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## CHARACTERIZATION OF A COMMUNITY CLUSTER OF GROUP A STREPTOCOCCAL INVASIVE DISEASE IN MAUI, HAWAII

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### Abstract

A community cluster of severe group A streptococcal skin infections occurred in Maui, Hawaii with 3 fatal cases of necrotizing fasciitis in 2002. *emm* types 1, 12, 58, 74, 85 and 109 were identified from 8 patients. *emm* types 74 and 109 have not been previously described in the United States according to the Centers for Disease Control and Prevention database. The identification of uncommon *emm* types suggested that group A streptococcal serotypes in Hawaii are different from those in the continental United States and can result in serious disease.

### Keywords

necrotizing fasciitis; community cluster; group A Streptococcus; *emm* typing

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Most cases of necrotizing fasciitis are associated with invasive group A streptococcal (GAS) infection.<sup>1</sup> In a recent population-based 5-state surveillance study, the annual incidence of invasive GAS disease was 2.2–4.8 cases/100,000 persons, with 7.1% of those developing necrotizing fasciitis.<sup>2</sup> The occasional clusters or outbreaks of necrotizing fasciitis have been mostly reported in hospital settings, and community-acquired clusters are rare.<sup>3,4</sup>

After 3 fatal cases of necrotizing fasciitis with toxic shock syndrome that occurred from February 2002 through April 2002, a cluster of severe GAS skin infections recurred in Maui, Hawaii (population 128,094) during the 3-month period of April 2002 through June 2002.<sup>5</sup> Molecular epidemiologic studies including *emm* typing, pulsed field gel electrophoresis (PFGE) and polymerase chain reaction (PCR) analysis of pyrogenic exotoxin A (*speA*) gene were undertaken to characterize this unusual cluster of isolates.

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## MATERIALS AND METHODS

### Patients and Bacterial Isolates

Hawaii State Department of Health (HSDOH) officials were notified after identification of patients with necrotizing fasciitis and invasive GAS infections by internists, surgeons and infectious disease specialists. The clinical data were obtained by diagnosing physicians. A case of GAS disease is considered invasive if the isolate was obtained from a normally sterile body site. Necrotizing fasciitis is defined as a rapid widespread necrosis of fascia and subcutaneous tissue with growth of GAS (or other bacterial pathogens) from deep tissue and/or blood. If GAS is isolated from the blood of these patients, in addition to hypotension and one of clinical criteria (renal impairment, coagulopathy, liver involvement and adult respiratory distress syndrome), it is classified as necrotizing fasciitis with streptococcal toxic shock syndrome (STSS).<sup>1,6</sup> Severe GAS skin infection is defined as deep, extensive cellulitis of the involved tissues, requiring hospitalization and intravenous antibiotic treatment. HSDOH officials obtained epidemiologic data for the area of residence and for history of contact with a patient with GAS clinical disease. The GAS isolates were collected from April 2002 through June 2002 and isolates were identified as *Streptococcus pyogenes* by standard methods.

### emm Typing

The *emm* gene sequencing was conducted by previously described PCR protocols.<sup>7,8</sup> The amplified PCR products were submitted to the University of Hawaii Biotechnology Facility for sequencing. The resulting sequences were compared with known *emm* types to determine the specific *emm* types using the Basic Local Alignment Search Tool (BLAST) program. The Centers for Disease Control and Prevention maintains a website containing known *emm* sequences with which the typed strains can be compared.<sup>7</sup>

### PCR Detection of *speA* Gene

The presence of the gene encoding *speA* was performed by PCR.<sup>9</sup> The 708-bp PCR product was detected by agarose gel electrophoresis. The streptokinase (*ska*) gene was amplified as a positive control.

### DNA Analysis by PFGE

All isolates were studied by PFGE after digestion with the restriction endonuclease *SmaI*.<sup>9</sup> The plugs were electrophoresed in a pulsed field apparatus (CHEF-DRII; BioRad Laboratories, Hercules, CA). An isolate with a unique set of bands was defined as a PFGE type. The DNA fingerprints were compared with the use of Molecular Analyst Fingerprinting plus DST, version 1.6.

