CASE REPORT

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Challenges in Diagnosing and Treating Early-Stage Streptococcal Toxic Shock Syndrome: about an Invasive Group A Streptococcal Case Report

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Keywords

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Abstract

We report the case of a 7-year-old girl with severe torticollis caused by invasive Group A Streptococcal infection (iGAS) complicated by early Streptococcal Toxic Shock Syndrome (STSS). Despite the absence of hypotension, she developed multiorgan damage. Imaging revealed multiple abscess at the base of the skull. Rapid intravenous antibiotics and supportive care led to full recovery. This case illustrates the diagnostic challenges of atypical STSS and emphasizes the importance of early recognition and treatment, particularly given the recent rise in paediatric iGAS cases across Europe following the COVID-19 pandemic.

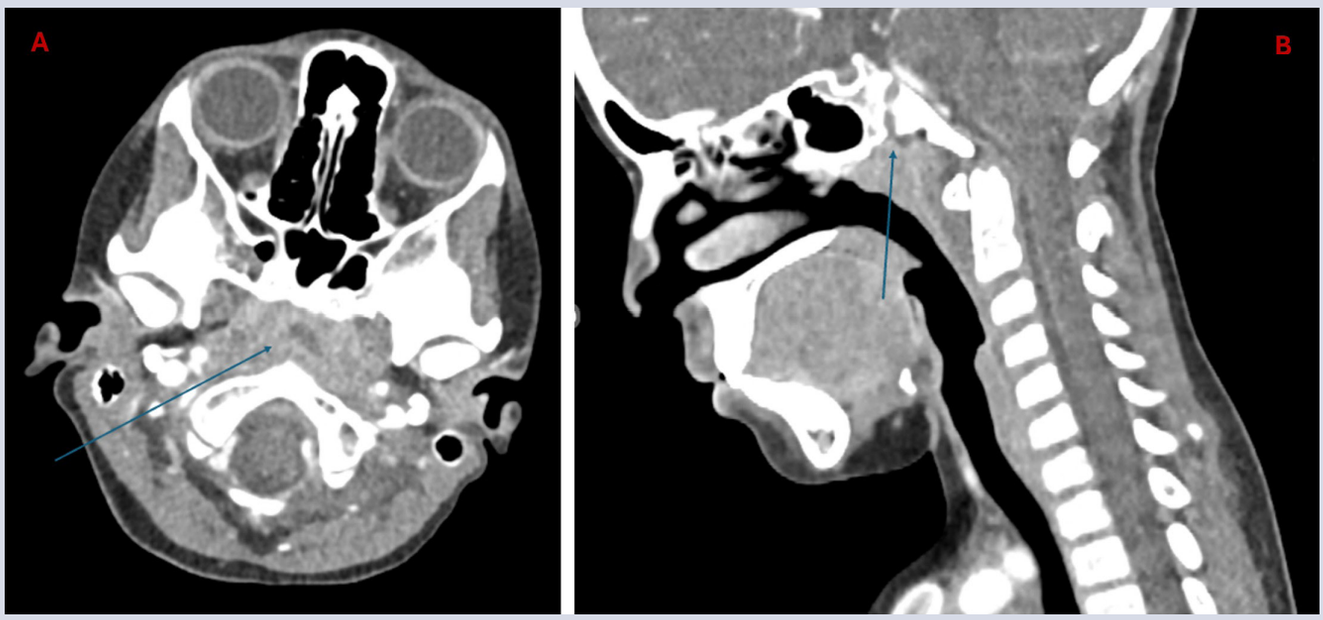
Introduction

Invasive Group A Streptococcal infections (iGAS) are defined by the presence of GAS in a normally sterile site or, in a non-sterile site when associated with toxin production leading to Streptococcal Toxic Shock Syndrome (STSS). iGAS carries a mortality rate of 8% to 17%, if not promptly treated. Among the key virulence factors of GAS protein M enables tissue colonization and immune evasion, while toxins trigger the massive immune response underlying STSS. Moreover, some strains produce toxins that act as superantigens, causing a massive immune response leading to STSS. iGAS combined with STSS is associated with a higher mortality rate estimated between 30% to 70% (1,2). After the COVID-19 lockdown, several European countries reported a marked increase in paediatric iGAS cases. In France and the Netherlands, the incidence was twice the pre-pandemic levels. Pneumonia with empyema, almost always linked to a respiratory virus, was the predominant presentation. The reasons for this surge remain unclear, though early data do not indicate association with a specific protein M type (3,4). We describe the case of a child with an iGAS osteoarticular infection who exhibited early signs of STSS. This occurred in Brussels during the early post-pandemic period and is therefore relevant in this epidemiological context. We aim to emphasise the importance of early recognition and treatment of iGAS and STSS.

