



Streptococcus Toxic Shock Syndrome Due to Non Haemolytic *Streptococcus pyogenes*

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Authors' contributions

The article was carried out in collaboration between all authors. Authors JS and JM equally contributed to the first draft of the manuscript and performed literature searches. Author AG helped with the laboratory analysis. Author LS revised, edited and performed further literature searches. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Aim: Describe the detection of an unusual pathogen associated with a common clinical presentation with abrupt worsening.

Case Presentation: We present the case of a 36-year-old Peruvian male who presented to the Emergency Department with a 24-hour history of fever, nausea, vomits and diarrhea. He received intravenous hydration and antibiotics. In the next eight hours he became toxic and developed septic shock. Despite intensive vasopressor therapy and broad-spectrum antibiotics, patient died of multiorgan failure within the first 48 hours. The first blood culture was positive for *Streptococcus pluranimalium*, but subsequent molecular testing of the strain showed non-beta-haemolytic *Streptococcus pyogenes*.

Discussion: *Streptococcus pluranimalium* is a gram positive cocci isolated from organ samples of different animals. It has been described few cases of this bacteria causing human infection. We discuss the similarities and differences between the reported cases and our findings. Surprisingly,

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after using more advanced tests, the isolated strain was identified as a non-beta-haemolytic *Streptococcus pyogenes*.

Conclusion: The detection of uncommon human pathogens in challenging clinical scenarios requires an early and accurate typification.

Keywords: *Streptococcus*; gastroenteritis; shock; septic.

1. INTRODUCTION

Streptococcus pluranimalium (Latin *pluris*: many and *animalium*: animals) is a non-motile, gram positive cocci arranged in chains or groups. It was first described in 1999 by Devriese et al. from samples of subclinical mastitis, genital tract and tonsils of cattle, from tonsils of a goat and a cat, and from the crop and respiratory tract of canaries. Colony size is less than 1 mm, produces greening hemolysis and grows at 37°C and 42°C [1]. It is remarkable for the large number of different biochemical characteristics; it is thought that the metabolic variability might be related to the very diverse habitats of this species. The divergent reactions may indicate the possible existence of multiple ecovars within *S. pluranimalium* showing typical host-specific or even site-specific characteristics, as is well known in other streptococci [2].

We report a case of gastroenteritis with subsequently septic shock leading to sudden death of an immunocompetent man, despite adequate management. In a first moment *S. Pluranimalium* was isolated, however results took a surprising twist when the strain was tested for molecular identification.

2. PRESENTATION OF CASE

A 36-year-old Peruvian male came to the Emergency Department (ED) of a private clinic in Lima, Peru with 24-hour history of fever, nausea, non-bilious vomits and abundant non-dysenteric, fetid diarrhea. The patient had just returned from a four-day beach trip to the Peruvian-coast where he stayed until two days prior to his arrival to the ED. One day before returning, the patient reported eating rotisserie chicken in a local restaurant. His past medical history was unremarkable. His vitals were BP 110/60, HR 74 x', RR 20 and T 37°C. Physical examination revealed mild lower abdominal tenderness to deep palpation without rebound or guarding. He was admitted with a diagnosis of gastroenteritis and started on intravenous hydration and Ceftriaxone 2 g QD.

Eight hours later, he became toxic with tachycardia, dyspnea, oxygen desaturation

(85%), hypotensive, febrile, with slightly distended and tympanic abdomen, reduced bowel sounds, and diffuse erythematous rash with conjunctival injection. He was transferred to the Intensive Care Unit with a presumed diagnosis of staphylococcal toxic shock syndrome. Laboratory analysis during the first and second day of hospitalization were significantly altered (Table 1).

