

## Case Report

A case of Pantón–Valentine leucocidin toxin-positive *Staphylococcus aureus*-mediated neonatal mastitis

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**Introduction:** Neonatal mastitis is an inflammatory condition of the breast frequently associated with *Staphylococcus aureus*. While Pantón–Valentine leucocidin (PVL), a B-pore-forming cytotoxin, is commonly associated with enhanced virulence in community-acquired methicillin-resistant *S. aureus* isolates, this is the first report to our knowledge of neonatal mastitis caused by PVL-positive *S. aureus*.

**Case presentation:** A 20-day-old full-term female neonate presented with bilateral mastitis, complicated by bilateral abscess formation. PVL toxin-positive *S. aureus* was cultured from aspirates of both breasts. All family members, none of whom presented with symptoms of infection, and, specifically, maternal vaginal samples proved negative for PVL-positive *S. aureus*. Successful resolution involved surgical drainage and clindamycin therapy.

**Conclusion:** While PVL toxin-positive *S. aureus* has previously been implicated in bovine and ovine mastitis, there may now be a need for vigilance with respect to human incidence. Due to PVL-mediated tissue necrosis, breast abscess formation and poor response to conventional antimicrobial therapy should, perhaps, be a cause for suspicion of PVL-bearing *S. aureus* and expediting of appropriate therapy to avoid potential for long-term consequences such as abnormal breast development.

**Keywords:** mastitis; neonatal; Pantón–Valentine leucocidin; *Staphylococcus aureus*.

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## Introduction

*Staphylococcus aureus* is a commensal skin organism, a major human and veterinary pathogen, and the most common cause of human mastitis (Osterman & Rahm, 2000; Peton & Le Loir, 2014; Rasigade & Vandenesch, 2014; Uhlemann *et al.*, 2014). As such, considerable emphasis has been placed on elucidating the mechanisms by which the virulence of *S. aureus* strains is mediated (Rasmussen *et al.*, 2013; Sollid *et al.*, 2014). Amongst these mechanisms are the horizontal transfer of the chromosomal cassette conferring resistance to methicillin (SCC<sub>mec</sub>) (Nubel *et al.*, 2008) and ability to produce toxins such as (but not limited to) Pantón–Valentine leucocidin (PVL) mediating tissue necrosis (Labandeira-Rey *et al.*, 2007; Diep *et al.*, 2010).

In the context of maternal and infant health, many studies have described incidence and transmission of community-associated and healthcare-associated strains, in addition to recommended antibiotic regimens, invasive and non-invasive management, and prevention strategies including decolonization (Saiman *et al.*, 2003; Fortunov *et al.*, 2007; Alsubaie *et al.*, 2012; Jahanfar *et al.*, 2013; Sheffield, 2013). With respect to mastitis specifically, most reports relate to incidence and treatment of *S. aureus* maternal infection (Branch-Elliman *et al.*, 2012; Chick *et al.*, 2012; Iatrakis *et al.*, 2013; Perez *et al.*, 2013) and, to a lesser degree, subsequent transmission of infection to (mostly pre-term and neonatal) infants (Behari *et al.*, 2004; Gastelum *et al.*, 2005; Kayiran *et al.*, 2014). Mastitis in children is less common and is largely related to neonates and pubescent/postpubescent age groups (Faden, 2005). A case series of neonates demonstrated that mastitis occurred most commonly in the fourth and fifth weeks of life, although

Abbreviation: PVL, Pantón–Valentine leucocidin.

age ranged from 12 to 45 days, and that parenteral antibiotics eradicated causative microorganisms (Stricker *et al.*, 2005). A larger review of neonatal cases from 2005 to 2011 (in Atlanta, USA) concluded that *S. aureus* was the most common cause of mastitis and that no infant with a positive breast culture had a concordant positive culture elsewhere (Montague *et al.*, 2013), arguing that urine, blood and spinal fluid cultures are unnecessary in otherwise well, afebrile infants with mastitis.

PVL-positive clones are emerging as virulent, multidrug-resistant *S. aureus* in Ireland (prevalence of PVL-positive MRSA increased from 0.2 to 8.8 %, and that of PVL-positive MSSA decreased from 20 to 2.5 % between 2002 and 2011) (Shore *et al.*, 2014). Despite this, we believe this report to be the first description of neonatal mastitis caused by PVL-bearing *S. aureus* and its successful treatment and, as such, will make a contribution to the emerging debate regarding management of neonatal mastitis (Al Ruwaili & Scolnik, 2012).

## Case report

A 20-day-old female infant was admitted to University Hospital Limerick (UHL) on 16 December 2013. She was born at 41 weeks gestation via spontaneous vaginal delivery. At day 7 of life, her mother noted that the baby's right breast was swollen and red. When it failed to settle spontaneously, she brought the baby to her general practitioner who diagnosed right breast mastitis and commenced what proved to be ineffective antimicrobial therapy with oral amoxicillin. The right breast continued to increase in size and the infant's condition deteriorated, with poor feeding, irritability, lethargy and vomiting. The infant's parents self-referred to the hospital. On arrival at UHL, examinations revealed discrete areas of erythema suggestive of mastitis on both breasts, more marked on the right. Under the right nipple there was a 4 cm swelling with underlying yellow-green discoloration of the skin. The area was warm and tender to touch, with pain elicited on superficial palpation. There was no obvious pointing over the right abscess. A 1.5 cm swelling was identified under the left nipple with no associated topical changes. The infant was diagnosed with bilateral mastitis, complicated on the right side with early abscess formation. She was apyrexial.