Case report

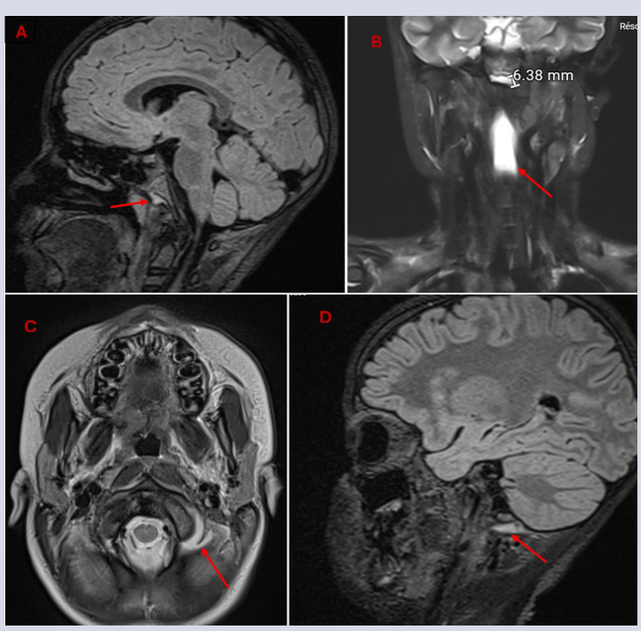
A seven-year-old girl was admitted to our paediatric department after suffering from torticollis for four days. She had been scratched in the neck by another child three days before the cervical pain started. She had no history of fever, no relevant medical background, and had not travelled recently. On the first day of cervical pain, a muscular contracture was identified and

FIGURE 1: Cervicofacial injected CT Scan: axial cut (A) and sagittal cut (B).



symptomatic treatment was recommended. She returned to the emergency room within two days because she started vomiting and her pain worsened. The physical examination revealed torticollis with impairment of both active and passive neck mobility. No cervical mass was identified clinically. She still had no fever, no rash and no neurological impairment. However, her blood sample showed significant inflammation with a C-reactive protein level of 200 mg/L (N ≤ 5,0 mg/L) and leukocytosis of 16400/μL (N 4500-13500/μL) of which 15300/μL were neutrophils (N 1500-7000/μL). She was admitted at this point to investigate the origin of such severe inflammation in the setting of a torticollis. Intravenous analgesics were given. She developed a sudden fever of 40°C six hours after admission. A cervical CT scan with contrast injections (Figure 1) revealed multiple small abscesses at the skull base, including one anterior to the clivus. A lumbar puncture showed no cerebrospinal fluid abnormalities. An MRI scan was performed on day 4 to evaluate the extent of the infection and assess for the presence of intramedullary lesions. Presphenoidal and multiple prevertebral collections extending from C1 to C4 were detected, associated with left occipito-atlantoid arthritis (Figure 2). The blood culture returned positive for Group A Streptococcus in less than 36 hours. Empirical ceftriaxone was initiated and subsequently switched to high-dose cefazolin once GAS had been identified. Early multiorgan involvement (liver, lungs, kidney and coagulation) in the absence of haemodynamic instability raised suspicion of STSS and prompted the addition of clindamycin on day one. No soft tissue necrosis or skin rash was observed. Indeed, hepatic cytolysis peaked at five times the baseline level within 48 hours. She also had altered hepatic function, with prothrombin time (PT) at 35% upon admission. On day two she developed a capillary leak syndrome with renal impairment. She presented with oedema of the face and extremities, became oliguric (diuresis less than 0.5 ml/kg/h), and gained 4% of her initial weight. Transient hypertension was noted during this period with a systolic blood pressure of 140 mmHg (> p 99). Furosemide and nifedipine were added. Laboratory tests showed hypoproteinaemia, hypoalbuminemia (minimal at 28 g/L on day two), microscopic haematuria and proteinuria (proteinuria/creatinuria ratio of 483 mg/g). Although her serum creatinine remained normal, the combination of these findings with addition of the renal ultrasound showing bilateral cortical hyperechogenicity suggested possible glomerular involvement. She also exhibited signs of acute respiratory distress syndrome (ARDS), with bilateral hypoventilation and desaturation to SpO2 85% requiring low-flow oxygen (maximum 2L/min). A chest X-ray on day two showed diffuse bilateral coalescent opacities (Figure 3). In this context intravenous methylprednisolone was added for three days, which allowed for a quick resolution of symptoms; oxygen was stopped after 36 hours. Echocardiography confirmed preserved cardiac function.

FIGURE 2: Cervicofacial MRI with multiple prevertebral presphenoidal collections (A: T1 FLAIR sagittal cut; B: T2 Coronal cut with fat suppression). Cerebral MRI with arthritis of the left occipito-atlantoid joint (C: T2 MRI axial cut; D: T1 FLAIR MRI sagittal cut).

