Occurrence of Wilms’ tumor in a child with hereditary spherocytosis

Derya Özyörük1, Hacı Ahmet Demir1, Suna Emir1, Esra Karakuş2, Bahattin Tunç1

1 Division of Pediatric Oncology, Department of Pediatrics, and 2 Department of Pathology, Ankara Children’s Hematology and Oncology Hospital, Ankara, Turkey.

Email: dozyoruk@yahoo.com

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Hereditary spherocytosis (HS) is the most frequent cause of congenital hemolytic anemia. It is an autosomal dominant genetic disorder characterized by cell membrane abnormalities, specifically in red blood cells. Although the association between benign, borderline and malignant tumors and HS is not clear, various tumors such as splenoma, adrenal myolipoma, pancreatic schwannoma, ganglioneuroma, extramedullary hematopoiesis, myeloproliferative disorders, multiple myeloma, B-cell lymphoma and acute lymphoblastic leukemia have been presented in case reports concerning HS patients. Here we describe a 6-year-old boy with HS who presented with a mass in the left kidney. Tru-cut biopsy revealed Wilms’ tumor (WT). To the best of our knowledge, this is the first case of WT associated with HS to be reported in the literature.

Key words: hereditary spherocytosis, malignant tumor, Wilms’ tumor.

Hereditary spherocytosis (HS) is the most frequent cause of congenital hemolytic anemia, occurring at a frequency of 1/5,0001,2. It is caused by a defect in the vertical relationship between the membrane skeleton and the lipid bilayer, which arises as a consequence of various deficiencies, primarily in ankyrin, spectrin and band 3 proteins, resulting in the loss of cellular architecture; red blood cells tend to develop spherical features and may subsequently undergo lysis. HS is a heterogeneous group of disorders with regard to clinical severity, protein defects and mode of inheritance1-4. Wilms’ tumor (WT), or nephroblastoma, an embryonal malignancy of the kidney, is the most common renal tumor of childhood. It usually presents as an abdominal mass in an otherwise apparently healthy child 5. To the best of our knowledge, HS associated with a malignant tumor has rarely been reported in the literature. We herein present the occurrence of WT in a child with HS.

Case Report

A 6-year-old male presented to our clinic with a left renal mass, which had been detected incidentally on abdomen ultrasonography. Abdominal computed tomography (CT) revealed a hypodense mass measuring 120x115x83 mm arising from the upper-middle part of the left kidney and extending into the inguinal area, with necrotic and cystic areas (Fig 1). The patient had a history of hereditary spherocytosis. Family history was unremarkable. The child was pale and had splenomegaly on physical examination. His laboratory findings were as follows: white blood cells 5.05×103/µl, hemoglobin 8.0 g/dl, platelets 250,000/µl, LDH 1600 IU/L; a peripheral smear showed spherocytes, anisocytosis and polychromasia. Tumor markers were within normal limits. Tru-cut biopsy was performed for differentiation from extramedullary hematopoiesis and/or any other malignancies. Histopathological and immunohistochemical analysis revealed Wilms’ tumor (Fig 2). (WT 1 strong positive, CD 99 focal positive, pan-CK weak positive, vimentine focal positive; sinaptophisine, CK 7, NB84, demsin and CD45 were negative). A metastatic workup revealed subpleural parenchymal
nODULES measuring 7 and 5 mm on the right lung, and 6 and 7 mm on the left lung on thorax CT (Stage IV). A left nephrectomy was performed after neoadjuvant chemotherapy with vincristine and dactinomycine according to SIOP criteria. After surgery, radiotherapy was administered for local tumor control, together with chemotherapy. After 2 cycles, the patient was in remission. After 4 cycles of chemotherapy, thorax CT revealed metastatic pulmonary nodules, and chemotherapy was switched to carboplatin and etoposide. After one year, imaging investigations showed metastasis to the liver, bone and lung. Topotecane, cyclophosphamide and adriamycine were started, but the patient died with progressive disease in the 20th month of treatment.

Discussion

Hereditary spherocytosis is an autosomal dominant genetic disorder characterized by cell membrane abnormalities, specifically in red blood cells. However, 25% of cases are found to be sporadic. It has been reported that among the genes that cause deficiency in membrane proteins in HS, the one affecting band 3 is located on chromosome 17q12-q21; that affecting ankyrin 1, on 8p21.1-p11.2; that affecting alpha-spectrin, on 1q21; that affecting band 4.2, on 15q15-q21; and that affecting beta-spectrin, on 14q23-q24.

Although Wilms’ tumor is, on the other hand, predominantly a sporadic disease, a genetic predisposition exists in a small number of individuals. Several genes have been implicated in the etiology of these lesions, including the Wilms’ tumor 1 (WT1) gene, which is located on the short arm of chromosome 11 (11p13), and the WT 2 gene, which is located on chromosome 11p15. In the present case, we were not able to find any genetic abnormalities due to technical limitations. We thought that the occurrence of Wilms’ tumor in our patient with hereditary spherocytosis might be a coincidental condition, but so far there has been no case reported in the literature in English that describes an association between hereditary spherocytosis and Wilms’ tumor.

Extramedullary hematopoiesis (EMH) is defined as the production of blood components outside the bone marrow. EMH may occur due to hematogenous spread of hematopoietic stem cells or activation of hematopoietic stem cells in other sites, or as a result of extramedullary hematopoiesis.
compensatory response to a reduction in blood components in a pathologic condition such as myelofibrosis. In the present case, however, radiologic findings on computed tomography were consistent with Wilms' tumor; tru-cut biopsy was performed to rule out EMH or any other problem related to HS. Histopathologic and immunohistochemical analysis revealed Wilms' tumor. Previously, non-Hodgkin's lymphoma, acute lymphoblastic leukemia, pancreatic schwannoma, ganglioneuroma, hepatoma, myeloproliferative disorders, Bence Jones-type multiple myeloma, splenoma, adrenal myolipoma, adenomatous polyposis coli and juvenile polyposis coli had been reported in patients with HS.

Because of the scarcity of such cases, no explicit relation between HS and malignancy has yet been reported. It has been suggested that malignancies in HS patients may result from remote ischemic or infectious/inflammatory insults or hematopoietic stimulation. One author speculated that lymphoma may develop due to chronic stimulation as a result of hemolysis. As cases of malignant and borderline benign diseases associated with HS are reported at an increasing rate, it is hoped that possible mechanisms may be elucidated by means of molecular and cytogenetic investigation.

Relapsed Wilms' tumor is often related to a poor outcome, and for patients who are burdened with various adverse prognostic factors, event-free survival is less than 15%. High-dose chemotherapy followed by autologous hematopoietic stem cell rescue has been used in small numbers of patients worldwide, and promising results have been reported. It has also been reported that HS in itself is not a contraindication for either donor or recipient in the matched sibling transplant setting. Our case relapsed during chemotherapy, but autologous hematopoietic stem cell rescue could not be performed.

In conclusion, although the occurrence of tumorigenesis in our patient may have been a coincidence, this is nonetheless the first case of Wilms' tumor associated with hereditary spherocytosis to be reported in the literature.

REFERENCES

