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Group A Streptococci: A rare and often misdiagnosed cause of spontaneous bacterial peritonitis in adults



Mark Malota^{a,*}, Thomas W. Felbinger^b, Reinhard Ruppert^a, Natascha C. Nüssler^a

^a Department of General and Visceral Surgery, Endocrine Surgery and Coloproctology, Klinikum Neuperlach, Städtisches Klinikum München GmbH, Munich, Germany

^b Department of Anesthesiology, Critical Care and Pain Medicine, Klinikum Neuperlach, Städtisches Klinikum München GmbH, Munich, Germany

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ABSTRACT

INTRODUCTION: Acute primary peritonitis due to group A Streptococci (GAS) is a rare but life-threatening infection. Unlike other forms of primary peritonitis it affects predominantly young previously healthy individuals and thus is often confused with the more frequent secondary peritonitis. A case series of three patients is presented as well as a review of the literature focusing on pitfalls in the diagnose and therapy of GAS peritonitis.

METHODS: A retrospective analysis of three patients with primary GAS peritonitis was performed. Furthermore a systematic review of all cases of primary GAS peritonitis published from 1990 to 2013 was performed comparing demographics and clinical presentation, as well as radiological imaging, treatment and outcome.

RESULTS: All three female patients presented initially with high fever, nausea and severe abdominal pain. Radiological imaging revealed intraperitoneal fluid collections of various degrees, but no underlying cause of peritonitis. Broad antibiotic treatment was started and surgical exploration was performed for acute abdomen in all three cases. Intraoperatively fibrinous peritonitis was observed, but the correct diagnosis was not made until microbiological analysis confirmed GAS peritonitis. One patient died within 24h after admission. The other two patients recovered after multiple surgeries and several weeks on the intensive care unit due to multiple organ dysfunction syndrome. The fulminant clinical course of the three patients resembled those of many of the published cases: flu-like symptoms, high fever, severe acute abdominal pain and fibrinous peritonitis without obvious infectious focus were the most common symptoms reported in the literature.

CONCLUSION: GAS primary peritonitis should be considered in particular in young, previously healthy women who present with peritonitis but lack radiological findings of an infectious focus. The treatment of choice is immediate antibiotic therapy. Surgical intervention is difficult to avoid, since the diagnosis of GAS peritonitis is usually not confirmed until other causes of secondary peritonitis have been excluded.

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1. Introduction

The vast majority of surgical patients with peritonitis suffer from secondary peritonitis due to perforation of hollow viscera or leakage from an intestinal anastomosis. In these cases, surgical clearance of the infectious focus is the treatment of choice. In contrast, patients with primary peritonitis rarely require surgical therapy and the mainstay of treatment is antibiotic therapy.¹ The mechanism of primary peritonitis is not completely

understood, but increased translocation of intestinal bacteria, retrograde inoculation from the genitourinary tract or hematogenous infectious routes have been discussed.² Since primary peritonitis is hardly seen in healthy individuals, impaired clearance of infectious pathogens due to medical conditions like liver cirrhosis, immunosuppression, or nephrotic syndrome is believed to predispose for the development of primary peritonitis.^{1–8}

Historically, primary peritonitis has been caused predominantly by gram-negative bacteria, but lately an increase of gram-positive bacteria including streptococcus pneumoniae has been observed. In contrast, Lancefield group A β-hemolytic Streptococci (GAS) which are typically associated with pharyngitis, erysipelas, scarlet fever or rheumatic, rarely cause primary peritonitis or life-threatening fulminant sepsis.³

Due to the scarcity of primary GAS peritonitis, only case reports and small case series have been published during the last

Abbreviations: GAS, group A β-hemolytic Streptococci; ICU, intensive care unit.

* Corresponding author at: Department of General and Visceral Surgery, Endocrine Surgery and Coloproctology, Klinikum Neuperlach, Oskar-Maria-Graf-Ring 51, 81737 Munich, Germany. Tel.: +49 089 67 94 25 01; fax: +49 089 67 94 3243.

