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Capsule switching in an outbreak of clonal complex 11 Neisseria meningitidis in Western Australia is associated with recombination events associated with virulence

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Background

Western Australia had an outbreak of invasive meningococcal disease (IMD) caused by clonal complex 11 serogroup W (cc11 MenW) between 2013-2020. Vaccination campaigns of the ACYW conjugate vaccine in young adults and children were conducted in 2017 and 2019. In 2019, the last five IMD cases were caused by serogroup C (MenC) isolates in individuals over 30 yrs old. We investigated the hypothesis that capsule switching from MenW to MenC had an effect on meningococcal virulence.

Aim/Methods

A recombination-adjusted timed phylogeny of cc11 outbreak isolates from 83 IMD cases from 2013-2020 was produced using Illumina paired-read sequencing aligned to the closed genome of type strain EXNM741. Recombination was assessed using the Genome Comparator tool from the Neisseria PubMLST database and

manual curation. To assess the impact of capsule switching on virulence, isolates were tested for colonization of Detroit 562 epithelial cells and survival in differentiated THP-1 macrophages. Mutants in sialic acid biosynthesis (cssB), capsule polysaccharide synthesis (csc/csw) and lipopolysaccharide (LOS) sialylation (lst) were compared between three MenW and three MenC isolates.

Results

Phylogenetic analysis demonstrated that the five cc11 MenC isolates were deeply nested within the cc11 MenW outbreak lineage and therefore were likely true capsule-switched mutants. Including the capsule synthesis locus, six recombination regions were observed either immediately before or during the capsule switching event. These regions encoded both metabolic and known virulence genes including lst, opaD, opaJ and pilI. Although adherence to Detroit cells was not significantly different between MenC and MenW isolates, invasivity changed in association with the distribution of the recombination events. MenC capsule expression inhibited epithelial invasion more than the MenW capsule (5.78-13.01-fold vs 0-3.01 reduction, respectively, $p< 0.05$), while no effect was seen for LOS sialylation (3/4 isolates). While survival in THP-1 macrophages remained similar, MenW isolates were internalised more frequently than MenC isolates ($p< 0.001$).

Conclusions

This study examined the impact of capsule switching on meningococcal virulence in the context of a meningococcal outbreak. We find support for the metabolic hypothesis of meningococcal virulence and show that compatibility of the meningococcal genome with a given capsule type is important for the maintenance of meningococcal virulence