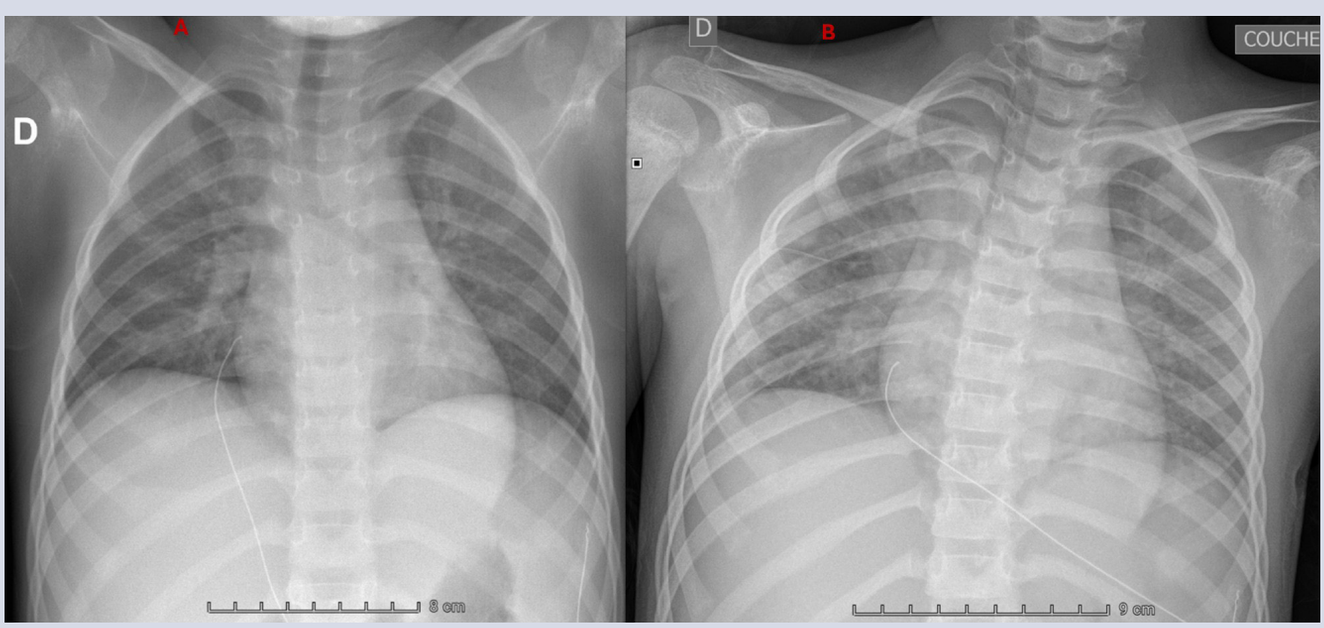


As her clinical status improved rapidly, the administration of intravenous immunoglobulins (IVIG) was cancelled. Cytolysis was fully resolved after one week, and PT returned to normal after three days. After one week, she had regained a good general state and full neck mobility. She received high-dose intravenous cefazolin for 28 days, while clindamycin was stopped after 10 days. Household contacts received 7 days of oral cefadroxil as post-exposure prophylaxis as soon as the GAS was identified in blood cultures. A follow-up MRI scan on day 13 showed resolution of the prevertebral collection, although the presphenoidal collection and occipito-atlantoid arthritis were still present. An MRI scan on day 21 showed only partial regression of the infectious lesions, so that IV treatment was continued for a total of 28 days. The girl was then discharged with a further four weeks of oral antibiotics. An MRI scan after 8 weeks confirmed complete resolution of both the abscesses and septic arthritis.

