2-2.

Cytokine profiles of newborns exposed to chorioamnionitis who developed chronic lung disease

（社会人大学院博士課程 4 年小児科・思春期科）
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INTRODUCTION : Neonatal chronic lung disease（CLD）is caused by intrauterine infections, pressure damage, and oxygen toxicity caused by postnatal respiratory management. Inflammatory cytokines are strongly induced in CLD, particularly when intrauterine infections, such as chorioamnionitis（CAM）occurrs. In this study, serum cytokine levels of newborns with CLD were comprehensively analyzed at birth, and the association between respiratory prognosis and severity were investigated.

METHODS : A total of 18 patients, diagnosed as having CLD36（CLD36 was defined as requiring oxygen at a corrected gestational age of 36 weeks, i.e., the need of auxiliary ventilation, such as positive pressure ventilation）after admitted in Neonatal Intensive Care Unit（NICU）between March 2018 and October 2019 were included in the study, and their cytokine levels were analyzed. The subjects were classified into 2 groups ; 9 CAM patients and 9 nonCAM patients, and their backgrounds were analyzed. Serum cytokines from samples on day 0 was measured and compared between the 2 groups. Levels of cytokines interluekin（IL）-1β, IL-6, IL-8, IL-10, and tumor necrosis factor（TNF）- were measured using the Bio-Plex suspension array（Bio-Rad Laboratories）. The number of white blood cells（WBC）, C-reactive protein（CRP）and serum IgM, duration of respiratory management were also compared between the 2 groups.

RESULTS : In the CAM group, there were 4 patients who received home oxygen therapy and 1 death. IL-8 levels were significantly higher in the CAM group than in the non CAM group（P<0.05）. The IL-8 / IL-10 cytokine ratio tended to be higher in the non CAM group, but the difference was not statistically significant.

CONCLUSION : IL-8 levels were significantly higher in the CAM group than in the nonCAM group. Patients with increased serum IgM levels or IL-8/IL-10 tended to require a longer duration of respiratory management. Therefore, IL-8/IL-10 may be a useful biomarker to predict the respiratory prognosis of extremely preterm infants.

2-3.

ゼブラフィッシュを用いた Loyes-Dietz 症候群の原因遺伝子と病態の解析

（社会人大学院博士課程 2 年小児科・思春期科）
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Loyes-Dietz 症候群（LDS）は常染色体優性遺伝形式をとる希少難病で、大動脈病変を主体とし、心血管系、骨格系、皮膚などに特徴的な症状を呈する全身性の結合織疾患である。その臨床像は、Marfan 症候群（MFS）や Shprintzen-Goldberg 症候群に類似した骨格系病変を主体とする症例から遺伝性大動脈瘤のみを呈する症例まで幅広い。しかし､大動脈瘤･解離、動脈蛇行などの血管病変はほぼ全例で認め、MFS に比しより若年期での大動脈瘤形成や解離が起こる傾向があるため、早期診断・経過観察を行っていく必要がある。LDS は、MFS の診断基準である Ghent 基準を満たすため MFS と誤診されることも多く、診断には LDS に特徴的な臨床所見の確認と遺伝子解析を行うことが重要である。これまで見出されている原因遺伝子は TGFBR1、TGFBR2、SMAD2、SMAD3、TGFB2、TGFB3 の 6 種類であり、これらの遺伝子産物はいずれも TGFβ シグナル伝達に関連している。

我々は、LDS の原因遺伝子、tgfbr2 をターゲットとして、スプライシング異常を引き起こすモルフォリノアンチセンスオリゴ（MO）を用いて LDS モデルフィッシュを作製した。1 細胞期の受精卵に tgfbr2 の MO をマイクロインジェクションしたところ、孵化 5 日後に、顔貌の異常、背中の湾曲、心奇