28PW-am213

筋ジストロフィー犬の骨格筋における筋線維タイプの解析

○湯浅　勝敏[1,2], 中村　昭則[2], 武田　伸一[2], 土方　貴雄[1]([1]武蔵野大薬, [2]国立精神・神経セ)

(**Background)** Skeletal muscles are composed of heterogeneous collections of muscle fiber types, and can adapt individual myofibers under various circumstances containing muscular disease, by changing fiber types. We examined the influence of dystrophin deficiency on fiber type composition of skeletal muscles in canine X-linked muscular dystrophy in Japan ($CXMD_J$), a large animal model for Duchenne muscular dystrophy (DMD). **(Methods)** We used tibialis cranialis (TC) muscles and diaphragms of normal and dystrophic dogs at various ages. For classification of fiber types, muscle sections were immunostained with antibodies against fast, slow, or developmental myosin heavy chain (fMHC, sMHC or dMHC), and MHC isoforms were also detected by gel electrophoresis. **(Results)** In comparison with TC muscles of $CXMD_J$, the number of sMHC fibers increased markedly and the number of fMHC fibers decreased with growth in the affected diaphragm. In populations of myofibers expressing fMHC and/or sMHC but not dMHC of $CXMD_J$ muscles, sMHC fibers were predominant in number and showed selective enlargement. Especially, in $CXMD_J$ diaphragms, sMHC fibers were significantly larger in populations of myofibers without dMHC. Analyses of MHC isoforms also indicated a marked increase of type I and decrease of type IIA isoforms in the affected diaphragm at ages over 6 months. In addition, expression of dMHC decreased in the $CXMD_J$ diaphragm in adults, in contrast to continuous high-level expression in affected TC muscle. **(Conclusion)** The affected diaphragm might be effectively adapted toward dystrophic stress by switching to predominantly slow fibers. Furthermore, the dystrophic dog would be a more appropriate model than a murine one, to investigate the mechanisms of respiratory failure in DMD.