Despite intensive vasopressor therapy and broad-spectrum antibiotics (Meropenem 1g TID, Vancomycin 1 gr BID and Oxacilin 1g Q4h), the patient persisted with hypotension and developed hypoxemia, acidosis, oliguric acute kidney injury and disseminated intravascular coagulation. Therapy was established for septic shock and drugs were titrated for renal clearance. Dengue and malaria were ruled out. Three blood cultures were collected in a BACTEC 9050 system. The first blood culture showed gram positive cocci on gram stain. Non-beta-haemolytic colonies were described on sheep blood agar. A Vitek system was used for processing and results were consistent with *Streptococcus pluranimalium* sensitive to Ampicillin, Ceftriaxone, Clindamycin, Erythromycin, Levofloxacin, Nitrofurantoin, Penicillin, Trimethoprim/Sulfamethoxazole and Vancomycin. The other two blood cultures were negative, as well as a second seed of the former blood culture. Further studies identified the isolated bacteria as non-beta-haemolytic *Streptococcus pyogenes*. Unfortunately, patient died of multiorgan failure on the second day of admission, before the strain was identified.

3. DISCUSSION

The main literature about *Streptococcus pluranimalium* comes from animal studies. Aside from above described, the organism has been found in ovine and bovine reproductive material including placentas and abortion materials [3,4]. It has been associated with mening oventriculitis in a calf, probably as a sequel of septicemia [5]. Cases of septicemia and valvular endocarditis in broiler parent stock are also reported [6].

Human infection by *Streptococcus pluranimalium* has been detailed in four case reports and one

diagnostic performance study. Paolucci et al. reported the first isolation in 2012 while analyzing a real-time polymerase chain reaction (PCR) test (SeptiFast) for early detection of bloodstream infection in febrile neutropenic patients [7]. In 2014, Jacob et al. described a case of a 53-year-old female with septic arthritis of the right knee who developed sepsis and multi organ dysfunction, causing the patient's death [8]. Aryasinghe et al. in 2014 reported the third case of *Streptococcus pluranimalium* in a 17-year-old French male who developed subdural empyema as a complication of a presumed asymptomatic sinusitis and recovered with no residual neurological deficit [9]. The fourth and fifth cases were reported as infective endocarditis in an intravenous drug user and a Down's syndrome man, respectively [10,11]. Some interesting facts among all cases, including the current report are presented below (Table 2).

Patients were in the age range of 17 and 53 years and were immunocompetent. Four cases (80%) had acute presentation as well as rapid progression of the disease. Intensive medical/surgical treatment were initiated with a fatality rate of 60%. All isolates were analyzed with VITEK 2 system, however only our strain was processed with additional molecular studies.

The antibiotic sensitivity of *Streptococcus pluranimalium* is available in 4 out of 5 cases; the antibiogram showed sensitivity to penicillin, first and second generation cephalosporins, erythromycin, aminoglycosides, linezolid and vancomycin among others. The most common antibiotics used were vancomycin and meropenem. Of note, two of the patients reported being on a tropical beach a week before the presentation of symptoms. It is important to mention that other diagnoses were considered, such as dengue and malaria because of the epidemiologic context, however they were ruled out. Furthermore, diabetes and human immunodeficiency virus were excluded to be predisposing conditions in this patient.

Surprisingly, the previous isolated strain obtained from the blood culture was identified as a non-beta-haemolytic *Streptococcus pyogenes* through more complex methods, including pyrrolidonyl arylamidase (PYR) test, a lateral flow test (ABON Strep A Rapid test device), and 16S ribosomal RNA sequencing confirmed by the reference laboratory of the National Institute of Health (INS -Peru).

It has been reported that the non-haemolytic *Streptococcus pyogenes* has a premature stop codon, modifying the gene of streptolysin S,

Table 1. Laboratory values

	Day 0	Day 1	Day 2
Hcto (%) / Hb (gr/dl)	40.5 / 13.9	36.9 / 12.2	32.2 / 10.9
Leuco	2630	2890	15390
(Ban,N,E,Bas,M,L)	(30,60,0,0,0, 10)	(26,32,4,1,11,24)	(24,65,0,0,0,3,8)
Platelets (10 ³ /mm ³)	174 000	79 000	91 000
PT / INR	> 180 / -	78.2 / 7.32	33 / 2.96
aPTT	> 200	172.7	131.1
Fibrinogen	< 80	< 80	-
Urea / Creatinine	44 / 2.49	64 / 4.52	85 / 5.82
Na / K	142 / 2.9	141 / 3.67	143 / 4.94
C-Reactive Protein	13.51	64.62	116.17
pH	7.2	7.24	6.99
PaO ₂	56	94.7	43.2
PaCO ₂	24.5	37.2	63.5
HCO ₃ ⁻	10.3	15.8	15.3
Pa/Fi	112	94.7	43.2
Lactate	11.42	11.64	16.02
AST / ALT	16 / -	233/55	1065 / 506
Alk Phos	91	129	152
Glucose	35*	213	151
CPK	165		
Blood Culture	1 positive for <i>S. pluranimalium</i>	2 negatives	-

