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Group B *Streptococcus* necrotizing fasciitis: an emerging disease?

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Necrotizing fasciitis is perhaps the most severe form of soft tissue infection primarily involving the superficial fascia and subcutaneous tissue. This condition is associated with severe sepsis, a fulminant course and high mortality. While group A *Streptococcus* (GAS) remains the most common etiologic agent in necrotizing fasciitis due to a single organism [1], we have recently noted an emergence of group B *Streptococcus* (GBS) or *Streptococcus agalactiae* as a causative agent. This report describes our recent experience with GBS necrotizing fasciitis seen in Singapore between the years 2000 and 2002.

Five patients with monomicrobial necrotizing fasciitis caused by GBS were identified during this time period. All patients were female, with ages ranging from 38 to 66 years. Diabetes mellitus was a frequent association and was noted in four of the patients. Early aggressive surgical debridement is the cornerstone management of necrotizing fasciitis and was performed in all cases. The procedure was repeated until all necrotic and non-viable tissues were excised. Two to three debridements were necessary to achieve this. The group B streptococci isolated from all five patients were susceptible to penicillin, ampicillin and erythromycin. Table 1 summarizes the clinical presentation, antimicrobial therapy and outcome of the five cases.

At our hospital, we generally treat patients with severe GBS soft tissue infections with high-dose parenteral penicillin once the organism has been isolated. High-dose intravenous penicillin is the drug of choice since

resistance to penicillin is not an issue with GBS. Once the infection has been controlled, the parenteral regimen is replaced by an oral β -lactam agent such as penicillin or amoxicillin. Antimicrobial therapy is continued for 4–6 weeks, until all wounds are covered with split thickness skin grafts. However, in the five cases reported here there were some variations in the antimicrobial therapy administered because of the preferences of individual treating physicians. Some authors have advocated the use of clindamycin in combination with penicillin in cases of GBS necrotizing fasciitis [2, 3], and there is now growing in vitro and in vivo evidence that clindamycin may be the preferred agent for treating streptococcal necrotizing fasciitis. While not used to treat our patients, the combination of clindamycin and penicillin may be superior to penicillin alone and should be considered in the treatment of future cases of invasive GBS infections [2, 3].

Skin and soft tissue infections are the most common manifestations of invasive GBS infection [4, 5]. However, monomicrobial necrotizing fasciitis caused by GBS in non-pregnant adults is extremely rare, with just over ten cases being reported in the English-language medical literature to date [2, 3, 6–9]. The addition of the five cases we observed make clear that GBS is capable of causing necrotizing fasciitis. While the virulence factors that enable GBS to cause necrotizing fasciitis have not yet been established, this emerging clinical entity has been reported increasingly in recent years [2, 3, 6–9]. All five of our cases occurred during a relatively short period of time, between 2000 and 2002.

Horizontal transfer of DNA encoding virulence factors (such as M1 or M3 surface proteins) among different strains of GAS have been demonstrated previously [10, 11]. Gardam et al. [2] postulated that a similar process may have occurred between group A and B streptococci, conferring the mutant strain of GBS with increased ability to spread through tissue planes, resulting in rapid tissue necrosis. This theory is supported by a report of the isolation of a 12,000-kD pyrogenic toxin similar to that found in GAS from a GBS strain in a case of toxic shock syndrome caused by this organism [12]. This sharing of

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Table 1 Summary of the clinical presentation, antimicrobial therapy and outcome of five patients with group B *Streptococcus* (GBS) necrotizing fasciitis