Haematological investigations demonstrated a normal white cell count ( $16.24 \times 10^9 \text{ l}^{-1}$ ), elevated neutrophils ( $8.48 \times 10^9 \text{ l}^{-1}$ ), mild thrombocytosis ( $427 \times 10^9 \text{ l}^{-1}$ ) and normal haemoglobin count ( $14.4 \times 10^9 \text{ l}^{-1}$ ). Renal function was normal. C-reactive protein was raised at  $11 \text{ mg l}^{-1}$ . Blood cultures were not completed, while urine was free of pathogens. A superficial swab of the right breast abscess resulted in growth of coagulase-negative staphylococci, but too few to enumerate accurately. Initially, the neonate was treated conservatively with intravenous flucloxacillin (220 mg four times per day) and intravenous benzylpenicillin

(220 mg three times per day), but exhibited minimal improvement. At 3 days, a small area of necrotic skin developed on the right breast in the periareolar area. Intravenous benzylpenicillin was discontinued, intravenous flucloxacillin was continued and oral clindamycin (25 mg four times per day) was introduced, as (due to increasing prevalence as described above) there was clinical suspicion of PVL toxin-mediated staphylococcal infection.

Subsequently, at 5 days, 5 ml aspirate was surgically removed from the infant's right breast abscess, which proved positive for *S. aureus* resistant to amoxicillin and gentamicin and sensitive to flucloxacillin, levofloxacin, linezolid, rifampicin, vancomycin and tetracycline. Intra-operative examination under anaesthesia confirmed a contralateral left breast abscess from which 2 ml *S. aureus*-positive aspirate was removed.

Post-operative antimicrobial therapy involved oral clindamycin and intravenous flucloxacillin. Both isolates of *S. aureus* subsequently tested positive for PVL toxin. Antimicrobial therapy was modified to oral clindamycin for a further 7 days, at which point full resolution had been achieved.

Subsequently, staphylococcal protein A (Spa) typing identified the isolate as being t005 (EMRSA-15) (<http://spa.ridom.de/spa-t005.shtml>), which has been reported mostly in Europe (including the UK and Ireland), ranked ninth in 2010 with respect to relative incidence (Grundmann *et al.*, 2010).

## Discussion

Reports of neonatal mastitis are relatively uncommon (Stauffer & Kamat, 2003) but most frequently (ca. 85 %) caused by *S. aureus* (Holmes & Zadoks, 2011). As such, there is some debate regarding best practice in its management (Al Ruwaili & Scolnik, 2012), but recommended treatment involves antibiotic therapy followed by surgical incision and drainage or needle aspiration if medical management fails (Sloan & Evans, 2003).

In this case, we describe the first incidence of PVL-positive *S. aureus*-caused neonatal breast abscess. It seems reasonable that risk factors for neonatal acquisition of PVL-positive *S. aureus* would be similar to those for other *S. aureus* strains, i.e. ingestion of infected breast milk, impaired skin integrity, or infection of breast tissue (engorged due to maternal hormones) via the nipple (Stauffer & Kamat, 2003). The long-term consequences of neonatal mastitis and its treatment were reported by Panteli *et al.* (2012), whereby development of the breast was characterized as involving intraductal dilatation, fibrous elements and calcifications or, where surgical incision was required, breast asymmetry and significant reduction in size compared with the uninfected breast. The emergence of PVL toxin-positive *S. aureus* (Labandeira-Rey *et al.*, 2007; Rasmussen *et al.*, 2013; Shore *et al.*, 2014)

is adding a new perspective to neonatal mastitis incidence due to its ability for tissue necrosis and the potential damage that this may cause to infected infants (Hsieh *et al.*, 1999; Nazir, 2005).

In this case, specifically, the neonate was breastfed successfully for 4 days postpartum and subsequently switched to bottle-feeding for convenience. The baby's mother did not have any underlying recurrent infective skin or soft tissue infections. This family had not been washing domestic items such as towels used for this neonate separately to those in use for other members of the family. During the course of the neonatal infection no other family member presented with signs or symptoms of a PVL-associated infection. Vaginal carriage of *S. aureus* is possible; however, samples obtained from high vaginal and groin areas proved negative. The potential for zoonosis (Holmes & Zadoks, 2011) was eliminated as the family did not have a household pet and did not live on a farm, and there was no other direct contact with animals. As this was an isolated incident, environmental (i.e. delivery room and equipment) and staff screening was considered unnecessary.

The vigilance of the infant's parents and the relatively early identification of PVL-positive *S. aureus* meant that appropriate targeted (rather than empiric) antimicrobial therapy resulted in eradication of the pathogen. The revision of therapy was influenced to no small part by the availability of aspirated pus, rather than topical swabs, which underwent on-site molecular and conventional susceptibility testing, as described elsewhere (O'Connor *et al.*, 2014), which reduced time to diagnosis by at least 24 h through avoidance of culture on non-selective solid media. It is debatable whether non-invasive assessment such as sonography would have been useful in this case, although its use has been described in differentiating between neonatal abscesses and mastitis (Borders *et al.*, 2009).

## Conclusion

Neonatal PVL toxin-positive *S. aureus* mastitis and breast abscess formation is uncommon but suspicion should arise with poor response to conventional antimicrobial therapy for mastitis. There is a need to improve awareness of PVL-positive *S. aureus*, particularly among those caring for neonates, as early diagnosis can prevent complications of invasive tissue necrosis and potential for long-term consequences such as abnormal breast development. Sending appropriate samples for testing can expedite diagnosis.

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