Hcto: Hematocrit, Hb: Hemoglobin, Leuco: Leukocyte, Ban: Bands, N: Neutrophils, E: Eosinophils, Bas: Basophils, M: Monocytes, L: Lymphocytes, PT: Prothrombin Time, INR: International Normalized Ratio, aPTT: activated partial thromboplastine time, Na: Sodium, K: Potassium, PaO₂: Partial pressure of oxygen in arterial blood, PaCO₂: Partial pressure of oxygen in arterial blood, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, Alk Phos: Alkaline Phosphatase, CPK: Creatine Phosphokinase. *Hemoglucotest

Table 2. Comparison of past research on *Streptococcus pluranimalium* human's infections

	Case 1	Case 2	Case 3	Case 4	Present case
Year of publication	2014	2014	2015	2016	2017
Country of origin	India	France (African ethnicity)	USA	Colombia	Peru
Age (years)	53	17	37	25	36
Onset of symptoms	4 days	2 days	15 days	3 months	1 day
Gender	Female	Male	Male	Male	Male
Symptoms /signs	Fever and right knee flogosis	Headache, nausea and lethargy	Left leg tenderness, and fever / murmur	Fever, dyspnea and weight loss	Fever, nausea, vomits and diarrhea
Epidemio. context	None	He was in Dubai 7 days prior to admission	None	Contact with farm animals	He was on the beach and ate rotisserie chicken 2 days prior to admission
Past medical history	Knee osteoarthritis and obesity	Long standing dental infection	IVDA	Down Syndrome, and chronic kidney disease	None
Initial site of infection	Right knee arthritis	CNS - Subdural empyema	Endocarditis with peripheral emboli	Endocarditis	Gastroenteritis
Specimen collection	Synovial fluid and blood	Subdural empyema	Peripheral emboli and vegetation	Blood	Blood
Characteristics of bacteria	Gram positive cocci identified as tiny no haemolytic colonies	Gram positive cocci and gram negative rods	Colonies of cocci	Gram positive cocci	Gram positive cocci identified as non-beta haemolytic colonies
Microbial identify. system	Vitek2	Vitek2	Vitek2	Vitek2	Vitek2, PYR test, ABON rapid Strep A rapid test and 16S RNA sequencing
Antimicrobial susceptibility pattern	Ampicillin, vancomycin, linezolid, rifampicin, erythromycin, amikacin, gentamicin, teicoplanin.	Penicillin, clindamycin, erythromycin, vancomycin, linezolid and cefepime	Vancomycin and gentamycin	Penicillin, clindamycin, erythromycin, cefotaxime and vancomycin	Penicillin, cephalosporins, erythromycin, aminoglycosides, linezolid and vancomycin
Therapy	IV antibiotics and drainage	IV antibiotics and drainage	IV antibiotics, embolectomy and cardiac surgery	IV antibiotics and cardiac surgery	IV antibiotics
Antibiotic	Not specified	meropenem and vancomycin	vancomycin and gentamycin	ampicillin/sulbactam	Meropenem and vancomycin
Outcome	Rapid deterioration and death on day 3	Total recovery	He died month after cardiac surgery	Total recovery	Rapid deterioration and death on day 2

Epidemio. Context: Epidemiological context

accounted for loss of hemolytic activity [12,13]. Although the hemolysis is characteristic for *Streptococcus pyogenes*, it is not fully understood the role in its pathogenicity [14,15].

4. CONCLUSION

The detection of uncommon human pathogens in challenging clinical scenarios requires an early and accurate typification.

CONSENT

All authors declare that written informed consent was obtained from the patient's parents for publication of this case report.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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