Figure S1. Levels of VMA, HVA, NSE, LDH, PB-MRD and BM-MRD in a relapsed NB case. A 25-month old male with an adrenal tumor was diagnosed with stage 4, MYCN non-amplified, high-risk NB and was treated with the standard regimen (JNBSG JN-H-11 protocol; UMIN000005045) consisting of induction chemotherapy, high-dose chemotherapy with autologous stem cell rescue, surgery, and radiotherapy. At 61 weeks following diagnosis, a new tumor mass had emerged in the brain and BM cytology revealed NB cells. He was clinically diagnosed with tumor relapse and was treated by salvage chemotherapy and high-dose chemotherapy with allogenic stem cell rescue. During the 25-month treatment period, 10 pairs of BM, PB and urine samples were collected. The levels of VMA (μg/mg creatinine) and HVA (μg/mg creatinine) in urine samples, as well as the levels of NSE (ng/ml) and LDH (IU/l) in PB samples were extracted from the patient's medical records. The levels of PB-MRD and BM-MRD were determined by measuring 7NB-mRNA (relative copy number) in PB and BM samples with droplet digital polymerase chain reaction. MRD, minimal residual disease; VMA, vanillylmandelic acid; HVA, homovanillic acid; NSE, neuron-specific enolase; LDH, lactate dehydrogenase; BM, bone marrow; PB, peripheral blood; NB, neuroblastoma.

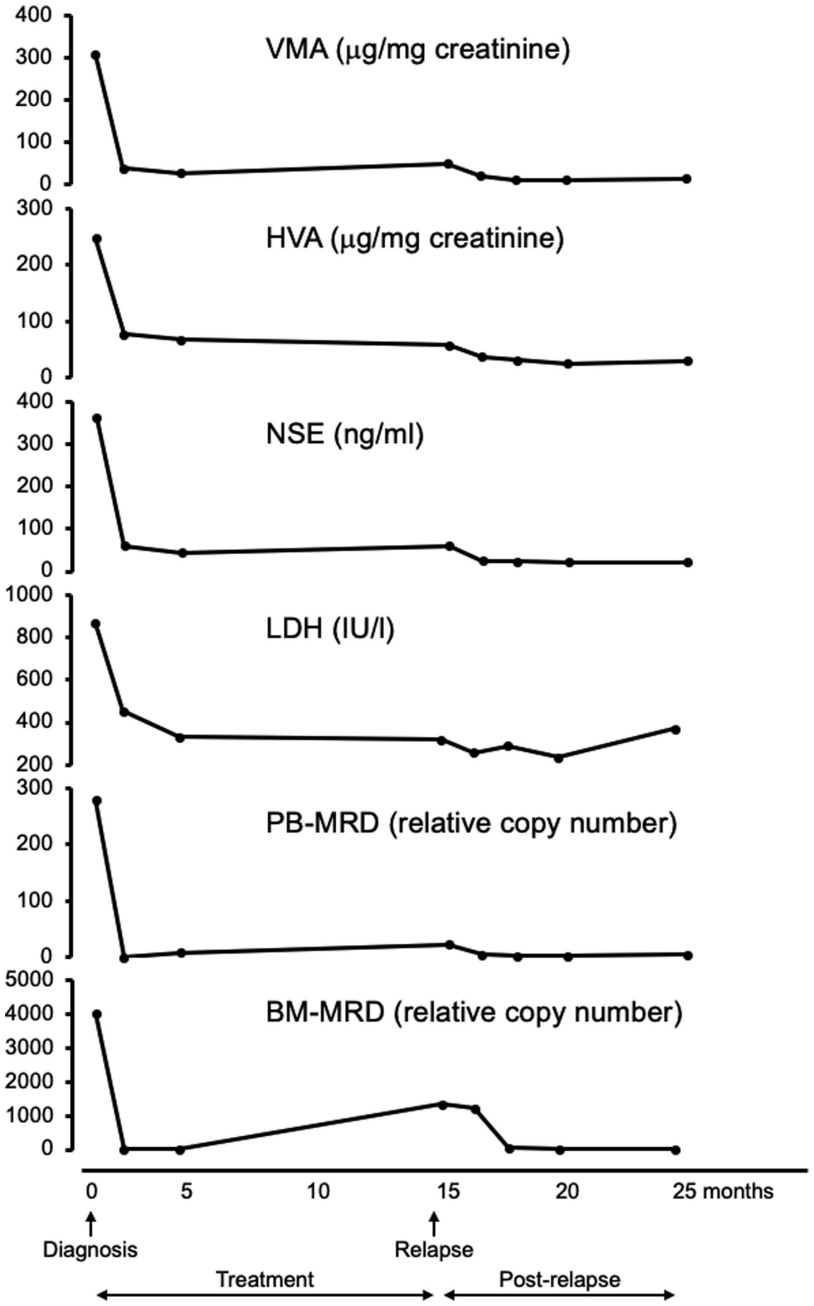

Figure S2. Correlations between tumor markers and MRD in subgroups of sample pairs according to each sample evaluation. Correlation between tumor markers and MRD in subgroups of sample pairs according to each patient evaluation. Levels of 7 neuroblastoma-mRNA (relative copy number) were determined by droplet digital polymerase chain reaction and their correlations with the levels of VMA (μg/mg creatinine), HVA (μg/mg creatinine), NSE (ng/ml) and LDH (IU/l) were assessed by Spearman's rank correlation coefficient in subgroups of concurrently collected BM, PB and urine sample pairs: Age at diagnosis (<18 months, 26 pairs; ≥18 months, 107 pairs), DNA ploidy (hyperdiploid, 33 pairs; diploid, 93 pairs), MYCN status (non-amplified, 88 pairs; amplified, 45 pairs) and recurrent tumor site (non-CNS, 55 pairs; CNS, 35 pairs). *P<0.05 (significant correclation). MRD, minimal residual disease; VMA, vanillylmandelic acid; HVA, homovanillic acid; NSE, neuron-specific enolase; LDH, lactate dehydrogenase; BM, bone marrow; PB, peripheral blood; CNS, central nervous system.