Comparison of Metaiodobenzylguanidine (MIBG) scintigraphy with microscopic bone marrow examination in patients with stage 4 neuroblastoma treated with autologous stem cell transplantation

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Objectives

In patients with neuroblastoma, bone marrow (BM) is the most common site of metastatic disease at diagnosis and is one of the most common sites of relapse. These patients are often treated with high dose chemotherapy followed by autologous stem cell transplantation as rescue. We evaluated the correlation between MIBG scintigraphy and microscopic BM examination (BM aspirate and biopsy) performed before autologous collection in patients with stage 4 disease, and the effect of BM contamination diagnosed by MIBG scintigraphy and/or microscopic BM examination on event free survival (EFS) and overall survival (OS).

Methods

We performed a retrospective analysis of children diagnosed with neuroblastoma between 1993 and 2019. Patients with incomplete data were excluded. This resulted in a group of 86 patients of which 47 had stage 4 disease. Thirty-seven of them were treated with an autologous hematopoietic stem cell rescue. The BM examination of three (3/37) patients gave inconclusive results and were excluded from further analysis. Mc Nemar was used to investigate the systematic difference of BM examination and MIBG scintigraphy and Cohen's kappa for measurement of agreement. Estimates of OS and EFS were based on Kaplan-Meier method. Log-rank test was used to compare OS and EFS distributions of patients with and without BM invasion diagnosed with both diagnostic tools.

Results

Thirty-four of 47 patients with stage 4 disease who had an autologous stem cell transplantation, were included. At the time of stem cell collection, BM metastases were still diagnosed with MIBG in 21% (7/34) and with microscopic BM examination in 6% (2/34) of the patients. More patients were diagnosed with BM invasion by MIBG scintigraphy compared to microscopic BM examination ($p = 0,0253$). There is a low agreement between the two diagnostic tests (kappa = 0,39). The 5-year OS of all patients (n=34) was 46,5% and the 5-year EFS 47,7%. Patients with BM invasion on MIBG scintigraphy and/or microscopic BM examination (7/34) at the time of stem cell collection had an OS at 5 years of 33,3% and a 5-year EFS of 28,6% and in the patients without BM invasion, 5-year 0S was 50,1% and 5-year EFS 53,2%. There was no statistically significant difference between both groups for OS ($p = 0,6$) and EFS ($p = 0,3$). When we compared patients (n=27) without BM invasion on MIBG scintigraphy and microscopic BM examination with patients with BM invasion on MIBG scintigraphy (n=5) but not with microscopic BM examination (5-year OS 50%, 5-year EFS 40%) and patients with BM invasion on both examinations (n=2) (5-year OS and EFS 0%), there was no statistical significant difference in OS ($p = 0,4$) and EFS ($p = 0,6$) between the 3 groups.

Conclusion

In our study population we found that statistically significant more patients were diagnosed with BM invasion with MIBG scintigraphy compared to BM examination and that there is a low agreement

between the two diagnostic tests. However, results of both examinations did not statistically significant effect OS and EFS.