肺炎鏈球菌對抗生素penicillin和ceftriaxone的抗藥機制及多重抗藥性血清型19A基因型ST320的演化機制

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摘 要

背景: 肺炎鏈球菌(Streptococcus pneumoniae) 為一重要的致病菌，而目前世界針對於肺炎鏈球菌有著兩個主要的問題: 1.越來越多的抗藥性菌株產生尤其是對盤尼西林以及頭孢黴素2.血清型19A的感染在全世界都有增長趨勢，在七價疫苗(7-valent pneumococcal conjugate vaccine, PCV7)施打後更有明顯增長趨勢。 材料方法: 共有82株臨床菌株(實驗一為80株，實驗二為2株)由長庚兒童醫院所收集(1)進行了抗生素MIC值測試以及抗生素結合蛋白(penicillin-binding protein, PBPs)的胺基酸序列分析(2)抗生素MIC值測試，並用multilocus sequence typing (MLST)比對菌株基因型以及分析pbp1a和pbp2x上下游1Kb基因序列。 結果: (1)在PBP1A靠近C-端有六個胺基酸突變點對於抗生素penicillin有顯著差異，而靠近N-端有十個胺基酸突變點對於抗生素ceftriaxone有顯著差異。PBP2B靠近活性位區有十二個胺基酸突變點對於抗生素ceftriaxone有顯著差異。PBP2X的胺基酸突變區在penicillin以及ceftriaxone MIC值小於0.19 μl/mg時幾乎都有共同的突變區域，PBP2X相較於PBP1A, PBP2B顯示有較早突變的趨勢。(2)因血清型19A與14的抗生素結合蛋白(PBP1A, PBP2X)突變點為相同的，但血清型19A與14的基因型為相異的，血清型19A基因型為ST320而血清型14基因型ST876 ，顯示一致性的突變區可能來自相同抗生素的篩選環境所造成的 。根據血清型19A與14的pbp1a, pbp2x上下游各1Kb的基因比對分析發現在pbp2x上游及pbp1a下游具有高度同源性(19A和14)。 討論: 本實驗結果顯示(1)PBP1A的C-端與提升penicillin MIC值有關，N-端與提升ceftriaxone MIC值有關。PBP2B的突變會影響ceftriaxone MIC值。而PBP2X比PBP1A 及2B會更早出現突變來影響penicillin及ceftriaxone 的MIC值。(2)推測血清型19A(ST320)與14(ST876)的PBP1A, PBP2X有相同的突變點，其產生是來自於相同的抗生素篩選壓力所造成的。

關鍵詞 : 肺炎鏈球菌、盤尼西林、頭孢黴素、血清型、基因型

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