Case Report

Urinary bladder leiomyosarcoma following radiotherapy in a patient with bilateral retinoblastoma: A case report

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ABSTRACT

Retinoblastoma patients have excellent survival following primary treatment by enucleation, radiotherapy or chemotherapy. Patients receiving chemotherapy or radiotherapy may develop second malignancies years later due to DNA damage or genetic mutations. Urinary bladder leiomyosarcoma is one among them and most such cases have been reported after chemotherapy. We report the third case occurring after isolated radiotherapy.

Key words: Bladder tumor, leiomyosarcoma, retinoblastoma

INTRODUCTION

Retinoblastoma is an uncommon childhood tumor with excellent cure rate following surgical enucleation or irradiation/chemotherapy. However, the long-term survival of these patients is reduced because of the occurrence of second malignancies, which ranges from 8.4% at 18 years after diagnosis to 90% after 30 years.[1] These second malignancies usually include soft tissue sarcomas, osteosarcomas, melanoma and brain tumors. The role of retinoblastoma gene (RB1) mutation, chemotherapy and radiotherapy as causative factors for these second malignancies is unknown due to the rarity of these cases.

Non-epithelial tumors of the urinary bladder account for less than 5% of all bladder malignancies, with leiomyosarcoma constituting less than 0.1%. About 100 cases of urinary bladder leiomyosarcomas have been reported so far, of which only 10 cases occurred as a second malignancy following treatment for retinoblastoma. Six of these patients were treated with chemotherapy, two received both chemotherapy and radiotherapy and two received radiotherapy alone as treatment for retinoblastoma. Herein, we report the third case of urinary bladder leiomyosarcoma occurring following radiotherapy.

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CASE REPORT

A 30-year-old male patient presented to us with a history of painless hematuria with clots of 2 month's duration. At 3 years of age, he was diagnosed to have retinoblastoma in both eyes and was treated with 18 cycles of radiation to both the orbits as his parents refused enucleation.

On examination, he had enlarged inguinal lymph nodes that were found to be inflammatory on biopsy. Ultrasonography and computed tomographic urography showed a large (6 cm × 6 cm) mass arising from the right anterolateral wall of the urinary bladder. The upper tract was normal. Cystoscopy revealed a large nodular lesion arising from the right anterolateral wall and hence only transurethral biopsy was performed. On histopathology, a high-grade sarcoma with only spindle cells and no epithelial cells was noted with possible differential diagnosis of high-grade sarcoma (leiomyosarcoma/malignant peripheral nerve sheath tumor) and sarcomatoid variant of urothelial carcinoma (carcinosarcoma) [Figure 1].

On immunohistochemistry (IHC), the tumor was strongly positive for cytoplasmic smooth muscle actin [Figure 2] and cytoplasmic vimentin, and focally positive for cytoplasmic desmin and cytokeratin, suggesting leiomyosarcoma. Further, negative IHC for epithelial membrane antigen

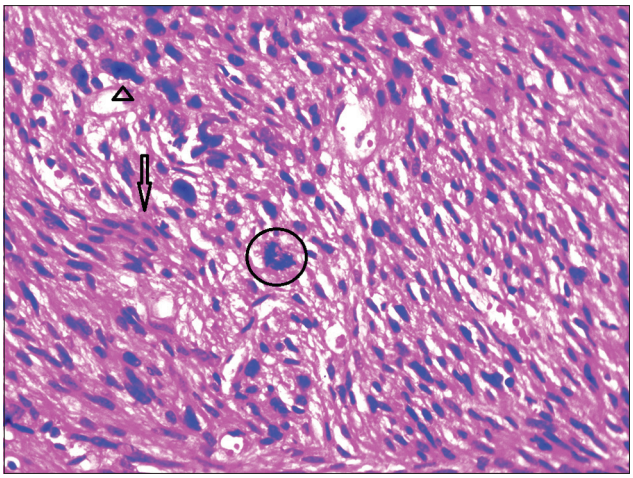

Figure 1: Hematoxylin and eosin staining X100: Showing bundles and fascicles of markedly pleomorphic spindly cells (marked by an arrow), bizzare cells (marked by an arrowhead) and atypical mitosis (marked by a circle)

