



## LETTER TO EDITOR

# Simultaneous Neuroblastoma and Acute Lymphoblastic Leukemia in an Infant

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## Dear Editor,

With improvements in treatment of childhood cancers, survival of children with different kinds of malignancies has dramatically increased. As a result, the oncologists are encountering increasing complications during the course of treatment. The development of second primary malignant neoplasms are predicted to be an overwhelming and serious consequence of childhood cancers.<sup>1</sup> Secondary malignancies may be of any type, from benign, low-grade tumors to different kind of malignancies.<sup>2</sup> Several studies have shown that secondary malignancies are one of the main causes of treatment-related complications in children who have underwent chemotherapy for their primary cancer or survivors of childhood cancers. Childhood acute lymphoblastic leukemia (ALL), retinoblastoma and Hodgkin lymphoma are among pediatric cancers that are well-known for development of secondary malignancies.<sup>3</sup> However, reports of multiple concurrent primary neoplasms in children are uncommon.

Here, we report an infant who developed ALL while he was on treatment for neuroblastoma. This is the second reported case of concurrent ALL and neuroblastoma; however, the previous one was an adrenal tumor,<sup>4</sup> while this case was originated from posterior mediastinum along with sympathetic ganglia in paravertebral region.

A 6-month-old boy was admitted to ICU with respiratory distress for which he was intubated and had assisted respiration with mechanical ventilation. After

initial management and supportive care, a thoraco-abdominopelvic CT-scan was performed which showed a huge paravertebral mass extending from T2 to T10 and retrocrural space. After receiving a short course of dexamethasone for alleviating presumed edema around trachea and major airways, a thoracotomy and debulking with the benefit of sacrificing vital structures was performed. The pathology was compatible with poorly differentiated neuroblastoma; MKI was 2%, however, we couldn't assess "DNA index" for the specimen. He was staged as stage 3. Hence, the patient was considered as "intermediate risk" neuroblastoma according to "International Neuroblastoma Risk Group Stratification". Bone scan and bone marrow study were within normal range. Due to partial response of the tumor and unsuccessful resection after second look surgery, N6 protocol was started for the patient. While he was on treatment for about 9 months, he referred to the emergency department with fever and hyperleukocytosis. Complete blood count revealed WBC: 122000/mm<sup>3</sup>, Hb: 9.5 g/dL and Platelet: 42000/mm<sup>3</sup>. A bone marrow aspiration was performed which showed complete infiltration of marrow with blasts which were confirmed by flowcytometry to be of hematopoietic origin. Immunophenotyping was compatible with pre B-cell ALL. Chest CT-scan of the patient was still indicative of the retrocrural mass of about 4×4.5 cm at this time. ALL-directed therapy with protocol for "high-risk ALL" including 4 courses of high-dose methotrexate (5 gr/m<sup>2</sup>) at consolidation phase was

started for the patient.

He is in good general condition at the time of this report into the maintenance phase of ALL treatment with evidence of bone marrow remission. Interestingly, the primary tumor is not visualized on chest and abdominal CT-scan. He is scheduled to undergo an MIBG scan.

Genetic scientists claim that 5-10% of cancers in pediatric age group occur in children with a genetic defect that increases the risk for development of neoplasm<sup>5</sup>. Secondary acute leukemia is a serious complication in children and adolescents who have been treated for cancer. There is convincing evidence that cytotoxic drugs are among the most strongly suggested etiologic factors of secondary leukemogenesis.<sup>1,2</sup> Secondary acute myeloid leukemia (s-AML) is reported much more common and many cases may in fact be second primary cancers. Treatment and host-attributed factors both have been identified as risk factors contributing to development of s-AML. The most commonly recognized chemotherapeutic agents are alkylating agents and topoisomerase II inhibitors (epipodophyllotoxins and anthracyclines).<sup>6</sup> ALL after primary cancer is reported very rarely. Again, it is not certain whether these cases of ALL are truly secondary to the primary cancer or represent a second primary malignancy. Secondary ALL is estimated to comprise about 5-10% of all secondary acute leukemia cases.<sup>7</sup> In the case series by Hunger and colleagues three cases of ALL have developed at least 6 months after treatment for neuroblastoma, Wilms' tumor, and Hodgkin's disease.<sup>7</sup> There is also a report of a case of stage 4 neuroblastoma in a 4-year-old boy who developed M4-AML after 12 months of therapy with cyclophosphamide, doxorubicin, cisplatin, and etoposide. He died while both malignancies were active.<sup>8</sup> Goudarzipour and co-workers reported a 8-year-old girl with Ewing's sarcoma who was successfully treated with chemotherapy and radiotherapy who developed secondary ALL four years later.<sup>9</sup> There is also a report of simultaneous diagnosis of ALL and brain tumor in a 5-year-old boy with no identified genetic syndrome.<sup>10</sup> The only concurrent case of ALL and neuroblastoma was also from Iran in which ALL occurred as a second primary neoplasm about 2 years after diagnosis and treatment for adrenal neuroblastoma in a 3.5-year-old girl. She also had received a cumulative dose of about 3000 mg/m<sup>2</sup> of etoposide.<sup>4</sup> Our case was an infant with primary mediastinal neuroblastoma stage 3 who developed secondary ALL, 9 months after treatment for neuroblastoma. He is in good condition at the time of this report with remission for ALL while awaiting an MIBG scan be performed.

**Conflict of Interest:** None declared.

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