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Article type : Case Report

Title: Diabetic Medicine

Created by: Maria Hale

Email proofs to: Peter.Colman@mh.org.au

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Article no.: DME-2017-00333

Article type: Case Report

Figures: 1; Tables: 0; Equations:0; References: 7

Short title/Authors running head: Fournier's gangrene, SGLT2 inhibitors and Type 2 diabetes • S. Kumar et al.

Case Report

Fournier's gangrene in a man on empagliflozin for treatment of Type 2 diabetes

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What's new?

- Fournier's gangrene is a life-threatening necrotizing infection and its occurrence in individuals with Type 2 diabetes on treatment with sodium glucose co-transporter 2 inhibitors has not been described previously in the literature.

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/dme.13508](https://doi.org/10.1111/dme.13508)

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Abstract

Background

Use of sodium glucose co-transporter 2 (SLGT2) inhibitors has been associated with an increased risk of genital infections secondary to increased glycosuria [1]. Our report highlights a case of Fournier's gangrene, the most severe and potentially fatal type of genital infection, which was preceded by multiple episodes of thrush in a man treated with empagliflozin for Type 2 diabetes.

Case report

A 41-year-old man with a 2-year history of Type 2 diabetes presented to his local doctor with scrotal swelling. He had been commenced on empagliflozin with an excellent glycaemic response (in conjunction with metformin 1000 mg twice daily) reducing his HbA_{1c} from 102 mmol/mol (11.5%) to 73 mmol/mol (8.8%) in the first 6 months of treatment. His past history was significant for obesity (BMI 38 kg/m²) and he was a current smoker. He was circumcised and sexually active with no previous history of genital infections. Approximately 2 years previously he had a diverticular perforation for which he required a Hartmann's procedure. His colostomy was reversed 5 months prior to this presentation and during the operative procedure an indwelling urinary catheter was used.

This man described his first episode of thrush approximately 7 months after commencement of empagliflozin. He did not seek medical attention and self-administered over-the-counter antifungal treatment. He described multiple subsequent episodes of thrush which were again self-treated with significant symptom improvement. He continued empagliflozin 25 mg daily during this time. After approximately 14 months on empagliflozin treatment, he presented to his local doctor with scrotal pain that had been present for 4 days and was urgently referred to our institution.

On presentation, he was hyperglycaemic (plasma glucose 19.9 mmol/l), afebrile and hemodynamically stable. Perineal examination revealed a grossly swollen and indurated scrotum with tender spermatic cord, epididymis and testicles. There was associated bilateral inguinal lymphadenopathy. Investigations showed elevated inflammatory markers [C-reactive protein 283.1 (< 5.0 mg/l) and white cell count 18.3 (4.0–11.0 × 10⁹/l)]. Scrotal ultrasound demonstrated enlarged left epididymis and hyperaemia consistent with epididymitis. A computed tomography (CT) scan of the pelvis revealed features consistent

with Fournier's gangrene (Fig. 1). Despite adherence to his oral hypoglycaemic agents, his HbA_{1c} on admission was 99 mmol/mol (11.2%); 3 months previously his HbA_{1c} had been 59 mmol/mol (7.5%).

An emergency exploration and debridement under anaesthetic identified an oedematous scrotum and a 10 × 10 cm abscess. There were no ischio-rectal abscesses, and the rectum and stoma site were healthy. He returned to theatre 96 h later for further exploration, washout and application of a vacuum dressing. On day 7 of his hospital stay, he received a split skin graft to his perineum. Operative cultures demonstrated heavy polymicrobial growth of *Streptococcus anginosus*, mixed anaerobes and Gram-negative bacilli. Initial antibiotic management included intravenous amoxicillin, gentamicin and vancomycin which was changed to intravenous meropenem for a total 14-day course.

Empagliflozin was ceased on admission and he was commenced on a basal bolus insulin regimen. He was counselled on smoking cessation and discharged home on day 15 on oral antibiotics.

Discussion

Fournier's gangrene is a necrotizing fasciitis involving the perineal and genital areas, and despite significant advances in treatment mortality rate remains high at ~ 10% [2]. This rapidly progressive polymicrobial infection is more common in men with the source of infection commonly originating from the gastrointestinal tract (49.2%), genitourinary tract (43.4%) and skin (7.5%) [3]. The most common risk factor for Fournier's gangrene is diabetes, however, it does not appear to be associated with a higher mortality rate [2,4]. Other risk factors include obesity, immunosuppressed states, smoking, alcohol abuse and end-stage renal or liver failure.

A high degree of suspicion is required to make the diagnosis as clinical presentation may vary from indolent cellulitis to severe pain, oedema and systemic features. Features that may assist in differentiating Fournier's gangrene from simple soft tissue infections include persistent severe pain, bullae, skin necrosis, ecchymosis, crepitus, extensive oedema, rapid spread and signs of systemic toxicity [5].

Fournier's gangrene is predominantly a clinical diagnosis, however, imaging techniques using ultrasonography, CT or magnetic resonance imaging can be used to confirm the diagnosis in uncertain cases. CT may demonstrate fluid collections, abscesses, subcutaneous emphysema, and show the origin and extent of infection [6]. Investigations usually show

leucocytosis, thrombocytopenia, electrolyte derangements and elevated inflammatory markers. Blood cultures may become positive with culprit pathogens such as *Escherichia coli*, *Staphylococcus*, *Streptococcus* and *Bacteroides* [5].

Treatment involves urgent aggressive surgical exploration and debridement of the necrotic tissue. Broad-spectrum antibiotics should be administered and multidisciplinary care involving urology, general and plastic surgeons and infectious disease teams may be required.

There has only been one other reported case of Fournier's gangrene in a man on an SGLT2 inhibitor which occurred 3 weeks after commencement of the agent in the context of chronic hyperglycaemia and poor perineal hygiene due to morbid obesity [7]. A wide clinical spectrum of genital infections is associated with SGLT2 inhibitors. These are usually mild and easily treated with over-the-counter antifungal agents, and occur soon after commencement of treatment. Adherence to follow-up is essential to ensure appropriate cessation of the SGLT2 inhibitor and optimization of glycaemic control using other suitable agents. However, multiple risk factors such as diabetes with poor glycaemic control, obesity, smoking, urinary catheterization, operative procedures, recurrent fungal infection together with continuing use of empagliflozin were present in our case and presumably led to the development of Fournier's gangrene. Furthermore, the significant deterioration in HbA_{1c} may have occurred due to subclinical infection leading to a vicious cycle of worsening hyperglycaemia and infection.

In conclusion, use of SGLT2 inhibitors in individuals with relevant co-morbidities may increase their risk of genital infections and timely cessation of these agents may help prevent progression to more severe infections such as Fournier's gangrene.

Funding sources

Competing interests

Acknowledgements

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FIGURE 1. Author to supply caption

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Title:

Fournier's gangrene in a man on empagliflozin for treatment of Type2 diabetes

Date:

2017-11-01

Citation:

Kumar, S., Costello, A. J. & Colman, P. G. (2017). Fournier's gangrene in a man on empagliflozin for treatment of Type2 diabetes. DIABETIC MEDICINE, 34 (11), pp.1646-1648.
<https://doi.org/10.1111/dme.13508>.

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