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Multi-drug resistant *Shigella sonnei* cluster (CTX-M-27) probably associated with MSM

Information for healthcare professionals

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Multi-drug resistant *Shigella sonnei* cluster (CTX-M-27) probably associated with men who have sex with men

Whole genome sequencing (WGS) has identified links between 17 cases of *Shigella sonnei* in England, Wales and Scotland between March and November 2018. Case isolates fall within the 10-SNP cluster CC 152 1.3.197.460.1360.% on WGS. A number of cases resident in multiple states across the USA that identify as men who have sex with men (MSM) have also been found to have *S. sonnei* within the 10 SNP cluster on WGS.

This strain is of concern due to its multi-drug resistant genotype; resistance markers include $bla_{\text{CTX-M-27}}$, which encodes an extended spectrum β-lactamase (ESBL), a single *gyrA* mutation associated with reduced susceptibility to fluoroquinolones and the macrolide resistance markers *erm*(B) and *mph*(A). Treatment of infections caused by this strain with first-line agents like quinolones, azithromycin and ceftriaxone may not be effective due to its multi-resistance; please see below for microbiological details.

Microbiologists should be aware that this strain of *S. sonnei* is phenotypically an ESBL producer, resistant to amoxicillin, co-amoxiclav, ceftriaxone, ceftazidime and co-trimoxazole. The azithromycin MICs have been >256 mg/L (epidemiological breakpoint of 16 mg/L) in all except 3/17 strains.It is consistently susceptible to chloramphenicol, ertapenem, temocillin, gentamicin, colistin, mecillinam and fosfomycin.

Laboratories should follow EUCAST protocols for susceptibility testing of Enterobacterales with these antibiotics.

Susceptibility testing for quinolones:
The strain has a single *gyrA* mutation, but may appear susceptible to ciprofloxacin on testing with gradient strips (MIC on screening has been 0.125 mg/L). Past experience with strains with this single *gyrA* mutation indicate that cases have a suboptimal response to treatment with ciprofloxacin and symptoms, especially diarrhoea, may be prolonged (beyond 7 days).
Further screening for quinolone resistance can be undertaken by using either
a) nalidixic acid; 30 μg disc (NAL30), looking for a zone size less than 20 mm or
b) pefloxacin disc (5 μg disc) looking for a zone size less than 23 mm is likely to work (currently under validation by EUCAST, work ongoing, personal communication G. Kahlmeter)
Zones sizes less than these should be interpreted as resistant and the isolate should be sent to GBRU for MIC determination.

Susceptibility testing for azithromycin:
The azithromycin breakpoint of S ≤16 mg/L can be used for *S.sonnei* based on the ECOFF for wild-type strains (CLSI).

Susceptibility testing for antibiotics such as mecillinam and fosfomycin can also be arranged on special request from GBRU and will be free–of-charge if the isolate is confirmed to belong to the outbreak strain, otherwise a charge will apply.

Treatment:
ESBL-producing *S. sonnei* can cause severe infection in MSM and treatment may be required in some cases that have prolonged dysentery or sepsis.

Oral treatment options for this strain are limited to antibiotics such as chloramphenicol, mecillinam and fosfomycin. Use of either mecillinam or fosfomycin would be off label or unlicensed, they should only be considered for treating uncomplicated cases such as prolonged diarrhoea. Due to a lack of evidence of their efficacy in severe infections, mecillinam and fosfomycin should not be used in the immunocompromised or cases with sepsis or severe colitis; consideration should be given to intravenous agents like ertapenem or temocillin.

For information on doses of these antibiotics please see attached references. Further queries should be addressed to the duty microbiologist at Colindale on: 0208 327 6736.

References / further information

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