Capsular Vi Polysaccharide Antigen in Salmonella enterica Serovar Typhi Isolates

Characterization of Salmonella enterica Serovar Typhi isolates for their Vi capsular polysaccharide antigen-related genetic sequences is desirable to define the role of isolates lacking such sequences in differential replication at unusual sites, including those coincident with human immunodeficiency virus (HIV). Infection with Vi-negative strains might produce typhoid fever among those immunized with various Vi vaccines.

S. enterica serovar Typhi isolates lacking Vi capsular polysaccharide antigen, evident during slide agglutination with Vi typing antisera, have been known for several decades. High molarity turns off expression of Vi antigen with a false label of Vi-negative S. enterica serovar Typhi. Genotypic sequences linked with an expression of S. enterica serovar Typhi Vi capsular polysaccharide antigen are located at three widely separated chromosomal loci, viaA, viaB, and ompB. The ViaB locus, an operon that contains two genes that encode enzymes for the biogenesis and translocation of Vi, is present in all Vi-positive strains. Enzymes encoded by genes tviB, tviC, tviD, and tviE catalyze intracellular Vi synthesis. The translocation and anchoring of Vi to bacterial surface is through export genes vexA, vexB, vexC, vexD, and vexE. Two other chromosomal regions, the ompB operon and viaA, which is allelic to resB-resC, have a role in expression of Vi capsular polysaccharide antigen in high molarity and other environmental signals (9).

Recently, even S. enterica serovar Typhi isolates that lacked ViaB sequences were responsible for an epidemic of multidrug-resistant typhoid fever in Calcutta, India (10).

S. enterica serovar Typhi strains devoid of capsular Vi antigen are frequently found at the National Salmonella Phage Typing Centre in the Department of Microbiology at the Lady Hardinge Medical College, New Delhi, India. During the year 2000, the facility received 1,289 isolates of Salmonella enterica serovar Typhi from different collaborating centers in India and Nepal. Upon receipt, each individual isolate was cultured in nutrient broth for a subculture on MacConkey agar. Biochemical, serological, and antibiotic sensitivity profiles were worked out. The presence or otherwise of Vi antigen was confirmed at room temperature by slide agglutination employing Vi typing antiserum (Murex Biotech Ltd., Dartford, England). The antibiotic sensitivity was carried out by disk diffusion method.

There were 113 Vi-negative Salmonella enterica serovar Typhi isolates drawn, including 88 isolates from blood, 3 isolates from bone marrow, and 1 isolate from a stool specimen. Such Vi-negative Salmonella enterica serovar Typhi isolates drawn from the patients presenting at the collaborating centers located in the northern, central, eastern, and southern parts of India and Nepal. Among the 113 isolates, 34 were resistant to ampicillin, tetracycline, chloramphenicol, and cotrimoxazole. None of the Salmonella enterica serovar Typhi isolates was resistant to ciprofloxacin or cephalaxin. There was no information regarding the HIV serological status of any of the patients.

Vi-negative Salmonella enterica serovar Typhi isolates, though less infective than Vi-positive isolates, can cause a disease indistinguishable from the one caused by Vi-positive isolates (3). They could replicate selectively at abnormal sites in immunocompromised individuals. S. enterica serovar Typhi and HIV coinfection is frequent (8). Vi-negative isolates are frequently associated with glomerulonephritis, hepatic dysfunction (5), common iliac artery occlusion, and perforation of terminal ileum and appendix (1). Salmonella enterica serovar Typhi even caused thyroiditis in a 62-year-old woman (4), multiple brain abscesses in a 2-month-old girl (2), and gluteal hematoma (7).

Vi-negative S. enterica serovar Typhi, on its entry to an intracellular niche, is protected from Vi antibody (3). Any prophylactic vaccine that does not elicit cellular immunity would be unlikely to confer protection against an intracellular replication of Vi-negative S. enterica serovar Typhi. That might have occurred during the trial with conjugated polysaccharide S. enterica serovar Typhi vaccine bound to nontoxic recombinant Pseudomonas aeruginosa endotoxin A (rEPA) in the Dong Thap Province in Vietnam. There were four isolations of S. enterica serovar Typhi from vaccinated children (6). Vi characterization, both phenotypic and genotypic, of S. enterica serovar Typhi isolates in prospective trials with any typhoid vaccine should be mandatory. That would reveal the role of Vi-negative S. enterica serovar Typhi in rare and unexpected failures with the vaccines presently in use, typhoid prophylactic vaccines.

The pathogenicity of typhoid fever is being evaluated intensively in Vietnam by Wain et al. (11). Among the 120 Vietnamese patients with enteric fever, there was a 30-fold higher concentration of S. enterica serovar Typhi in bone marrow. Furthermore, bacterial counts were elevated further with an increasing duration of illness. There were no details about a presence or absence of Vi antigen in the Vietnamese S. enterica serovar Typhi isolates. Such an investigation, retrospective and prospective, on S. enterica serovar Typhi isolates in Vietnam and elsewhere would be essential to evaluate any intracellular accumulation and dissemination of Vi-negative S. enterica serovar Typhi isolates. A deficient cellular immunity in the host could encourage even prolonged persistence of S. enterica serovar Typhi at aberrant locations.

To conclude, fiscal input for a microbiological surveillance for genotypic characterization of S. enterica serovar Typhi would be cost-effective. Apart from gaining fundamental information regarding pathogenesis of typhoid fever, with such support it would be possible to assay the efficacy of the newer conjugated typhoid vaccines. Moreover, Vi genotypic characterization of S. enterica serovar Typhi would be an asset to reference centers associated with any in-depth investigations performed with Salmonella enterica serovar Typhi.

REFERENCES


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