Clinical

An invisible enemy: Panton-Valentine Leukocidin Staphylococcus Aureus on deployed troops

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Abstract

Over the last seven years Primary Care establishments in the Royal Navy and Royal Marines have dealt with a number of severe and fatal infections caused by Panton-Valentine leukocidin (PVL) producing Staphylococcus aureus, and appear to be seeing these infections more commonly than their civilian colleagues. This retrospective study looked at the levels of PVL S. aureus isolated in deployed personnel during Op HERRICK 14 to determine if the levels seen in British military troops are higher than the national average. We found that the percentage of PVL positive S. aureus isolates sent to the UK HPA reference laboratory from the Camp Bastion laboratory during OP Herrick 14 was 41%, considerably higher rate than the UK civilian rate. Future research, including a larger study into the carriage levels of PVL S. aureus in the military will hopefully shed more light on the spread and transmission of this potentially deadly bacterium.

Introduction

Over the last seven years Primary Care establishments in the Royal Navy and Royal Marines have dealt with a number of severe and fatal infections caused by Panton-Valentine Leukocidin (PVL) producing Staphylococcus aureus, and appear to be seeing these infections more commonly than their civilian colleagues. In this report we present a breakdown of PVL testing for all S. aureus isolates sent to the HPA Reference Laboratory from the Role 3 Camp Bastion Medical Facility in Afghanistan during Op Herrick 14. We compare these results with the reported percentage of PVL positive S. aureus isolates received by the UK national reference laboratory.

Background

Staphylococcus aureus is a Gram positive coccus, able to cause a wide spectrum of disease, from toxic shock to pneumonia to food poisoning and skin sepsis. Different strains of S. aureus produce different virulence factors. These virulence factors can be divided into enzymes (haemolysins, staphylokinase, phospholipase, coagulase, etc) and exo-toxins (proteins excreted from within the bacterium itself, i.e. not part of the cell wall as in Gram negative endotoxins). Some strains secrete exo-toxins (exfoliative toxins A and B) leading to staphylococcal scalded skin syndrome or toxic shock syndrome, whilst some produce pore-forming toxins (such as PVL) which punch holes in the membranes of white blood cells.

S. aureus is a common skin coloniser, and is carried by a proportion of healthy people in the anterior nares. From there it spreads to the hands and body. People can be categorised as either:

i. persistent carriers, approximately 20% of people (range12-30%)
ii. intermittent carriers, approximately 30% (range 16-70%)
iii. non-carriers, approximately 50% (range 16-69%) (1).

Whilst persistent Staphylococcal aureus carriage is thought to be due to host characteristics (such as male sex and young age) combined with host genetics, it is strongly associated with specific risk factors, such as damaged skin; hence infections with S. aureus are seen commonly in diabetics and intravenous drug users (2).

Persistent carriers are often colonised by a single strain of S. aureus over long time periods, but intermittent carriers may carry different strains over time. There is evidence that PVL-producing S. aureus strains are being carried by some RN and RM personnel. S. aureus cells can survive for months on any type of surface. Hands are the main vector for transmitting S. aureus from surfaces to the nose. Whilst it is less common for S. aureus to reach the nose directly through the air, airborne transmission is important for the dispersal of staphylococci to different reservoirs from where they may be transmitted by hands. Within a particular group, for example a sports team or a troop of marines, a single clone may spread to and colonise all the group members (3). Studies looking at transmission of PVL S. aureus between members of sports teams have found that turf burns, body shaving, shared bathing facilities and repeated physical contact were associated with increased transmission and infection (4). Poor hygiene and
Clinical S. aureus and larger abscesses. Studies from national reference PVL may affect otherwise healthy young people. Necrotising pneumonia which has a high mortality and necrotising fasciitis, osteomyelitis, septic arthritis invasive infections including necrotising pneumonia, Like other methicillin-sensitive. are S. aureus country (8, 9). However in the UK there are a variety of cause of civilian skin and soft tissue infection across the USA 300 strain (also known as ST8 clonal lineage), is currently a major producing methicillin-resistant S. aureus, USA 300 strain used by Wright in 1936. PVL-producing (7). The term Panton Valentine leukocidin toxin was first came to S. aureus phage PVL strains – crowding, cuts, colonisation with S. aureus (17). A possible model for the mechanism is that PVL attacks the PMN and prevents the body from destroying the bacteria, thus allowing further bacterial growth leading to the tissue damage. However soft tissue infection models show that PVL toxin can also cause significant muscle damage via the induction of pro-inflammatory mediators leading to necrotic tissue damage (17, 18, 19). Some mouse models of PVL pneumonia show PVL increasing the adherence factors produced by the bacteria to allow greater bacterial adherence to tissue (20).

