, Winfield DA, Reilly JT. Scrotal Ulceration during all-*trans* Retinoic Acid (ATRA) Therapy for Acute Promyelocytic Leukaemia. *Clin Lab Haematol.* 2000; 22: 171- 4.
4. Mori A, Tamura S, Katsuno T, et al. Scrotal Ulcer Occuring in Patients with Acute

Promyelocytic Leukemia during Treatment with all-*trans* Retinoic Acid. *Oncol Rep.* 1999; 6: 55- 8.

5. Goto H, Tsurumi H, Kasahara S, Hara T, Yamada T, Sawada M, et al. Acute Promyelocytic Leukemia Accompanied by Scrotal Fournier's Gangrene during ATRA Treatment and Relapsed as External Ear Tumor. *Rinsho Ketsueki.* 1998; 39(12): 1169- 74.

6. Naithani R, Kumar R and Mahapatra M. Fournier's Gangrene and Scrotal Ulcerations during all *trans*-Retinoic Acid Therapy for Acute Promyelocytic Leukemia. *Pediatric Blood & Cancer.* 2008; 51(2): 303- 4.

7. Fukuno K, Tsurumi H, Goto H, Oyama M, Tanabashi S, Moriwaki H. Genital Ulcers during Treatment with ALL-*trans* Retinoic Acid for Acute Promyelocytic Leukemia. *Leuk Lymphoma.* 2003 Nov; 44(11): 2009- 13.

8. Koga H, Fujita I, Miyazaki S. Effects of all-*trans* Retinoic Acid on Superoxide Generation in Intact Neutrophils and a Cell free System. *Br J Haematol.* 1997. 97: 300- 5.

9. Degos L, Dombret H, Chomienne C, et al. All-*trans*-Retinoic Acid as a Differentiating Agent in the Treatment of Acute Promyelocytic Leukemia. *Blood.* 1995. 85: 2643- 53.