Gastrointestinal Stromal Tumor (GIST), Cajal Cell Phenotype of the Stomach : A Clinicopathologic Study and Comparative Genomic Hybridization Analysis

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Abstract : Recently, there has been a remarkable change in the concept of gastrointestinal stromal tumors (GISTs). GIST is a major subset of mesenchymal tumors of the gastrointestinal tract, but their definition, histogenesis, biological behavior, and clinical handling remain controversial. As a result, we herein defined GIST as a c-kit positive mesenchymal tumor of the gastrointestinal tract, with a "cajal cell phenotype". In this study, we examined 44 cases of cajal cell phenotypes arising in the stomach, to clarify the clinicophatholgic and immunohistochemical features. In addition, we employed comparative genomic hybridization(CGH)to detect any relative chromosome copy number changes in the cajal cell phenotype. According to our results, the age of the patients ranged from 42 to 87 years old (median 67). Almost all of the tumors were located in the upper parts of the stomach (70%). The median size of the cajal cell phenotype was 4.4 cm, including ten intramural small microscopic lesions (median 0.7 cm), that were incidentally detected. The tumors were classified into three groups, according to their predominant light microscopic appearance as benign (n=10, 23%), borderline malignancy (n=25, 57%), and malignant (n=9, 20%), mainly based on the presence of cellular and nuclear atypia and pleomorphism. Distant metastasis, direct invasion, or recurrence was observed in five cases, and all were histologically classified as malignant. The possibility of the presence of pluripotential stem cells was suspected to be the histogenetic orign of the tumor. In the immunohistochemical analysis, all tumors are diffusely stained for both c-kit and CD34. Caldesmon (h-CD), a novel smooth muscle maker, was also expressed in 36 (81%), while epithelial makers, such as epithelial membrane antigen (EMA) and cytokeratins, were only positive in one malignant case. It seems that the presence of epithelioid cells is thus one of the most important prognostic indicators for an aggressive behavior, in addition to tumor size, the mitotic index and/or Ki-67 labeling index. We confirmed the previously reported findings by observing losses on chromosome 14q, 22q, 1p, 9q and gains on 8q, 5q to be present in the cajal cell phenotype. In addition, several new chromosomal changes such as a deletion of 16p, 17q, 19p and a gain of 4q, 6q were frequently observed. The possibility that these quantitative genetic changes participated in tumor growth and development was therefore suggested.

Key words : GIST, Cajal cell phenotype, C-kit, Caldesmon, Cytokeratin, Clinicopathologic study, CGH