Emergence of telithromycin resistance in Haemophilus influenzae in Japan

An isolate of Haemophilus influenzae type d from a Japanese patient with pneumonia was found to have a MIC of 64 μg telithromycin ml⁻¹. Emergence of telithromycin resistance in H. influenzae is an important clinical problem, although reports concerning resistance to telithromycin in clinical isolates of H. influenzae are few (Bogdanovich et al., 2006).

A 76-year-old man with a history of asthma and smoking was admitted to a hospital because of fever, cough and coxalgia in November 2004. No antimicrobial agent had been administered since December 2003 for the treatment of pneumonia, bronchitis, pharyngitis, tonsillitis and sinusitis. In 2004, however, telithromycin resistance emerged rapidly in H. influenzae in Japan. To the best of our knowledge, this report is the first detailed account of telithromycin-resistant H. influenzae in Japan. In this report the mechanisms conferring telithromycin resistance have been partially characterized. Multiple mutations in 23S rDNA from domains I to VI were identified, as well as an amino acid mutation in G65A in L4. However, no mutation was found in L22. In the present isolate the effect of efflux on telithromycin resistance remains unclear.

In Japan, telithromycin has been approved since December 2003 for the treatment of respiratory tract infections, such as pneumonia, bronchitis, pharyngitis, tonsillitis and sinusitis. In 2004, however, telithromycin resistance emerged rapidly in H. influenzae in Japan. To the best of our knowledge, this report is the first detailed account of telithromycin-resistant H. influenzae in Japan. In this report the mechanisms conferring telithromycin resistance have been partially characterized. Multiple mutations in 23S rDNA from domains I to VI were identified, as well as an amino acid mutation in G65A in L4. However, no mutation was found in L22. In the present isolate the effect of efflux on telithromycin resistance remains unclear.

In recent studies (Bogdanovich et al., 2006, 2004), H. influenzae isolates showing MICs >0.5 μg telithromycin ml⁻¹, which include those ‘susceptible’ according to CLSI (2006) categories, had telithromycin efflux mechanisms. High-level telithromycin resistance in H. influenzae is rare, but has been characterized by alterations of ribosomal proteins and/or 23S rDNA, as well as efflux mechanisms (Bogdanovich et al., 2006). Although continuing studies are required, multiple mutations in 23S rDNA from domains I to VI may play some role in conferring high-level telithromycin resistance, in addition to ribosomal protein alterations and telithromycin efflux. These mechanisms differ from those conferring high-level macrolide resistance, that is, ribosomal protein alterations combined with macrolide efflux, and/or specific mutations in domain II and V of 23S rDNA (Peric et al., 2003). Control and prevention of telithromycin resistance will require further epidemiological investigation and characterization of the underlying mechanisms.

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References