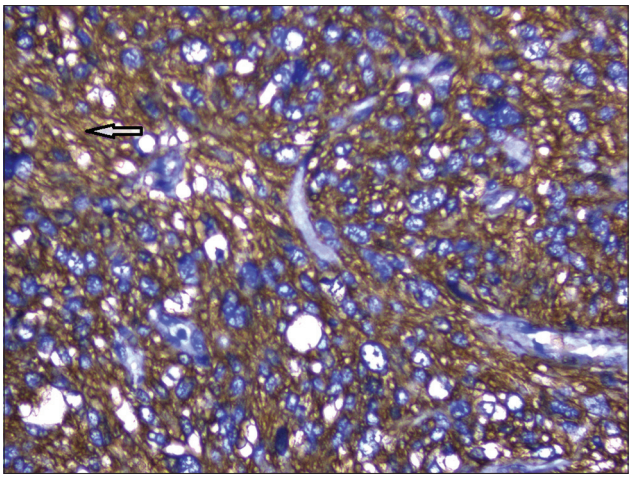

Figure 2: Immunohistochemistry (magnification X100) showing strong smooth muscle actin cytoplasmic positivity (marked by an arrow)

and S100 ruled out carcinosarcoma and malignant peripheral nerve sheath tumor, respectively, thus confirming urinary bladder leiomyosarcoma. The patient refused further genetic analysis. He was not willing for radical surgery and was referred to the oncologist for further management and subsequently lost to follow-up.

DISCUSSION

Retinoblastoma is the most common intraocular malignancy of childhood and is usually diagnosed by 3 years of age. Hereditary retinoblastoma is usually bilateral (10–15% unilateral) and occurs as a result of mutation in the RB1 gene. It has an excellent prognosis following extirpation or radiotherapy/chemotherapy. However, these patients are at a 20-fold increased risk of developing subsequent second malignancies due to long-term survival, genetic mutations and effects of radiation and chemotherapy.[2] These malignancies include soft tissue sarcomas, brain tumors, melanomas, etc., Risk of bone and soft tissue sarcomas begins within 10 years of treatment for hereditary retinoblastoma and continues throughout adulthood, especially for soft tissue sarcomas. The incidence of these cancers is strongly associated with the dose of radiotherapy used to treat their retinoblastoma.[3] Survivors of non-hereditary retinoblastoma are at a much lower risk of a subsequent primary cancer.

Mutations in RB1 or altered expression of p105 Rb (a protein encoded by RB1) have been found in many sarcomas, small-cell lung and bladder cancers, breast tumors, glioblastomas and, less frequently, in other cancers. p105 Rb functions in multiple cellular processes, including proliferation, DNA replication, DNA repair and cell-cycle checkpoint control.

Minogawa *et al*.,[4] reported a case similar to ours wherein a 27-year-old woman with bilateral retinoblastoma had been treated with surgery and radiation. They suggested that along with RB1 gene and chemotherapy, other genetic factors might also be associated with bladder leiomyosarcoma in retinoblastoma patients.[4]

Al Zahrani *et al*.,[5] reported a 16-year-old girl who developed leiomyosarcoma of the bladder after enucleation of the eyeball and cyclophosphamide therapy at 6 months of age. The authors claimed that both genetic alterations as well as cyclophosphamide led to the development of leiomyosarcoma.

Because of the excellent survival of these retinoblastoma patients, it is necessary that survivors, their caretakers and health care providers are aware of the second malignancy risks, especially for hereditary patients. Research is ongoing to identify specific RB1 mutations or location of mutations predisposing to sarcomas and may help in the identification of survivors at greater risk. Increased risk of sarcomas associated with pre-operative diagnostic evaluation using ionizing radiation and therapeutic radiation has led to modifications in the current diagnostic protocol and treatment. For diagnosis, magnetic resonance imaging and ocular ultrasonography have been recommended. In the treatment of retinoblastoma, there is a growing trend toward increased use of chemotherapy, focal therapies and, recently, chemosurgery. However, guidelines for long-term follow-up that are specifically designed for the detection of sarcomas and other second primary malignancies in retinoblastoma survivors are needed.

REFERENCES

1. Draper GJ, Sanders BM, Kingston JE. Second primary neoplasms in patients with hereditary retinoblastoma. Br J Cancer 1986;53:661-71.
2. Marees T, Moll AC, Imhof SM, de Boer MR, Ringens PJ, van Leeuwen FE. Risk of second malignancies in survivors of retinoblastoma: More than 40 years of follow-up. J Natl Cancer Inst 2008;100:1771-9.

3. Abramson DH, Ellsworth RM, Kitchen FD, Tung G. Second non-ocular tumors in retinoblastoma survivors. Are they radiation-induced? Ophthalmology 1984;91:1351-5.
4. Minagawa T, Okaneya T, Kamigaito M, Nishizawa S, Ogawa T, Kawakami M, *et al*. Leiomyosarcoma of the urinary bladder in a patient with bilateral retinoblastoma. Int J Urol 2008;15:548-50.
5. