Natural history of ganglioneuroma (GN) and intermixed ganglioneuroblastoma (iGNB): An International Neuroblastoma Risk Group (INRG) project

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Background and introduction.

GN and iGNB represent the benign extremes of the neuroblastic tumour spectrum. Historically surgical resection was recommended, and in some cases chemotherapy. Recent reports suggest that a more conservative approach, including watchful observation, could be adequate and avoid surgical morbidity. However, large studies are lacking.

Aims

To describe the natural history of a large cohort of GN and iGNB, with a focus on presentation, treatment, outcomes and patterns of relapse.

Methods / materials

Eligible (diagnosis of GN and iGNB, age 0-24 years, diagnosed 1990-2016) patients were identified in the INRG Data Commons and descriptively analysed. Kaplan-Meier curves of event-free survival (EFS) and overall survival (OS), were generated, and the outcome of subgroups was compared using a log rank test. Treatment data reported to the INRG Data Commons are the initial assigned treatment, and not the actual treatment administered.

Results

945 eligible cases were identified, 198 (21%) GN and 747 (79%) iGNB. 323 (39%) were males. Median age was 4.5 years (range: 0-20.5 years), with 893 (94.5%) ≥18 months at diagnosis. The primary tumour was thoracic in 346 (39%) cases, abdominal in 261 (29%) cases, and adrenal in 184 (21%) cases. The majority (526 cases, 56%) were INSS stage 1, 241 (26%) were stage 2, 122 (13%) were stage 3, 2 (0.2%) were stage 4S, and 49 (5%) were stage 4. Only 51/945 cases (21%) presented with metastases (INSS stage 4 or 4S): 16 (31%) in bone marrow, 20 (39%) in bone, 18 (35%) in distant lymph nodes, 11 (22%) in other sites and 21 patients with unknown site of metastasis. *MYCN* was studied in 847 cases (90%) and was amplified in 17 (2%). None of the cases had other molecular investigations. The initial assigned treatment was: observation (16, 6%), surgery and observation (174, 61%), conventional-dose chemotherapy (2-8 cycles) plus surgery (66, 23%), and only 29 (10%) were treated with intensive chemotherapy. Of these 29, 17 were reported to have received stem cell transplant, and 4 received immunotherapy. The 5-year EFS survival was 94±0.9%, and 5-year OS was 96±0.8% (n=945).

Summary / conclusion

Patients with GN and iGNB have excellent survival outcomes. The majority of patients underwent an attempt at surgical resection. Further studies focusing on long term morbidity of the disease and/or treatment will be important, in order to inform more accurate 'balance of risk' for future treatment recommendations.