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Case report

# Unusual cause of severe diabetic ketoacidosis precipitated by *Streptococcus bovis/equinus* (SBSEC) bacteremia: Case report and review of literature

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ABSTRACT

Diabetic ketoacidosis is a feared complication in patients with diabetes mellitus and poses high risk of mortality and morbidity unless treated in timely manner. Infection is one of the most common precipitating factors for the development of diabetic ketoacidosis. Bacteremia with Group A and Group B beta hemolytic streptococcal strains are well known, however nonenterococcal Group D strains such as the *Streptococcus bovis/Streptococcus equinus complex* (SBSEC) still remains an understudied entity. Here we present a case of a 35-year-old Type I diabetic female presenting with severe diabetic ketoacidosis with overlapping features of hyperosmolar hyperglycemia, precipitated by *Streptococcus alactolyticus* bacteremia, successfully treated with four-week course of parenteral ceftriaxone. This case report emphasizes the potential importance of SBSEC as an emerging pathologic strain and culprit for triggering diabetic ketoacidosis which requires prompt diagnosis and targeted therapy.

## Introduction

Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic states (HHS) are the two most common life-threatening complications of diabetes mellitus [1]. Although there are significant differences in the underlying pathophysiology, the basic mechanism for both complications is a relative or absolute state of insulinopenia. Under conditions of extreme stress such as infections, myocardial infarctions, cerebrovascular accidents, medication non-compliance, drug abuse or trauma, an increase in counter-regulatory hormones such as cortisol, catecholamines, glucagon and growth hormone can precipitate DKA and HHS. Therefore, prompt evaluation and management of the underlying precipitating factors forms the cornerstone of successful treatment [2].

The *Streptococcal bovis/Streptococcal equinus complex* (SBSEC) compromises a highly diverse group of bacteria including commensal colonizers of the human and animal gastrointestinal tract and opportunistic pathogens [3]. Associated bacteremia, infective endocarditis, neonatal meningitis, fulminant neonatal sepsis and chorioamnionitis have been reported in the literature [4–7]. In the new taxonomy of SBSEC, *Streptococcus alactolyticus* was included in SBSEC as phenotypically indistinguishable and an earlier synonym of *S. intestinalis*, grouped under Salivarius group of Streptococcal viridans species based on phenotypic characteristics [8]. *Streptococcus alactolyticus* has been isolated from intestinal flora of pigs, chicken, cows, pigeons and dogs, making it an animal associated species [9–11]. Here, we describe a rare case of *Streptococcus alactolyticus* bacteremia as a precipitating cause for severe diabetic ketoacidosis.

## Case report

A 35-year-old African American female with past medical history of poorly controlled Type 1 diabetes mellitus (Hba1c 9.6%) complicated by diabetic gastroparesis, diabetic retinopathy, hypertension and end stage renal disease on hemodialysis, presented to our emergency department with complaints of epigastric abdominal pain, 8/10 in severity, crampy, intermittent with associated nausea and vomiting of 1-day duration. She denied any aggravating factors and reported minimal relief with analgesic regimen. Review of system was negative for fever or change in bowel habits. Her last hemodialysis session was one day prior to admission and she had been compliant with her insulin regimen as well as dietary restrictions. Additional history was significant for 10 packs year of smoking.

On physical examination, temperature was 36.1° C, heart rate of 110/min, blood pressure of 142/63 mmHg, respiratory rate of 30/min and oxygen saturation of 97% on ambient air. The abdomen was soft and non-distended with normoactive bowel sounds. Laboratory parameters revealed leukocytosis (17 × 10^3/mcL), anion gap metabolic

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**Table 1**
SBSEC delineation in four DNA homology clusters based on 16S ribosomal DNA sequences [8].

| DNA cluster | Current (genotypic) Denomination | Synonym | Former (phenotypic) Denomination |
|---|---|---|---|
| I | *S. bovis* | | |
| | *S. equinus* | | |
| II | *S. gallolyticus* | *S. gallolyticus subsp. gallolyticus* | S. bovis biotype I |
| | *S. macedonicus* | *S. gallolyticus subsp. macedonicus* | S. bovis biotype II.2 |
| | *S. Pasteurianus* | *S. gallolyticus subsp. Pasteurianus* | S. bovis biotype II.2 |
| III | *S. infantarius* | *S. infantarius subsp. infantarius* | S. bovis biotype II.1 |
| | *S. lutetiensis* | *S. infantarius subsp. coli* | S. bovis biotype II.1 |
| IV | *S. alactolyticus* | | |

