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<u>Sex as a biological variable</u>
not detected.
<u>Subject Demographics</u>
Age: not detected.
Weight: not detected.
<u>Randomization</u>
not detected.
<u>Blinding</u>
not detected.
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Invasive *Streptococcus pyogenes* Infection:

A case report

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Abstract

The Group A Streptococcus (GAS), also known as *Streptococcus pyogenes*, is a human pathogen causing various infections, ranging from mild, such as tonsillitis and impetigo, to severe and invasive conditions like septicemia and necrotizing fasciitis. Despite a decline in incidence and severity during the 20th century due to antibiotics, there has been a reported increase in severe cases since the 1980s in industrialized countries.

Streptococcus pyogenes (*S. pyogenes*) is a human pathogen with a natural reservoir in the pharynx and skin, exhibits asymptomatic carriage in various body sites. It is responsible for a spectrum of clinical manifestations, from asymptomatic carriage to severe invasive infections. Transmission occurs through respiratory droplets or direct contact with skin lesions. Bacteriologically, *S. pyogenes* is gram-positive β -hemolytic streptococcus. This summary highlights a case of invasive Group A Streptococcus infection in a 28-year-old diagnosed at the microbiology laboratory of the Mohammed V Military Training Hospital in Rabat, Morocco.

A 28-year-old patient, with a history of chickenpox, presented with acute febrile oligoarthritis. Following a recent flu-like syndrome and febrile tonsillitis, the patient experienced asymmetric inflammatory oligoarthritis affecting the left knee, left ankle, and right shoulder, accompanied by functional impairment of the left lower limb. Upon admission, clinical examination revealed swelling, positive patellar tap, and sternal involvement. Laboratory and imaging findings indicated an abscessed collection in the left knee and anterior mediastinitis. Emergency aspirations revealed Group A Streptococcus, specifically *Streptococcus pyogenes*, leading to a diagnosis of septic arthritis. Dual antibiotic therapy and knee joint drainage resulted in symptom resolution after 45 days.

The rise in severe Group A Streptococcus infection underscores the need for early detection and treatment. Widely sharing the French High Council for Public Health's antibiotic prophylaxis recommendations is crucial for awareness. Collaborating between clinicians and microbiologists is essential for effective management.

52

53 **Key words:** Invasive infection, Streptococcus pyogenes, Septic arthritis.

54

55 **Data Summary**

56

57 No data was generated during this research or is required for the work to be reproduced.

58

59 **Introduction**

60

61 The Group A Streptococcus (GAS), or *Streptococcus pyogenes*, is a strictly human pathogen
62 capable of causing a wide range of infections, either benign such as tonsillitis [1] and impetigo,
63 or severe and invasive such as septicemia, streptococcal toxic shock syndrome (STSS), and
64 Necrotizing fasciitis [2].

65 In the course of the 20th century, these infections experienced a significant decrease in both
66 their incidence and severity, primarily due to the advent of antibiotic therapy. However, an
67 increase in the frequency of severe infections, sometimes in the form of clustered cases, has
68 been reported since the early 1980s in several industrialized countries [3]. We present a case of
69 invasive Group A Streptococcus infection in a 28-year-old adult diagnosed at the microbiology
70 laboratory of the Mohammed V Military Training Hospital in Rabat Morocco.

71

72 **Case Presentation**

73

74 This concerns a 28-year-old patient admitted to the emergency department for acute febrile
75 oligoarthritis evolving for 7 days. In his medical history, a history of chickenpox at the age of
76 7 was noted, with no history of recurrent sore throats, scarlet fever, or allergic rhinitis. One
77 month before hospitalization, he had presented with a flu-like syndrome associated with febrile
78 tonsillitis, symptomatically treated with good clinical improvement.

79 Twenty-one days later, the patient reported the rapid onset of asymmetric inflammatory
80 oligoarthralgia involving the left knee, left ankle, and right shoulder, leading to total functional
81 impairment of the left lower limb, associated with swelling of the sternocostal region. This
82 evolution occurred in the context of a general state alteration, unquantified fever, anorexia, and
83 unquantified weight loss.

