初期未分化型胃癌の遺伝子異常の研究

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研究代表者　服　部　隆　則

（滋賀医科大学医学部・教授）

はしがき

研究組織

研究代表者：服　部　隆　則（滋賀医科大学医学部・教　授）

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研究成果

初期未分化型胃癌とくに印環細胞癌の遺伝子異常はほとんど知られていなかった．平成８年度に印環細胞型の早期と進行癌を用いて，癌部のDNAを抽出し10箇所のmicrosatelliteについてPCRを施行し，microsatelliteのinstability(MSI)とloss of heterozygosity(LOH)を調べたところ，MSIと接着分子関連遺伝子のLOHは一部の胃印環細胞癌における早期からの遺伝子異常の一つであることを示した．同時にDNA ploidyを調べたところ，早期癌ではほとんど二倍体であったが，進行癌では異倍体のパターンを示した．平成9年度はcomparative genomic hybridization (CGH)法を用いて早期と進行期の印環細胞癌の全染色体における遺伝子異常を検索した．その結果，早期癌ではCGH法では染色体変化は認めなかったが，進行期癌では７番染色体のコピー数の増加が検出された．一方，早期の表層拡大型印環細胞癌を対象として，X染色体不活化現象を用いてクロナリティー解析をしたところ，ほとんどの症例でモノクローナルのパターンを示した．こられの癌はほとんどが二倍体癌であった．以上から，初期未分化型癌のほとんどは二倍体癌で，しかもMSIと接着分子関連遺伝子の異常以外には明かな染色体異常がなく，モノクローナルに表層拡大性に増生し，７番染色体に存在する未知の遺伝子に異常が生じ，異倍体化し下方に浸潤性に増殖・進展していくものと考えられた．