E-mail addresses: mark.malota@klinikum-muenchen.de, markmalota@hotmail.com (M. Malota).

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decades.^{4–30} In almost all published cases, as well as in our small series of three patients, similar clinical symptoms are reported. The most striking observation however, was the high incidence of exploratory laparotomies or laparoscopies. In retrospect many of these surgical procedures may have been avoidable, if the primary nature of the peritonitis had been recognized.^{9–11} We therefore try to highlight the predominant symptoms as well as the preferable diagnostic procedures for timely diagnosis and therapy of GAS peritonitis.

2. Case reports

#1: A 23-year-old female student was admitted to the emergency department with severe abdominal pain in the right lower quadrant, a temperature of 39.1 °C; tachycardia (98/min) and mild hypotension (100/60 mmHg). Six hours prior to admittance she had been treated by her general practitioner with non-steroidal anti-inflammatory drugs and penicillin for suspicion of tonsillitis despite a negative Rapid Strep Test. She had no relevant medical history and did not take any regular medication. Upon physical examination she displayed a localized peritonism in the right lower quadrant. Blood analysis revealed massive leukocytosis (25/nl) and an elevated C-reactive protein (115 mg/l). Due to the provisional diagnosis of acute appendicitis, antibiotic treatment with piperacillin and sulbactam was initiated and she was taken to operating room. Laparoscopic examination revealed small amounts of free intra-abdominal fluid and a moderately inflamed appendix vermiformis. Therefore, laparoscopic appendectomy was performed. In contrast to the moderate inflammatory findings upon laparoscopy, the patient's postoperative condition deteriorated rapidly and a second-look laparotomy was performed 8 h after the first operation after stabilization in the ICU. During the second operation massive purulent ascites was found. However, neither hollow visceral organ perforation nor any other focus could be detected. Despite all efforts, the patient remained in septic shock and died within 24 h after admission from multiorgan failure. Blood cultures of the peritoneal fluid were positive for GAS. Furthermore, histological examination of the appendix confirmed infection with β -hemolytic group A Streptococci.

#2: The second patient (female, 34 years old) presented with unspecific abdominal pain and septic shock (tachycardia 100/min, RR 85/60 mmHg, Leucocytes 55/nl, CRP 200 mg/l) eight days after hysteroscopic removal of an intrauterine pessary. Abdominal ultrasound revealed free intra-abdominal fluid and edematous swelling of the small intestine. Computed tomography (CT) confirmed the small intestinal edema. An unspecific bowel infection was suspected and antibiotic treatment with cefazolin and metronidazole was initiated. Within hours, the patient developed rhabdomyolysis, acute renal and acute hepatic failure with disseminated intravascular coagulation. Laparotomy became necessary for abdominal compartment syndrome. Intraoperatively, fibrinous peritonitis was observed, but no focus could be identified. An intra-abdominal vacuum dressing was applied. The antibiotic therapy was escalated to imipenem and vancomycin when blood cultures and ascites were positive for gram-positive cocci. Multiple consecutive abdominal lavages with intra-abdominal vacuum dressings were required until the abdomen could be closed seven weeks later after complicated postoperative treatment on the ICU. The patient was discharged on the 58th postoperative day.

#3: A 36-year old woman was admitted with petechiae, peritonitis of the lower abdomen and septic shock (tachycardia 100/min, RR 90/50 mmHg, Temp 38.9 °C). Five days before her husband had suffered from a GAS pharyngitis but she had no clinical findings in the upper respiratory tract. Blood analysis showed leukocytosis (21/nl), elevated C-reactive protein (152 mg/l) and rhabdomyolysis (CK 8211 U/l). CT scan revealed large amounts of

intra-abdominal fluid, but no infectious focus could be detected. Purulent ascites was retrieved by ultrasound guided abdominal paracentesis. Antibiotic therapy with piperacillin and tazobactam was initiated and since secondary peritonitis was suspected, the patient was taken to the operating room. Laparotomy confirmed fibrinous purulent peritonitis, but no obvious source of infection could be identified. Blood cultures and ascites culture showed gram-positive cocci, which were further characterized as GAS. During the following weeks, multiple laparotomies were necessary and eventually a Hartmann's procedure was performed for ischemia of the sigmoid colon. 56 days after the first operation, the patient could be discharged. Gastrointestinal continuity was restored eight months thereafter. The source of GAS infection remained unclear.

