Increased incidence of *Staphylococcus aureus* bacteraemia among people who inject drugs in Oxfordshire reveals a polyclonal outbreak.

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INTRODUCTION

- People who inject drugs (PWID) are at increased risk of viral and bacterial infections, including of Staphylococcus aureus bloodstream infections.[1]
- 11% of all methicillin susceptible *S. aureus* (MSSA) bacteraemia in England in 2015 occurred in PWID.[1]
- A clonal outbreak of MRSA causing bacteraemia among PWID has previously been demonstrated in the UK.[2]

- Aim: After observing an increased number of PWID admitted to Oxford University Hospitals NHS Foundation Trust with *S. aureus* bacteraemia (SAB), we conducted a retrospective examination of SAB in Oxfordshire to investigate the apparent outbreak

METHODS

Case identification

- We reviewed mandatory surveillance data on all SAB cases in the trust 2011-2016 to quantify the number of cases with injecting drug use documented as a risk factor.
- We reviewed electronic patient records (EPR) of all admissions with an episode of SAB in 2015-6, including a detailed Infectious Diseases/Microbiology consultation document and electronic discharge summary to assess the accuracy of surveillance-reported drug use

Case review

- We reviewed the EPR of all admissions with documented history of injecting drug use in 2015-6 to document clinical features of cases

Research ethics committee approval was not required for this public health surveillance exercise.

Microbiology and Genomics Methods

- One bacterial isolate from each 2015-16 episode in PWID was retrieved for whole genome sequencing.
- Single colonies were picked, DNA extracted and randomly allotted a well in the sequencing plate
- All isolates were sequenced on the Illumina HiSeq 4000; reads mapped to a reference genome (MRSA252[3)] using Stampy[4], and assembled using Velvet[5.]
- Maximum likelihood phylogeny was constructed using RAxML[6] assuming a general time reversal model.
- Multi-locus sequence type (MLST) was determined *in silico* by interrogating the de novo assembly for each of the 7 MLST loci.[7]

RESULTS

A true increase in cases was observed. Between 2011-2014, surveillance reporting data recorded 101-143 episodes of SAB per year, with 2-8 episodes (median 3) in PWID. In 2015 there were 10/151 episodes, and 27/154 in 2016 (P= <0.0001, χ^2-test). Surveillance-reported drug use closely matched 2015-16 EPR data, with EPR-recorded drug use in 35/37 episodes, and in no others. Mandatory surveillance identifies cases in PWID with high sensitivity (100%) and specificity (95%).

Recurrent and complicated SAB is common in this population. Seven recurrences >14 days after last positive culture occurred in 6 PWID, after a median of 140 days (range 18-667). Six of 35 (17.1%) episodes were complicated by endocarditis. Musculoskeletal infection was confirmed in 3/35 episodes (8.6%) and discitis was suspected in a further 3 patients who elected to leave hospital prior to imaging.

Blood culture isolates were available for 34/35 cases. Whole genome sequencing revealed a polyclonal outbreak with no dominant strain (Figure 1). Despite multiple cases with the same sequence type (ST), we found no evidence of transmission: at least 250 polymorphisms separate isolates from different patients. Comparing isolates from recurrent episodes, 4 recurrences were closely related (0-17 bp), and 3 recurrences involved genetically distant isolates (17kb-45kb). Time between isolates did not predict recurrence with a new strain (Table 1).

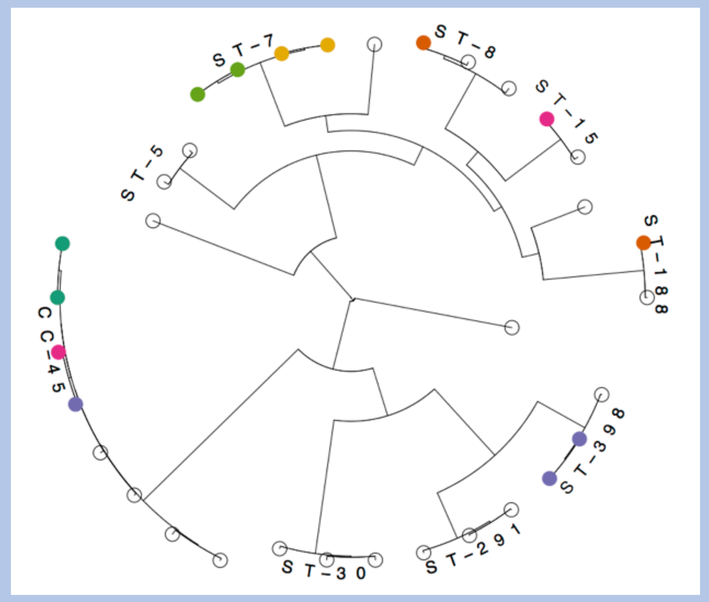

Figure 1: Maximum likelihood phylogeny of 34 isolates, each isolated in a separate episode of SAB. Filled circles of identical colour represent isolates from the same individual

Days between episodes	SNPs between isolates
18	45361
57	0
87	2
140	36427
220	17
535	17009
667	3

Table 1: Time between positive blood cultures and estimated number of SNPs between isolates for 7 recurrent episodes.

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CONCLUSIONS

The incidence of SAB in PWID in Oxfordshire has recently increased and this is associated with significant morbidity.

Whole genome sequencing reveals no evidence of an outbreak strain.

Increasing number of cases may be due to either a greater number of PWID or increasing risk of injecting practice.