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LETTER TO THE EDITOR

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Fournier's gangrene that initially mimicked pubic cellulitis in an elderly woman administered a Janus kinase inhibitor, methotrexate, and prednisolone for rheumatoid arthritis

Dear Editor,

An 82-year-old woman, with rheumatoid arthritis (RA), was referred to us with a painful reddish swelling on the right-hand side of the genitalia. She had been administered 10 mg/d tofacitinib (TOF) (a Janus kinase [JAK] inhibitor), 4 mg/wk methotrexate (MTX), and 5 mg/d prednisolone for RA. She started feeling a painful sensation on the right-hand side of the genital region, 4 days prior to the first examination. General examination revealed a body temperature of 38.6°C, blood pressure of 117/60 mm Hg, and heart rate of 100 bpm/min. Physical examination revealed a painful reddish swelling in the pubic area (Figure 1A). Neither fluctuation nor snow-ball crepitation was palpable. Blood examination revealed a white blood cell count of 11 600/mm^3 and C-reactive protein (CRP) level of 9.53 mg/dL. Contrast-enhanced computed tomography detected gas (arrows) and an increased adipose tissue accumulation extending from the right labia majora to the right lower abdomen (Figure 1B). TOF and MTX were discontinued. Meropenem and clindamycin were administered, and an incision into the lesion was performed. Symptoms worsened rapidly and became serious; blood pressure dropped to 87/47 mm Hg on day 2, and a tremendously painful reddish swelling with CRP level of 30.76 mg/dL developed on day 3. Emergent debridement was performed on day 3 (Figure 1C). Deep brown, nonviscous, and foul-smelling liquid was excreted during debridement. Blood and pus culture tests were unable to detect infectious organisms. Anaerobic cultures were performed on blood but not on pus from the wound. The reddish swelling spread to the proximal right thigh on day 4 (Figure 1D) but resolved on day 6. The lesion was washed daily and gradually developed into reddish granulation tissue without signs of infection. The granulated wound was sutured on day 23 (Figure 1E), and the recovered lesion persisted for 7 months (Figure 1F).

To the best of our knowledge, this is the first reported case of Fournier's gangrene (FG)[1] during administration of a JAK inhibitor. The case appeared to be a less serious manifestation when first examined; however, serious clinical features developed immediately after the withdrawal of TOF.

The JAK family is involved in the immune-related intracellular transduction of signals from extracellular cytokines via receptors. TOF is an inhibitor of JAK protein activities, mainly JAK1 but also, less potently, JAK2 and Tyk2.[2,3] TOF administration can lead to serious infections, as it blocks type I interferons and interleukin-6 via the inhibition of JAK1.[3]

JAK signaling is involved in inflammatory and autoimmune diseases.[4] TOF can inhibit airway neutrophilia stimulated by inhaled lipopolysaccharides, the predominant component of gram-negative bacterial cell walls.[5] JAK inhibitors can potentially suppress inflammation due to infection by gram-negative bacteria. In this case, withdrawal of TOF probably led to severe inflammation, which manifested as necrotizing fasciitis.

We report a case of FG that initially mimicked pubic cellulitis in an elderly woman administered a JAK inhibitor and other immunosuppressive agents. Accumulation of cases of necrotizing fasciitis during the administration of JAK inhibitors would be highly beneficial for characterizing the clinical course of this clinical entity.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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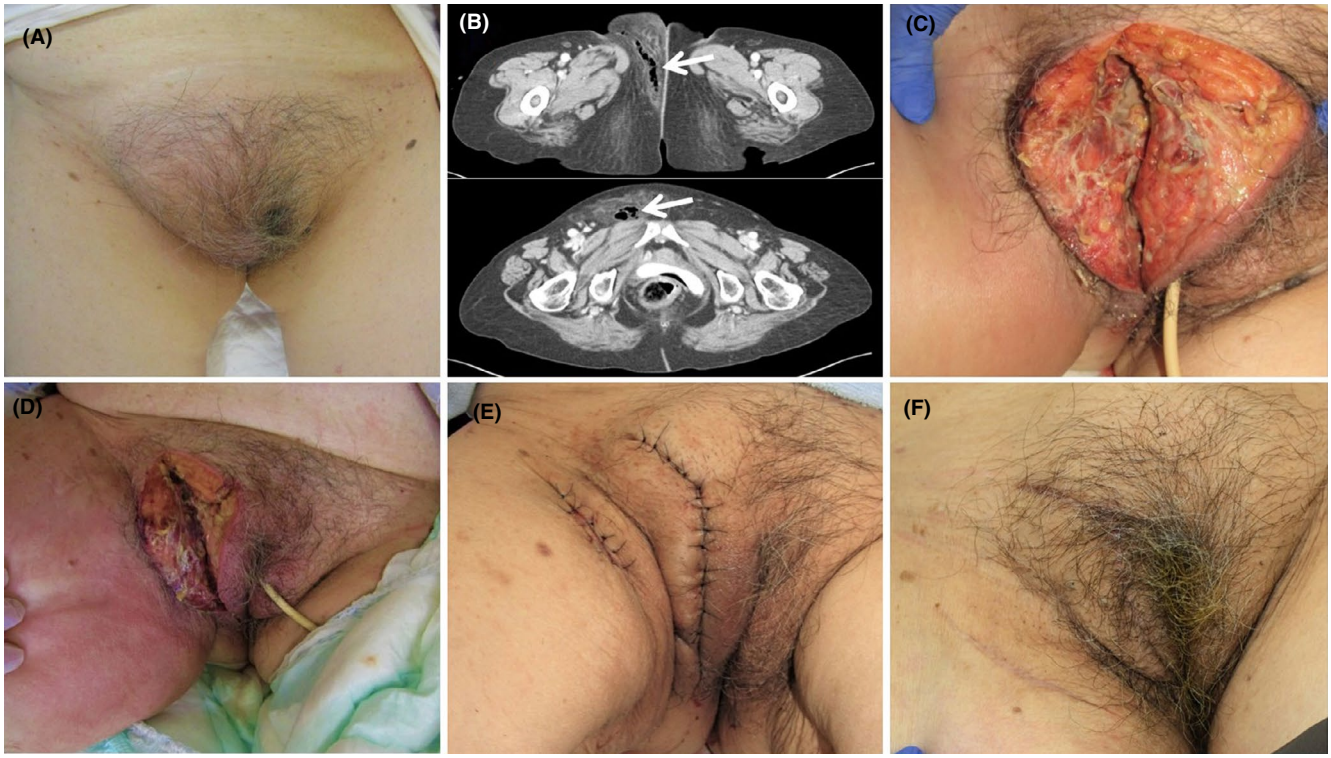

FIGURE 1 A, A painful reddish swelling in the pubic area. B, Gas (arrows) and an increased adipose tissue accumulation extending from the right labia majora to the right lower abdomen. C, Necrosis until adipose tissue and Colles' fascia. D, The reddish swelling spreading to the proximal right thigh. E, At the moment of the suture of the granulated tissue. F, The recovered lesion 7 mo later from the suture

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