Some people believe that PVL in fact plays no part in the pathogenesis of the severe infections, but is merely a marker associated with virulent strains. This is based mainly on gene knockout mice models of PVL infections (21, 22). However the validity of many of these models has been questioned after the discovery that the PVL toxin affects different animals' PMNs differently. In mice and non-human primates PVL does not seem to have the same toxic effect as is seen in rabbits and humans (17, 23). Whilst in the UK community PVL S. aureus has low incidence of methicillin resistance, worldwide the picture is complicated by MRSA PVL producers, such as USA 300, which have spread rapidly through US cities in the last 5 years (24). An Alaskan community medical centre study looked at the proportion of S. aureus samples that were MRSA 300 in 2003 and then again in 2006, and found an increase from 16% to 100% (25). USA 300 appears to have an incredible ability to displace the locally endemic S. aureus strain, which has allowed it to become pandemic across most American States and Canada (17).

Studies performed in 1994 and 2002 at National Reference laboratories in the UK and France showed that about 2% of S. aureus isolates received were PVL positive (12, 26). The Health Protection Agency found that about 21% of received invasive S. aureus isolates were positive for PVL in 2006 and a London study observed similar numbers, with 20.8% of SSTI S. aureus isolates being PVL gene positive (24). It is felt that both these numbers may be an underestimate, as many patients with suspected PVL infections are treated based purely on suspected PVL infections are treated based purely on clinical findings without confirmatory testing (27). Both studies found that levels of methicillin resistance were low, between 0.8 and 5%. Data from the Staphylococcus Reference Unit of the HPA shows that 65% of S. aureus from boils and abscesses are PVL-positive and one third of these are associated with recurrent episodes of infection (12).

There have been several reports of severe PVL infections in UK military personnel since the death of a young Royal Marine in 2004 (28, 29). This retrospective study looked at the levels of PVL S. aureus isolated in deployed personnel during Op HERRICK 14 and questioned whether the levels seen in the British military troops are higher than the national average.
Method
We reviewed the results for all S. aureus isolates from May-Oct 2011 that were sent from the pathology laboratory in the UK Role 3 Hospital at Camp Bastion to the Staphylococcus Reference Unit at HPA Colindale for PVL and resistance testing. Samples are received by the Camp Bastion laboratory directly from the Role 3 Hospital, the Camp Bastion Primary Health Care Department, and other ISAF medical care facilities throughout Helmand province. Samples from local civilians, contractors, Afghan Army and Afghan Police were excluded. Samples lacking the basic clinical details were also excluded from this study.

Results
Initial number of samples = 127
Remaining samples after exclusion criteria applied N = 98
Number samples reported as PVL positive. N = 40 (41%)

Discussion
This study found that the percentage of PVL-positive S. aureus isolates sent to the UK HPA reference laboratory during OP Herrick 14 was 41%.

S. aureus isolates are referred back to the UK Reference Laboratory if PVL testing is requested directly by the clinician, or if the clinical details on the pathology form indicate that PVL testing is appropriate. Therefore the high rates could be due to collection and sampling bias. Military medical staff, especially RN personnel, are acutely aware of the dangers of PVL S. aureus and may be more accurate at selecting which patients to test. Additionally the military biomedical scientists are more aware than their civilian colleagues of the need to test high risk patients for PVL.

Although we have tested samples from a predominantly RM population, the levels of PVL may be mirrored in the other branches of the military. PVL infections are not only a problem for our military personnel, but may spread to and affect their families (29). Other nations’ armed services are facing a similar problem. The US military has published extensively on its problem with PVL infection, looking to identify the risk factors and identify possible areas for intervention. It is understandable why PVL would be more likely to spread through a military population: armed forces personnel, particularly during basic training, spend large amounts of time in crowded environments with multiple abrasions to their skin.

Clindamycin resistance in S. aureus tends to result from changes to 23S part of the ribosome which is caused by a plasmid-carried gene (erm). Resistance to clindamycin is not always obvious on initial testing of an isolate, as the resistance mechanism is inducible (that is to say it will turn on following exposure to certain antibiotic groups). The level of clindamycin resistance identified in this study are similar to the levels reported in a study of UK isolates in 2005 (12).

Conclusion
PVL within the military is an issue that needs further research. There are a number of actions that can be implemented to help in the day to day management of our patients. Firstly, military clinical staff must continue to have a high level of suspicion for all cases of recurrent skin and soft tissue infection, remembering that family members as well as serving personnel are at risk. Secondly, they should continue to take swabs from high risk patients and specifically request PVL testing when submitting the sample. It is important to be aware that not all NHS hospital laboratories will perform PVL testing as a matter of routine; it has to be a specific request.

Further information on PVL infections and their management will be available in a Joint Service Publication to be released soon. Further areas of research, including a larger study into the carriage levels of PVL S. aureus in the military, and the epidemiology of the military PVL-positive strains, will shed more light on the spread and transmission of this potentially deadly bacterium.

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References


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