84 Upon admission, the patient was stable neurologically, hemodynamically, and respiratorily,
85 with a GCS of 15, normotensive at 11/7, tachycardic at 108 beats/min, polypneic at 22
86 cycles/min, SaO₂ at 98%, and a central temperature at 38°C. Conjunctivas were normally
87 colored, the throat was clean with poor oral hygiene.

88 The musculoskeletal examination showed painful swelling of the left ankle and left knee with
89 filling of the subquadriceptal recess and a positive patellar tap on palpation. The Womac score
90 was 88. The hips were free and painless, but there was a painful satellite adenopathy in the left
91 inguinal region.

92 In the thorax, there was a painful anterior sternal swelling, irregular in contour, soft and mobile
93 in the deep plane. The skin examination revealed an erythematous, edematous patch on the
94 anterior surface of both ankles and legs with infiltration of the soft tissues of the left leg (Figure
95 1). Additionally, there were no wounds, fistulas, or pustules.

96 The rest of the clinical examination was unremarkable. The initial biological assessment
97 showed leukocytosis at 19,500 cells/mm³, with 89.4% neutrophils and lymphopenia at 1300
98 cells/mm³. There was a clear inflammatory syndrome with a serum C-reactive protein (CRP)
99 level of 453 mg/L, ferritin above 1600 ng/mL, corrected calcium at 104 mg/L, uric acid at 24
100 g/L. Renal function was normal, proteinuria was 435 mg/L, and the hepatic assessment was
101 unremarkable. HIV, HCV, and HBV serologies were negative.

102 The infectious assessment noted negative aerobic-anaerobic blood cultures and a sterile urine
103 culture.

104



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Fig. 1. Painful swelling of the left ankle and left knee

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The Magnetic Resonance Imaging (MRI) of the left knee revealed an abscessed collection
122 extending from the subquadriceptal recess to the lateral external recess, measuring 22x99 mm
123 and showing hypodensity, associated with infiltration of adjacent soft tissues (**Fig. 2**).

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Fig. 2. MRI of the left knee showing an abscessed collection extending from the
127 subquadriceptal recess to the lateral external recess, measuring 22x99 mm, with hypodensity.