3. Published case reports and case series

A PubMed literature search for “primary peritonitis” and “streptococcus group A” for publication years from 1990 to 2014 was performed. 26 publications of case reports or small case series with a total of 35 adult patients as well as one review could be identified.^{4–30} Publications about pediatric patients were not included in this analysis. The demographic characteristics and the clinical symptoms of the published patients are summarized in Table 1.

Predominantly, young women were affected resulting in a female:male ratio of 4:1. The median age was 38 years (range 22–87 years). Five patients were older than 50 years and one female patient was 87 years at the time of diagnosis.^{4,5,18,28} Medical history of almost all patients had been uneventful prior to GAS peritonitis. Risk factors for primary peritonitis (immunosuppression, liver cirrhosis, diabetes) were reported in 8 of the 35 (23%) patients.

On admission, severe abdominal pain and high fever were the most frequent symptoms. In some patients, diarrhea and flu-like symptoms (fatigue, muscle aches) have been reported. Toxic shock syndrome was observed in 13 of 35 patients (Table 1).^{4,7,13,17–19,22,24,25}

CT scan was performed in 29 patients (83%) (Table 2) and revealed various amounts of intra-abdominal fluid collections, as well as intestinal edema, but no obvious cause of infection such as appendicitis, diverticulitis or perforation. The lack of an infectious focus led to the suspicion of primary peritonitis only in 2 patients whereas 34 patients (97%) were taken to the operating room despite negative results of the CT scan (Table 2).¹⁸

Broad-spectrum antibiotic treatment was initiated in all patients. However, in 10 patients no information was provided whether the initially chosen antibiotic was effective against Streptococci (Table 2). In 19 of the remaining 24 patients (79%) the initial antibiotic regimen was already effective for the treatment of GAS infection.^{4,6–11,14,16,18,20,21,24,27} In 14% ($n=5$) antibiotic therapy was altered during the course of the disease. In all but one patient final antibiotic therapy was effective for the treatment of GAS infection.²⁶ Blood cultures were positive in 29 patients (83%) (Table 2).

In most patients, the source of infection remained unclear. Among those with confirmed sources, ascending vaginal infections and pharyngitis were most the frequent (Table 2).^{6,8,9,11,12,19}

All patients published in the literature were reported to have recovered from GAS peritonitis, whereas in our series one of three patients died within 24 h after admission.

4. Discussion

Group A Streptococci predominantly cause upper respiratory tract and cutaneous infections, whereas spontaneous primary peritonitis in adults caused by GAS is rare.²⁹ The scarcity of this disease is reflected by the small number of patients reported in the

Table 1
Demographics and clinical presentation of patients with GAS peritonitis.

