

LETTER TO THE EDITOR

Burkitt Lymphoma in a Child With Osteogenesis Imperfecta

To the Editor: We read with interest the report of Burkitt lymphoma in a child with Joubert syndrome [1], which highlights the observation that patients with congenital malformations may be at increased risk of developing malignancies [2,3]. We recently cared for a 5-year-old boy with osteogenesis imperfecta who also developed a Burkitt lymphoma. The family history was significant for a father and two older siblings with a known diagnosis of osteogenesis imperfecta type I. The patient had sustained only one fracture at age 3, involving the left radius and ulna. He presented with progressive abdominal distention, tachypnea, and shortness of breath. Chest X-ray showed bilateral pleural effusions, and a computed tomography scan revealed soft tissue masses at the right cardiophrenic angle and at the right postero-lateral aspect of the thoraco-abdominal junction. There was a large amount of ascites throughout the abdomen with thickened areas of peritoneum and confluent lymph node enlargement. Malignant fluid removed from a thoracentesis and paracentesis revealed a clonal B cell population expressing CD10 (dim), CD19, CD20, FMC7, and lambda light chains, consistent with aggressive B cell lymphoma. Histologically, the fluid sample revealed markedly atypical cells with prominent nucleoli and darkly basophilic cytoplasm with very prominent cytoplasmic vacuolization. Cytogenetic analysis revealed a t(8;14) translocation. There was no bone marrow or central nervous system involvement.

The patient was diagnosed with stage III Burkitt lymphoma and was treated according to Children's Cancer Group protocol no. 5961, regimen B1. Induction chemotherapy was complicated by profound abdominal ascites and mild respiratory compromise which required several thoracenteses and paracenteses. He tolerated the remainder of his 4 months chemotherapy course without problems. He remains in clinical remission 2 years following diagnosis. Since the diagnosis of Burkitt lymphoma, he has sustained several additional fractures secondary to trauma: bilateral mandible fractures, T5 and L2 compression fractures, and a T9 burst fracture.

Osteogenesis imperfecta is a rare congenital connective tissue disorder with considerable phenotypic variability. Prognosis ultimately depends on the degree of severity. The incidence of fractures varies widely with age [4], level of activity, and success of surgical interventions [5]. There is no known increased risk for developing a malignancy in children with osteogenesis imperfecta. Rare pediatric patients with osteogenesis imperfecta have developed

osteosarcoma [6] or familial leukemia [7]. There have also been case reports of adults with osteogenesis imperfecta who have developed osteosarcoma [8], breast carcinoma [9], ovarian serous carcinoma [10], and multiple myeloma [11].

Osteogenesis imperfecta is associated with deletion of or mutation in the collagen type I, alpha-1 or alpha-2 genes (COL1A1 or COL1A2) [12,13], located at chromosomes 17q21.31-q22 and 7q22.1, respectively. Burkitt lymphoma results from chromosome translocations that involve the *c-MYC* oncogene (chromosome 8q24) and regulatory regions of immunoglobulin (Ig) heavy chains (14q32), kappa (2p12), or lambda light chains (22q11) [14], resulting in t(8;14), t(8;2), and t(8;22). Since there have not been any previous reports of Burkitt lymphoma in osteogenesis imperfecta patients, it is likely that this association is a random occurrence. However, since collagen is a key component of the hematopoietic microenvironment, it is possible that alteration of the extracellular matrix could have perturbed hematopoiesis and contributed to malignant transformation. From a clinical perspective, our patient's underlying condition did not affect his ability to tolerate and respond to chemotherapy. Should future cases arise, this knowledge may be of interest.

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