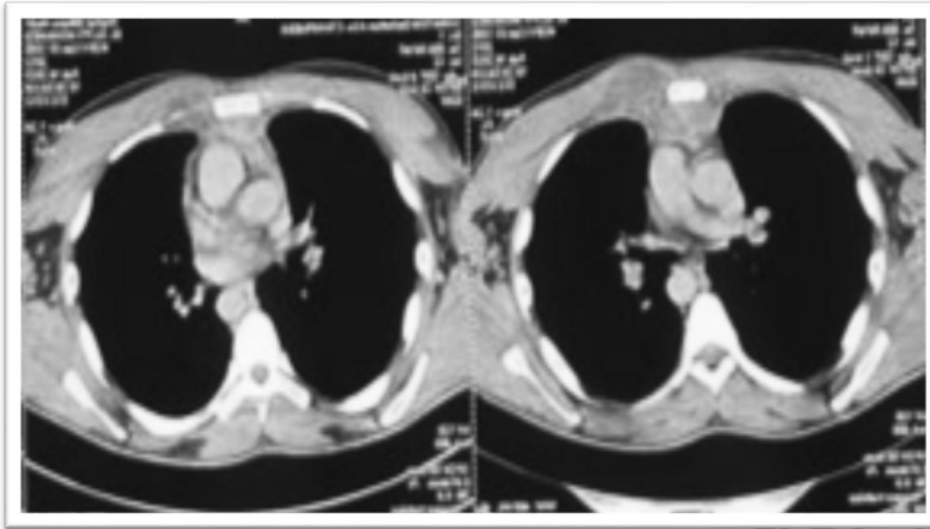
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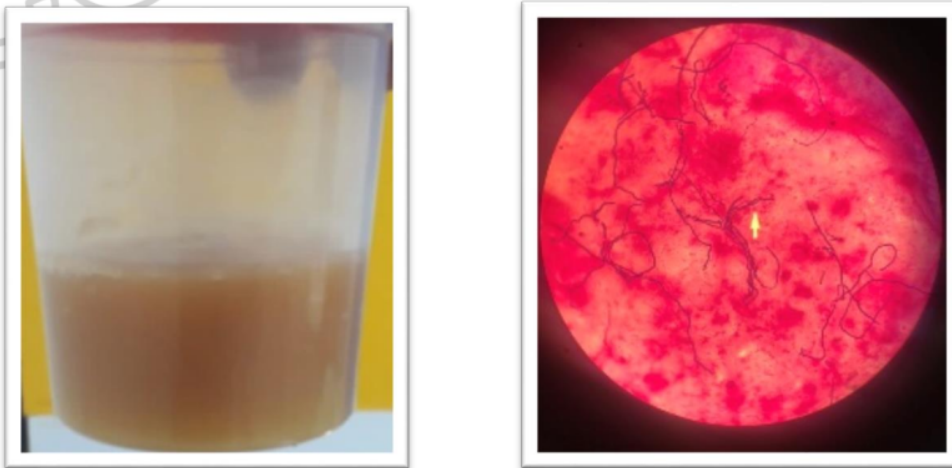
The thoraco-abdomino-pelvic computed tomography showed a pre- and retrosternal collection
131 extending towards the cervicothoracic orifice, measuring 63x74x97 mm, with sternal erosion
132 and the onset of anterior mediastinitis (**Fig. 3**).

133



134
135 **Fig. 3.** Thoracic CT scan showing a pre- and retrosternal collection extending towards the
136 cervicothoracic orifice, measuring 63x74x97 mm, with sternal erosion and the onset of
137 anterior mediastinitis.
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139 Faced with this clinical presentation of left knee arthritis associated with a probable infectious
140 anterior mediastinitis, emergency joint and mediastinal aspirations were performed,
141 supplemented by a cyto-bacteriological examination of the samples, revealing a turbid aspect
142 (**Fig. 4**). Cytology showed 28,800 mm³ of lymphocytes, 4,800 mm³ of erythrocytes, with a
143 leukocytic formula consisting of 99% polymorphonuclear neutrophils (PMNs).
144 Aerobic-anaerobic culture yielded a strongly positive result for numerous Group A
145 *Streptococcus*. The aerobic-anaerobic culture was positive, isolating and identifying
146 *Streptococcus pyogenes*.
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148
149 **Fig. 4.** Microbiological examination of the joint aspiration
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The antibiotic sensitivity study was determined using the agar diffusion method on Mueller-Hinton agar (MH), following the recommendations prescribed by the European Society of Clinical Microbiology and infections Diseases (CA-SFM) [4]. (Table I)

Table I. The antibiotic sensitivity.

Group A Streptococcus		
	Categorization	Minimum Inhibitory Concentration (MIC) mg/L
Penicilline G	Sensitive	≤ 0,25
Gentamycine	Sensitive	≤ 256
Tetracycline	Sensitive	4
Erythromycine	Sensitive	< 0,06
Pristinamycine	Sensitive	0,0625
Clindamycine	Sensitive	= 0,5
Linezolid	Sensitive	0,25
Vancomycine	Sensitive	= 2
Teicoplanine	Sensitive	= 2
Moxifloxacin	Sensitive	= 0,5

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Thus, the diagnosis of septic arthritis due to Group A streptococcus (pyogenic) was established, and the patient received dual antibiotic therapy comprising ceftriaxone 2 g/day and ciprofloxacin 500 mg twice daily. This was followed by knee joint drainage. The clinical and biological response to treatment was marked by the resolution of inflammatory symptoms after 45 days of antibiotic therapy.