Author	Publication year	Demographics		Symptoms on admission			
		Sex	Age	Acute abdomen	Fever at >38.5°C	Toxic shock syndrome	Additional symptoms
Gribbin	1990	M	44	Yes	Yes		Nausea
Christen	1990	F	50		Yes	Yes	
		F	58	Yes	Yes	Yes	Vomiting and diarrhea
Casadevall	1990	F	87	Yes	Yes		
		F	42		n.d.		
Graham	1995	F	39	Yes	Yes	Yes	
Moskovitz	2000	F	39	Yes	Yes		Diarrhea and myalgia
Legras	2001	F	22	Yes	Yes		
Vuilleumier	2001	F	33	Yes	No	Yes	
Borgia	2001	F	36	Yes	n.d.		
Fox	2002	F	36		Yes	Yes	
Ueyama	2001	F	39	Yes	Yes		Vaginal discharge
Sanchez	2001	M	34	Yes	n.d.		
Okumura	2004	F	29	Yes	No		
Kanetake	2004	M	40	Yes	n.d.	Yes	
Brivet	2005	F	54	Yes	Yes	Yes	Renal failure
		F	82	Yes	Yes	Yes	Vomiting and diarrhea
Jarvis	2006	F	38	Yes	Yes	Yes	Vomiting and diarrhea
		F	30	Yes	n.d.		Nausea and rigors
Saha	2006	F	23	Yes	Yes		Vomiting and diarrhea
van Lelyveld-Haas	2008	F	28	Yes	Yes		
Doloy	2008	F	35		Yes		
Thomas	2009	M	36		n.d.	Yes	
Kinsella	2009	M	38		n.d.		n.d.
Haap	2010	F	27	Yes	n.d.		Nausea and diarrhea
Tilanus	2010	F	39		Yes	Yes	
		M			n.d.	Yes	
		F		Yes	No		
		F		Yes	n.d.		
		F		Yes	Yes		
Legras	2011	F	32	Yes	Yes		Pharyngitis
Nogami	2014	F	40	Yes	Yes		Flue-like symptoms
Min	2014	F	51	Yes	Yes		Gastitis

literature: only 35 cases of GAS peritonitis have been published since 1990.^{4–30} The vast majority of these 35 patients were young previously healthy women. On admission most of them presented in septic condition with severe abdominal pain and high fever and secondary peritonitis was suspected. Based on this erroneous diagnosis all but one patient¹⁸ were operated despite negative results of the radiologic imaging. We here report about another three patients suffering from GAS peritonitis. Their clinical presentation as well their treatment bear a close resemblance to the published cases: all three young women presented with severe abdominal pain and fever. Secondary peritonitis was suspected and this false diagnosis was pursued even though CT scans failed to identify an infectious focus.

It has to be noted though, that a negative CT scan does not exclude secondary peritonitis which may be due to various diseases such as perforated appendicitis ruptured ovarian cyst or diverticulitis.^{18,31} Immediate surgery and removal of the infectious focus is the mainstay of treatment of secondary peritonitis and any delay of surgical therapy is likely to impair the recovery of these patients.² Therefore exploratory laparotomy despite negative radiologic imaging is a well-accepted treatment option in septic patients. This strategy may explain the high rate of exploratory surgery in patients with GAS peritonitis. In these predominantly young patients with acute onset of peritonitis, most surgeons would have suspected secondary peritonitis rather than any type of primary peritonitis.^{31–33}

It remains unclear however, whether surgical exploration and lavage of the abdominal cavity is beneficial or detrimental for patients with GAS peritonitis. One could assume that removal of infectious ascites and reduction of intra-abdominal bacterial load

support the healing process. However, in cirrhotic patients with spontaneous bacterial peritonitis, surgery does not improve the course of the disease.¹ Given the fact that GAS peritonitis is also a form of primary peritonitis, it is conceivable that surgery may carry more risks than benefits for patients with GAS peritonitis. Thus, prevention of surgery in these patients would be desirable and a rapid antigen detection test should be considered prior to surgery in young female patients, who present with acute onset of peritonitis but lack an infectious focus in radiologic imaging. In patients with positive rapid antigen detection test, surgery should be postponed and antibiotic therapy should be initiated as soon as possible.³⁴ GAS are sensitive to beta-lactam antibiotics and penicillin is recommended for uncomplicated GAS infections.^{34–37} However, there seems to be little consensus regarding the antibiotic treatment for GAS peritonitis and only little information has been published about the antibiotic regimens chosen for the treatment of patients with GAS peritonitis.² In general, any septic patient will be treated initially with broad-spectrum antibiotics. Similarly, our patients received a combination of piperacillin and tazobactam according to our institutional guidelines. Once results of blood cultures were available, antibiotic therapy was adjusted accordingly. Fortunately, most patients survive and recover completely from this life-threatening disease after a long hospital stay.