Discussion

After the COVID-19 pandemic, a rise in paediatric iGAS was reported across Europe. iGAS may progress to severe manifestations such as STSS, whose early recognition is critical for prognosis. According to the CDC criteria, a confirmed case of STSS requires isolation of GAS from a sterile site, hypotension, and at least two additional clinical or laboratory abnormalities, including renal impairment, coagulopathy, hepatic involvement, ARDS, macular rash or soft tissue necrosis. However, these criteria were primarily designed for epidemiological surveillance and may lack sensitivity in early clinical stages. Although mandatory in formal definitions, hypotension may be delayed and should not preclude early treatment when clinical suspicion is high (2,5). In our case, iGAS was confirmed by positive blood cultures, and STSS was suspected based on multiple organ involvement (liver, lungs, kidney and coagulation). The absence of skin rash, a frequent and early sign of STSS in children, complicated the distinction between STSS and sepsis with multiorgan failure. However, the absence of haemodynamic instability prior to or concurrent with multiorgan damage was considered consistent with STSS. In STSS, the GAS toxins act as superantigens triggering uncontrolled T-cell activation and massive cytokine release through dysregulation of immune signalling pathways. This exaggerated host immune response drives organ dysfunction and contributes substantially to mortality (6). Failure to identify STSS may delay targeted toxin-suppressive interventions and worsen prognosis. Of note, although our patient did not strictly meet the CDC creatinine threshold for renal impairment, she exhibited oliguria, haematuria, proteinuria, oedema, transient hypertension, all suggestive of glomerular involvement. Toxin-mediated renal injury may precede measurable renal failure and remain clinically significant even without fulfilling formal thresholds. In our case, the favourable outcome following timely antibiotics and supportive therapy suggests that early intervention may prevent progression to haemodynamic shock. Clindamycin was promptly added on day one upon suspicion of STSS. Its efficacy lies in its ability to inhibit streptococcal toxin and cytokine production, and it also has excellent tissue penetration, particularly relevant in deep cervical infection. Unlike beta-lactams, its activity is not affected by high bacterial inoculum (Eagle effect). In combination with high-doses beta-lactams, conferring rapid bactericidal activity, clindamycin constitutes the best synergistic regimen to reduce STSS-related mortality, as highlighted by the meta-analysis of Laho et al. (7). Although bactericidal antibiotics such as beta-lactams may theoretically increase toxin release through bacterial lysis, this concern is outweighed by the well-established survival benefit of early and aggressive antimicrobial therapy, as delays are consistently associated with increased mortality. The role of intravenous immunoglobulins (IVIG) in severe iGAS, particularly STSS, remains controversial. Given their safety profile and the severity of the disease, many experts, including in our country, recommend IVIG for cases of involving haemodynamic instability, ICU admission, STSS or necrotizing fasciitis (7). Although our patient fulfilled criteria suggestive of STSS and received clindamycin, the absence of shock and the rapid clinical improvement under antibiotic therapy led to withhold IVIG administration, balancing potential benefit against uncertain evidence in non-fulminant presentations. Invasive GAS infections are often considered more difficult to eradicate and are associated with a high risk of recurrence, often justifying prolonged antibiotic courses, particularly in deep-seated infections. In osteoarticular infections, treatment duration is generally guided by radiological and clinical evolution.

FIGURE 3: Chest X Ray (A: the day of admission; B: on day two of the stay).



However, imaging abnormalities may persist despite clinical recovery. As highlighted in paediatric guidelines, this can lead to unnecessarily prolonged antibiotic therapy (8). In our case, the persistence of cervical arthritis on imaging led us to continue the treatment until resolution was achieved, given the limited reliability of clinical assessment for our patient's deep-seated infection. The recent PEGASUS study, covering 1721 paediatric iGAS cases across 14 European countries, reported a marked post-pandemic surge of iGAS with heterogeneous clinical presentations. Ear, nose and throat (ENT) infections, in particular deep cervical and head and neck infections, as in our patient, accounted for over a quarter of cases in this outbreak. Their data also illustrated the wide range of iGAS presentations, identified previous chickenpox as a risk factor and further emphasized the importance of recognising atypical or incomplete presentations of STSS (9). Our patient was infected with a strain of GAS carrying emm4 gene. This is one of the five most common protein M gene subtypes associated with iGAS. Strains belonging to this emm-type are frequently capsule negative. Flores et al. reported that such capsule-negative emm-types are increasingly associated with invasive paediatric infections, possibly through enhanced toxin production and alternative virulence mechanisms compensating for the absence of a capsule (10). In the Netherlands, a novel capsule-negative emm4 lineage was identified and associated with the post-pandemic increase in iGAS incidence, suggesting that specific genetic lineages may have contributed to this epidemiological pattern (11). In Belgium, however, data from the national surveillance system did not reveal significant pattern in emm-type distribution during this period (12). Although the absolute risk of secondary iGAS infection among contacts remains low, it is significantly higher than in the general population. This justifies targeted prophylaxis for close contacts of patients with severe GAS infection including STSS. However recommendations for post-exposure prophylaxis remain inconsistent across European countries, despite evidence supporting its effectiveness (7). In our case, household contacts received 7 days of oral cefadroxil.

Current Belgian guidance also emphasises prompt case notification to health authorities, as well as prophylaxis for close contacts (12). This case highlights the diagnostic challenge of early or atypical STSS and underscores the importance of prompt recognition to guide appropriate management. Although iGAS incidence has declined following the post-pandemic surge, recent Belgian data indicate that rates remain persistently elevated in children (13). The underlying reasons for this sustained increase remain incompletely understood. This case report aims to contribute to ongoing clinical awareness and supports the need for continued surveillance and systematic reporting of iGAS to better characterize its evolving epidemiology.

Statement

Written informed consent was obtained from the parents of the children who served as subjects of this case report study.

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