acidosis (ABG: pH 6.8, pCO2 17, HCO3 not measurable, anion gap > 30, lactate 7 mmol/L) with hyperkalemia of 8.8 mmol/L, hyponatremia 121 mmol/L (corrected 133), chloride of 79 mmol/L, hyperphosphatemia 11.9 mg/dL, blood glucose of 1562 mg/dl, elevated serum ketones, BUN 148 mg/dl, serum creatinine 9.5 mg/dl, serum bicarbonate of < 10 mmol/L and albumin of 4.0 gm/dL. Urine toxicology screen was negative and serum ethanol levels were less than 10 mg/dl. EKG was suggestive of peaked T wave, wide QRS and ventricular bigeminy. She was managed as a case of severe diabetic ketoacidosis with overlapping features of hyperosmolarity with emergent hemodialysis. She was not started on antimicrobials initially pending blood cultures.

On hospitalization day 1, blood cultures were reported to be positive for Gram positive cocci in chains and pairs. She was started on IV vancomycin and after species identification of *Streptococcus alactolyticus* switched to IV ceftriaxone. Upon further evaluation, she did admit to having a dog in good health for the past 3 years, who licked her face and mouth frequently. She denied any exposure to farm animals or wild life and denied ingesting anything directly from hunting, farming or from the field. Abdominal ultrasound as well as CT abdomen and pelvis were unremarkable. Transthoracic echocardiography was also negative for infective endocarditis however whole-body gallium scan was suggestive of increased tracer uptake in the lower abdomen/upper pelvis, concordant with infectious focus. She received antimicrobials for total of 4 weeks. Repeat blood cultures remained negative.

## Discussion

Prevalence of hyperglycemic emergencies which encompasses DKA, HHS and overlap hyperosmolar ketoacidosis is rising in the United States despite preventive strategies [1]. Mortality rates associated with HHS (5–20%) are significantly higher than that for DKA (1–5%), however the overlapping features of hyperosmolarity and ketoacidosis result in worst outcomes even though these patients tend to be younger [12]. Increased mortality rates are usually a cause of underlying precipitating factors rather than the consequence of the metabolic derangements [1]. Inadequate insulin therapy and infections are among the two most common precipitating factors with infections accounting for 30–50% of DKA cases [2]. Therefore, prompt evaluation and management of underlying precipitating factors are keys to successful treatment.This is particularly true for bacteremia, given the increased severity of infections in diabetic patients. Patients with poorly controlled diabetes are predisposed to infections due to various immune deficiencies as it may be the case in our patient [13]. Bacteremia with beta hemolytic streptococcal is well known, however SBSEC still represents an understudied group.

Currently, the SBSEC is classified within the non-beta hemolytic streptococcus and Lancefield group D streptococci. There have been intensive revisions in the classification because of the phenotypic diversity with efforts taken to streamline the nomenclature. The latest is based on 16S ribosomal DNA sequences and delineates SBSEC in four DNA homology clusters [Table 1]. *Streptococcus alactolyticus*, only species in DNA cluster IV, is infectious pathogen which is described in this case report [8]. Alactolyticus is typically an animal associated species, isolated from the gut flora of canines, pig, chicken or horse. Rinkinen et al. were able to demonstrate that *Streptococcus alactolyticus* is the dominating culturable lactic acid bacterium in canine jejunum and feces [11]. Human infections by *Streptococcus alactolyticus* are extremely rare and often virulent as evidenced by few human cases described in literature. Recently, Almeida et al. described a case of infective endocarditis complicated by septic emboli [4] and Toepfner et al. described a fatal case of fulminant neonatal sepsis caused by this pathogen [6].

To best of our knowledge, this is the first case report of severe diabetic ketoacidosis precipitated by *Streptococcus alactolyticus* bacteremia. Data is lacking regarding the virulence mechanism and antimicrobials resistance pattern in this strain. However, our patient responded favorably to 4 weeks course of ceftriaxone.

## Conclusion

SBSEC have wide spectrum of habitats and functional roles and are lately emerging as virulent pathogen with little literature on their virulence mechanism, host preference, zoonotic potential and antimicrobials resistance that is causing an alarming situation. As physicians, we should be aware of this taxonomical group, to promptly identify and treat in a timely fashion.

## Conflict of interest

The authors declare they have no conflict of interest.

## Consent

“Written informed consent was obtained from the patient for publication of this case report.”

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