The entry site of GAS in patients with peritonitis is not well understood.³⁵ The predominance of women among patients suffering from GAS peritonitis foster the suspicion of ascending infections of the genitourinary tract, since GAS are often part of the vaginal flora.³⁸ Increased virulence of some GAS serotypes as well as an impaired humoral response may further contribute to the increasing frequency of invasive GAS infections.³⁶ Other potential entry

Table 2
Diagnostics and therapy of patients with GAS peritonitis.

Author	Radiological imaging	Surgical interventions		Blood cultures	Antibiotics effective against GAS?		Source of GAS infection
		Laparoscopy	Laparotomy		Initial therapy	Final therapy	
Gribbin	Ultrasound		+	Pos	n.d.		Pharyngitis
Christen	Ultrasound		+	Pos	(+)	+	Unidentified
	Ultrasound		+	Pos	+	+	Unidentified
Casadevall	Ultrasound		+	Pos	n.d.		Unidentified
	CT	+		Neg	n.d.		Unidentified
Graham	CT		+	Pos	+	+	Pharyngitis
Moskovitz	CT		+	Pos	(+)	+	Vaginal
Vuilleumier	CT		+	Pos	+	+	Vaginal
Borgia	CT		+	Pos	+	+	Vaginal
Fox	CT		+	Pos	–	+	Unidentified
Ueyama	CT		+	Pos	+	No change	Unidentified
Sanchez	CT	+		Neg	+	No change	Unidentified
Okumura	CT		+	Pos	n.d.		Pharyngitis
Kanetake	CT		+	Pos	n.d.		Pharyngitis
Brivet	CT	+	–	Neg	+	(+)	Unidentified
	CT	–	–	Neg	+	No change	Unidentified
Jarvis	CT		+	Pos	n.d.		Unidentified
	CT		+	Pos	n.d.		Vaginal
Saha	CT		+	Pos	+	+	Unidentified
van Lelyveld-Haas	Ultrasound		+	Pos	+	+	Vaginal
Doloy	Ultrasound	+		Neg	+	+	Unidentified
Thomas	CT		+	Neg	n.d.		Unidentified
Kinsella	CT		+	Pos	n.d.		Insect bite
Haap	CT		+	Pos	+	No change	Unidentified
Tilanus	CT		+	Pos	+	+	Unidentified
Monneuse	CT		+	Pos	n.d.		Unidentified
	CT		+	Pos	+		Unidentified
	CT		+	Pos	–	+	Unidentified
	CT		+	Pos	+		Unidentified
	CT		+	Pos	+		Fasciitis
	CT		+	Pos	–	+	Fasciitis
	CT		+	Pos	–	n.d.	Pharyngitis
Legras	CT	+		Pos	–	n.d.	Pharyngitis
Nogami	CT		+	Pos	+	No change	Pharyngitis
Min	CT		+	Pos	–	+	Unidentified

sites of GAS include the upper respiratory tract, superinfections of insect bites or other minor skin lesions with hematogenous spread of GAS, as well as the direct transluminal spread from the bowel, especially in patients with streptococcal proctocolitis have also been reported.³⁹ However, in many of the published cases, the source of GAS infection remained obscure rendering preventive measures impossible.^{37–43}

5. Conclusion

GAS peritonitis is a rare type of primary peritonitis, which may be easily confused with secondary peritonitis. In young, previously healthy women who present in septic condition but lack radiologic signs of secondary peritonitis, an infection with GAS should be considered. The treatment of choice is the fast initiation of antibiotic therapy. Although surgical therapy is generally not required for the treatment of GAS peritonitis, it may be necessary to exclude secondary peritonitis.

Conflict of interest

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Ethical approval

Written informed consent was obtained from the patient for publication of this case report and its accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contributions

Mark Malota contributed to acquisition of data and writing manuscript. Nüssler and Felbinger contributed to writing manuscript. Ruppert contributed to study conception and design and writing manuscript.

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