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Stage IV-S neuroblastoma with liver metastases - case report

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Abstract

Purpose: Stage IV-S neuroblastoma with metastatic dissemination to liver (Pepper's syndrome) is a very rare finding in infants. Our aim was to present patients with this syndrome with good prognosis.
Methods: During 2003-2004 3 infants (2 boys and 1 girl) with stage IV-S neuroblastoma, with liver metastasis were diagnosed and treated in our institutions. While the primary tumor in both boys was found to originate from the right adrenal, in the third patient the primary tumor was not localized. The latter patient had skin involvement, bone marrow infiltration (below 10%) and a solitary skull lesion. The diagnosis was defined after surgical removal of the adrenal tumors and by skin and bone marrow aspiration biopsies, respectively. The chemotherapy used included 6 cycles of vincristine, day 1, and cyclophosphamide, days 1-3.
Results: After completing chemotherapy all 3 infants are in complete clinical and laboratory disease remission.
Conclusions: Stage IV-S neuroblastoma with metastatic dissemination to the liver generally has good therapeutic outcome. Our experience also proves the favorable prognosis of this well defined patient group in infants.
Key words: infants, liver metastases, neuroblastoma

Introduction

Neuroblastoma is the most common embryonal tumor in childhood (incidence 1:10 000 of children's population; comprising about 8-10% of all paediatric malignancies). The potentiality to originate from various part of sympathetic nervous system, make possible the registration of primary tumors in different anatomical sites – adrenal glands and retroperitoneal region (in 70%); mediastinum and cervical region (20%); paravertebral regions (8%) and rarely (about 2%) in other sites.

Neuroblastomas are typical childhood tumors. They can be diagnosed prenatally, even with placental metastases. About 50% are children younger than 2 years; 75% are below 4 yrs. of age, 97% are diagnosed before the age of 10. At diagnosis 50% of infants and 70% of older children may have metastatic spread of tumor in lymph nodes, bones, bone-marrow, subcutaneous tissue, liver etc. These characteristic findings are reason for defining syndromes such as Pepper's Syndrome (in youngest infants with diffuse liver metastases), Smith's Syndrome (with skin involvement) etc.

In the most popular neuroblastoma staging system (Evans et al. 1971) beside the main grades from I to IV, there is a distinct Stage IV-S applied for infants, otherwise classified as I or II stage but with dissemination either in liver or skin, without bone metastases and no more than 20% neuroblasts in bone marrow. All these patients form a distinct prognostic group with survival comparable with Stage I and II neuroblastomas. Among them, patients

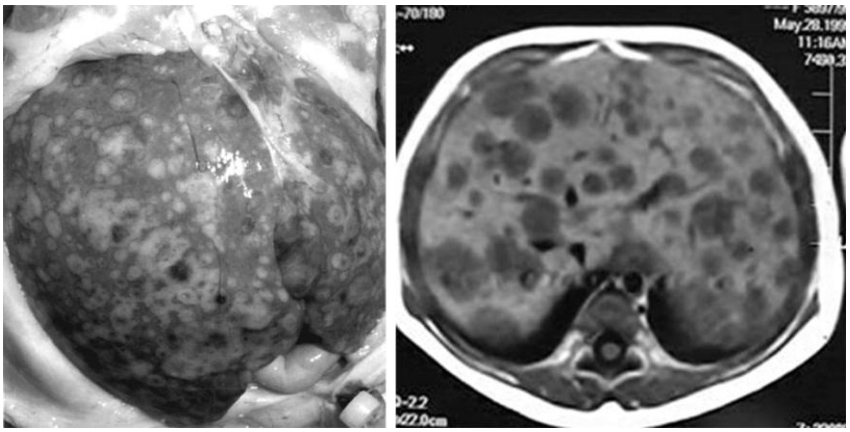
below 1 year of age have excellent survival (up to 75%) while children above 2 years survive poorly (35%).

Purpose

Our aim is to share our experience with a very rare form of clinical presentation of Neuroblastoma. In a period of 2 years (2003-2004) we have diagnosed, treated and followed-up 3 infants (2 boys and 1 girl) with Neuroblastoma stage IV-S with liver metastases.

Patients and Methods

Case1. A boy, 4 months of age, was referred (May 2003) to our hospital with a tumor mass in right abdominal half. The CT and ultrasound scans revealed a tumor, 8x5 cm in size, located in right adrenal gland and a massive enlargement of liver with multiple hypoechogenic zones consistent with liver metastases ***(fig.1)***. Laboratory findings have shown normal CBC, LDH, serum ferritin and no BM infiltration. NSE levels were elevated - 72.68 ngr/ml (norm – 16.7 ngr/ml).



After 2 cycles of chemotherapy (VCR 0.3 mg iv 1-st day; Cyclophosphamide 70 mg for 3 days) a primary tumor total surgical extirpation was performed (July 2003). Histology has proven neuroblastoma with metastases in liver. Post operative chemo was done for 6 more courses with VCR and Cyclophosphamide every 45 days. The follow-up for 3 years and 3 months show no evidence of the disease.

Case 2. A girl, 6 months old, (august 2004) had several bluish subcutaneous nodules on the front chest wall. Physical examination revealed liver enlargement with multiple hypoechogenic zones on ultrasound in both hepatic lobes. CT scan has not localized primary tumor, but proved the multiple metastases in liver. A skin nodule fine needle biopsy proved the skin involvement. Aspiration biopsy has registered below 10% neuroblasts in bone marrow. A single X-ray detectable solitary lesion on the skull was found. Laboratory tests showed no deviation in LDH and serum ferritin, while NSE was elevated – 169 ng/ml (norm – 16.7 ng/ml). A chemotherapy including 6 cycles of VCR (1 day 0.4 mg iv) and 6 days Cyclophosphamide – 100 mg iv was initiated. Follow-up shows a full clinical and laboratory remission for 2 years.

Case 3. A 2 months old boy (December 2004) was referred for a right-sided abdominal tumor. CT and ultrasound have registered tumor (6x8 cm) in right adrenal gland and multiple hypoechogenic lesions in liver. Laboratory data showed normal levels for CBC,

LDH, serum ferritin and elevated NSE – 100 ng/ml. After 2 cycles of VCR (1 day) and Cyclophosphamide (3 days), a reduction of the primary tumor helped radical surgical extirpation. Histology of the tumor and liver biopsy proved neuroblastoma. Chemotherapy with additional 6 cycles of the same cytostatic combination was performed after surgery. The boy is still in clinical and laboratory remission for 1 year and 9 months.

Results

After completion of therapy, all 3 infants are in clinical and laboratory remission. The control image follow-ups show no evidences of tumors.

Conclusion

Neuroblastoma stage IV-S with metastatic dissemination to liver generally has good therapeutic outcome. Our experience also proves the favorable prognosis of this well defined infant patient group.