## RESULTS

### Patients and Bacterial Isolates

Ten cases of invasive GAS disease were observed after January 2002, including the first 3 cases with necrotizing fasciitis and STSS who died shortly after minor skin trauma. One isolate from these fatal cases was available for further studies (identified in April). This isolate was studied with 7 additional isolates, from patients with nonfatal, invasive GAS disease from April 2002 through June 2002. One of these 7 isolates was from a nonresident who had onset of symptoms before arriving in Maui. The patients ranged in age from 18 to 74 years. The mean age was 51.9 years. All patients with necrotizing fasciitis had STSS, and the case fatality rate for necrotizing fasciitis was 100%. All of the necrotizing fasciitis patients had histories of recent, minor skin trauma before development of their disease. No epidemiologic link was identified among the cases (Table 1).

Two of the isolates were from blood, 1 was from joint fluid and 5 were from deep wound cultures. One of the blood isolates was from the individual who died with necrotizing fasciitis and STSS. *emm* Typing. *emm* types 1, 12, 58, 74, 85 and 109 were identified from 8 patients. *emm* 74 was found in the fatal necrotizing fasciitis case and in another case with cellulitis. *emm* 85 was identified from the second bacteremia case and from a case with cellulitis. *emm* 85 and 109 have been rarely isolated and according to the Centers for Disease Control and Prevention database *emm* 74 had not been previously described in the United States.<sup>7</sup>

### speA Gene Analysis

The *speA* gene was present in 2 isolates (*emm* 74). DNA Analysis by PFGE. Two *emm* type 85 isolates had the same PFGE pattern. *emm* 74 isolates were also clonal.

## DISCUSSION

We have observed a very unusual cluster of necrotizing fasciitis cases in Maui, HI, followed by several cases of invasive and serious skin infections during a 3-month period. Epidemiologic data have not been previously reported for necrotizing fasciitis outbreaks, and few studies have been done in the rare community-acquired outbreaks of other invasive GAS disease. Outbreaks have occurred over prolonged periods, and they have been caused by several GAS serotypes.<sup>4</sup> In some studies, an association between infections from certain types like *emm* 1 and 3 or from strains possessing pyrogenic exotoxins has been reported.<sup>1,2</sup> In the cluster we studied, we found several different, unusual GAS serotypes.

We reported a community-acquired cluster of invasive GAS cases after 3 fatal cases of necrotizing fasciitis with STSS. This was the first molecular epidemiologic analysis of an invasive GAS disease cluster from Maui, HI. Similar to the data obtained in Oahu,<sup>10</sup> several different and unusual serotypes were observed. Although the study included a limited sample with one isolate available from the fatal cases, previously reported *emm* types like *emm* 1 were infrequent. The unusual *emm* type 74 appeared to be an invasive GAS type based on this cluster.

The identification of other uncommon *emm* types like *emm* 85 and 109 suggested that GAS serotypes in Hawaii were different from those isolated in the continental United States. This may have further significance for any future vaccine formulations containing M proteins or other serotype-specific molecules. The *speA* gene, which has been associated with invasive GAS infections in some studies, was found in only 2 isolates (both *emm* 74), suggesting that it is not an essential virulence factor.<sup>9</sup>

Our results suggest that the seroepidemiology of GAS isolates in Hawaii differs from those in the continental United States. This might, in part, explain the unusual occurrence of a community-acquired necrotizing fasciitis cluster.

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TABLE 1

Patient Characteristics and *emm* Typing of Isolates

Patient	Disease Onset	Sex	Age (yr)	Diagnosis	Predisposing Factors	Outcome	Culture Site	<i>Emm</i> Type	<i>speA</i>
1	2/15/02	M	48	NF, STSS	Insect bite	Died	NA	NT	NT
2	3/5/02	M	51	NF, STSS	Minor trauma to left knee, splenectomy	Died	NA	NT	NT
3	4/11/02	F	57	NF, STSS	Coral reef cut	Died	Blood	74	+
4	5/11/02	F	60	Cellulitis	Insect bite	Alive	Leg	12	-
5	5/12/02	F	66	Cellulitis	Schizophrenia	Alive	Leg	85	-
6	5/13/02	F	58	Cellulitis	None	Alive	Leg	109	-
7	5/22/02	M	54	Cellulitis	Alcoholism, schizophrenia, homeless	Alive	Toe, shin	74	+
8	6/8/02	M	33	Cellulitis	Coral reef cut	Alive	Foot	58	-
9	6/12/02	M	74	Cellulitis	None	Alive	Blood	85	-
10	6/22/02	M	18	Septic arthritis	Fall to right knee, streptococcal pharyngitis	Alive	Knee fluid	1	-

NA indicates not available; NF, necrotizing fasciitis; NT, not tested.