IS-3  Heterogeneous subgroups in human neuroblastoma for clinically relevant risk stratification

Grants-in-Aid the Ministry of Health, Labor and Welfare of Japan (H16-012)\(^1\), Committee on Tumor Registration, JSPS\(^2\)

Eiso Hiyama\(^{1,2}\), Yutaka Hayashi\(^{1,2}\), Masahiro Fukuzawa\(^{1,2}\), Fumiaki Sasaki\(^{1,2}\), Masahiko Sugiyama\(^{1,2}\), Satoshi Kondo\(^{1,2}\), Tatsuro Tajiri\(^{1,2}\), Akihiro Yoneda\(^{1,2}\), Kouhei Akazawa\(^{1}\), Megu Ohtaki\(^{1}\)

Purpose: Neuroblastoma is a biologically heterogeneous tumor and demonstrates favorable or unfavorable outcomes. In Japan, nation-wide neuroblastoma mass-screening (MS) project had been performed at 6-months-age infants during 20 years. To evaluate the heterogeneous subgroups of human neuroblastoma, we analyzed the neuroblastoma patients who were diagnosed in this period. Methods: The clinical course of 3600 patients including 2000 MS detected patients whose tumors were diagnosed between 1981 and 1998 were registered on Japanese Society of Pediatric Surgeons and Japanese Society of Pediatric Oncology. A total of 33 clinical factors including age at diagnosis, histopathology, and stage were assessed in our population. Results: Univariate analysis revealed 24 factors were significant (p<0.001). Multivariate analysis revealed that stage at diagnosis, bone metastasis, bone marrow metastasis, serum ferritin, MYCN amplification, and Shimada’s histology were the most significant (p<0.001). The prognostic contribution of age to outcome is continuous in nature. The simulation study using multitarget model revealed that distribution of clinical neuroblastoma was divided into three groups. Conclusions: Japanese neuroblastoma survey revealed several risk factors for clinically relevant risk stratification. Our proposal model could qualitatively explain distribution of neuroblastoma consisting of one favorable and two unfavorable subgroups. For clinically relevant risk stratification, an age cutoff should be considered by the distribution of heterogenous subgroups.