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論文内容の要旨

Synopsis of Thesis

〔論文題名 : Thesis Title〕 Genotypic Profile of *Streptococcus suis* Serotype 2 and Clinical Features of Infection in Humans, Thailand

(タイ国におけるヒト感染例由来豚レンサ球菌血清型2型遺伝子型プロフィールとその臨床学的特徴)

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〔目的(Purpose)〕

To examine associations between clinical features of *Streptococcus suis* serotype 2 infections in humans in Thailand and genotypic profiles of isolates.

〔方法ならびに成績(Methods/Results)〕

From January 2006 through August 2008, a total of 1,154 unidentified streptococcal isolates from blood or CSF were collected from hospitals in all 76 provinces of Thailand. Biochemical testing, *S. suis*-specific and *S. suis* serotype 2- or 1/2-specific PCR confirmed 165 isolates from 34 hospitals in 25 provinces as *S. suis*. The final serotype of all strains was confirmed by coagglutination tests that used rabbit antiserum. Multilocus Sequence Typing (MLST), Pulsed-Field Gel Electrophoresis (PFGE), and PCR determination of 89Kb pathogenicity island (PAI), virulent-associated genes (*epf/sly/mrp*) were done for 165 isolates. Clinical data was collected from these 34 hospitals by using clinical case record form. MLST enabled classification of 165 strains into 4 ST complexes: the ST1, ST27, ST29, and ST104 complexes. The largest cluster of 89K PAI-carrying strains was ST1 ($n = 81$, 49.1%), which had the *epf+/sly+/mrp+* genotype. Another large cluster of non-89K PAI-carrying strains was ST104, which had the *epf-/sly+/mrp-* genotype. PFGE analyses identified 20 pulsotypes. Analysis of the dendrogram for these 20 pulsotypes revealed at least 16 clusters (I to XVI). 5 pulsotypes of A were identified for the ST1 and ST126 strains while 4 pulsotypes (H, H1, H2, and H3) were identified for ST104 strains. PFGE showed diverse DNA patterns for strains in ST27 complex. Of the 165 isolates, 136 (82.4%) were from the northern region, 19 (11.5%) from the central region, 7 (4.2%) from the northeast region, and 3 (1.8%) from the eastern region. The dates of isolation suggest that human cases occur more frequently during the rainy season, June–August of each year. The clinical features of the 158 human cases of *S. suis* serotype 2 infection are meningitis category ($n = 93$) included 22 cases of confirmed meningitis, 44 cases of bacteremic meningitis, and 27 cases of probable meningitis. The nonmeningitis category ($n = 65$) included sepsis with focal signs other than meningitis ($n = 9$) and sepsis ($n = 56$). The ST1 strains were significantly associated with the meningitis category ($p < 0.0001$), the ST104 strains were significantly associated with the nonmeningitis category ($p < 0.0001$). The median age (range) of the 155 patients for whom age was known was 55.0 (18–93) years; 72.8% were male. No cases in children were identified in this study. All 158 patients had been hospitalized; median duration (range) of hospitalization for the 158 patients was 11 (1–45) days; 15 (9.5%) patients died. No significant differences were found between the fatal and nonfatal cases with respect to patient age or period of admission.

〔総括(Conclusion)〕

This study of the clinical features of 158 cases of *S. suis* serotype 2 infection in humans in Thailand showed that the disease occurs sporadically in adults and results in a mortality rate of $\approx 9.5\%$; the major clinical manifestations include meningitis and sepsis. MLST analyses of 165 isolates from humans indicated that the major STs were ST1 followed by ST104. Although both ST1 and ST104 strains cause sepsis, it is likely that only the ST1 strain causes meningitis.

論文審査の結果の要旨及び担当者

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論文審査の結果の要旨

豚レンサ球菌感染症は獣医学領域では古くから知られた病原細菌であるが、近年、世界的に重篤なヒト感染例が多く報告され、注目を集めている。一方でその細菌学的知見、臨床病態、疫学等、未だ不明な点が多い。

申請者は、本論文においてヒトにおける豚レンサ球菌感染症の実態を明らかにするために、タイ国における本菌感染症の後方視的解析をおこない、分離菌の主要な血清型が2型であること、また主要なMLST (multi locus sequence typing) はST1およびST104であることを明らかにした。各症例を病態により髄膜炎カテゴリー (58.9%) と非髄膜炎カテゴリー (41.1%) に分類した場合、ST1株は髄膜炎カテゴリーに、ST104株は非髄膜炎カテゴリーに対して有意に関連することが明らかとなった。

以上の知見は豚レンサ球菌感染症の実態を理解する上で大変重要であり、また本菌感染症発症機序解明に大いに貢献するもので、学位の授与に値すると考えられる。