Case no.	Age/sex	Underlying comorbidities/ predisposing conditions	Site(s) affected	Culture results for GBS		No. of wound debridements	Type and duration of antimicrobial therapy	Outcome
				Tissue biopsy	Blood			
1	48/F	Diabetes mellitus, peripheral vascular disease	Right thigh	+	-	3	Parenteral penicillin for 2 weeks followed by amoxicillin for a total duration of 60 days	Survived
2	66/F	Diabetes mellitus	Left foot and calve	+	-	3	Parenteral penicillin and cloxacillin for 21 days followed by oral penicillin for a further 14 days	Survived
3	44/F	Diabetes mellitus, peripheral vascular disease	Left lower limb	+	-	2	Parenteral penicillin and cloxacillin for 21 days followed by oral amoxicillin for a further 21 days	Survived
4	51/F	Diabetes mellitus	Right lower limb	+	+	3	Parenteral penicillin for 16 days followed by oral amoxicillin for 21 days	Survived
5	38/F	Nil	Right hand	+	+	3	Parenteral penicillin for 14 days followed by oral amoxicillin/ clavulanate for 14 days	Survived

F female, + positive, - negative

virulence factors may also explain the recent reports of increased invasiveness of GBS [4, 5]. In addition, certain serotypes of GBS, such as serotype V, may have a predilection for invasive behavior [13]. Due to the retrospective nature of the present review of five cases, however, the GBS isolates were no longer available for serotyping and pulsed-field gel electrophoresis analyses.

One of our patients (case 5) fulfilled the definition of streptococcal toxic shock syndrome (STSS), as defined by the Working Group on Severe Streptococcal Infections [14], with fever, hypotension and multiple organ failure. Intravenous immunoglobulin (IVIG) therapy was given in this case because of the associated STSS. IVIG has been demonstrated to be of benefit in cases of STSS due to severe invasive GAS infections [15]. Since the postulated mechanism for toxic shock due to GBS may be similar to that due to GAS, IVIG should be considered as an adjunctive treatment of potential benefit in cases of GBS necrotizing fasciitis associated with toxic shock [3]. Why some patients with invasive GBS develop necrotizing fasciitis while others develop both necrotizing fasciitis and streptococcal toxic shock-like syndrome remains to be elucidated [2, 3]. It is clear, however, from the limited literature available, that GBS necrotizing fasciitis can occur in isolation or in association with a streptococcal toxic shock-like syndrome [2, 3, 6-9].

Reports in the medical literature to date have focused on GBS as a disease of pregnancy and the neonatal period. While the emergence of invasive GBS in adults has been highlighted recently [1, 4, 5], awareness should be raised regarding the spectrum of soft tissue infections caused by GBS and, in particular, the danger of progression to necrotizing fasciitis. The essential component in the management of this serious condition is early operative debridement in order to improve the chances of survival of these patients. However, this is difficult to achieve, since the disease is often clinically indistinguishable from cellulitis or other more benign soft tissue infections in the early stages of its evolution [1]. Therefore, when wound cultures yield GBS, awareness of the danger of progression to necrotizing fasciitis should heighten the treating physician's index of suspicion.

In non-pregnant adult patients, necrotizing fasciitis due to GBS occurs almost exclusively in immunocompromised hosts, such as patients with diabetes mellitus, cirrhosis, renal failure and malignant neoplasms [2, 3, 6-9]. These conditions are also well-established risk factors for invasive GBS infection [4]. Four of our patients were diabetic. It is not known why diabetics are more prone to invasive GBS infections, but one study demonstrated that serum samples from patients with type 1 diabetes have reduced phagocytic activity against GBS in vitro [16].

Our series adds to the limited available literature underscoring the potential for GBS to cause necrotizing fasciitis and indicates that the microbiological differential of monomicrobial necrotizing fasciitis should be expanded to include GBS. Awareness of this possibility should heighten the treating physician's index of suspicion when managing these soft tissue infections. Early recognition,

aggressive surgical debridement and high-dose intravenous penicillin therapy are imperative for decreasing the morbidity and mortality of this disease [1]. The use of clindamycin (in combination with a β -lactam antimicrobial agent) and IVIG (when associated with STSS) may be of potential benefit and should be considered. Factors that confer increased invasiveness to GBS need to be further elucidated.

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