Discussion

S.pyogenes is a human pathogen with a natural reservoir in the pharynx and skin. It can be isolated in asymptomatic carriers from the nasopharynx, skin, vagina, or rectum. The bacterium is responsible for a wide range of clinical manifestations, from asymptomatic carriage to severe invasive infections that can rapidly compromise the prognosis [5]. Interhuman transmission of *S. pyogenes* occurs through droplets from the upper respiratory tract or direct contact with skin lesions. Bacteriologically, *S. pyogenes* is a gram-positive β-

178 hemolytic streptococcus, catalase-negative, and oxidase-negative. It is a facultative anaerobe,
179 grows better in 5 to 10% carbon dioxide, and forms distinct colonies on blood agar plates.
180 Among the numerous virulence factors of *S. pyogenes*, the M protein holds a special place. It
181 is a surface protein that constitutes a major virulence factor, and it plays a fundamental role in
182 typing *S. pyogenes* strains [5].

183 Globally, invasive *S. pyogenes* infections are estimated at 663,000 new cases and 163,000
184 deaths annually. Comparable incidences ranging from 1.5 to 5.2 cases per 1,000,000 inhabitants
185 are reported in European and North American countries. The mortality associated with these
186 invasive *S. pyogenes* infections is estimated between 12.5% and 19%, rising to 45% when
187 streptococcal toxic shock syndrome (STSS) complicates the clinical form [5].

188 Prevention strategies for community-acquired invasive SGA infection were established on
189 November 18, 2005, by the French High Council of Public Hygiene (CSHPF) [6].

190 The prevention strategy for isolated or clustered cases relies primarily on defining a case of
191 invasive SGA infection, distinguishing between certain, probable, or possible cases. Our
192 observation can be defined as a certain case of invasive SGA infection since *S. pyogenes* was
193 isolated from a usually sterile fluid (joint fluid collected upon patient admission). The
194 uniqueness of our observation lies in establishing the diagnosis of invasive SGA infection after
195 isolating and identifying the microorganism through culture.

196 The CSHPF has defined several risk factors for acquiring invasive SGA infection in adults
197 (Table II) [7].

198 **Table II: Risk Factors for Invasive Group A Streptococcal Infection In Adults [7].**

200• Age > 65 years
201• Progressive chickenpox
202• Extensive skin lesions, including burns
203• Intravenous drug use
204• Underlying medical conditions (diabetes, cancer, hematologic disorders, HIV infection, heart 205 failure)
206• Significant oral corticosteroid use (prednisone 5 mg/kg/day > 5 days (recent treatment) or 207 prednisone 0.5 mg/kg/day for 30 days)

208 In our case, the patient had no risk factors and no identifiable infectious entry point despite
209 thorough investigation. In France, the CSHPF (French High Council for Public Health)
210 recommends initial antibiotic prophylaxis with an orally administered 2nd or 3rd generation
211 cephalosporin for a duration of 8 to 10 days [6]. In case of cephalosporin contraindication, the
212 use of an oral macrolide (as in our case, following confirmation of strain sensitivity) is
213 recommended (Azithromycin for 3 days or Clindamycin for 10 days). Lastly, in the presence
214 of macrolide-resistant strains, penicillin prophylaxis for 10 days is suggested, combined with
215 rifampicin during the last 4 days of treatment [6].

217 Conclusion

218 The current resurgence of invasive infections with Group A Streptococcus (GAS), their
219 severity, and the urgency of initiating specific treatment underscore the importance of early
220 recognition of these infections. The recommendations for antibiotic prophylaxis from the
221 French High Council for Public Health (CHSPF) in cases of invasive GAS infections should be
222 widely known and disseminated.

223 Given the complexity of the implicated pathogens and the issue of resistance, the safest
224 approach is to collaborate closely between clinicians and microbiologists to ensure the best
225 possible patient care.

228

1
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Conflicts of interest:

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The authors declare that there are no conflicts of interest.

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Consent to publish:

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4
Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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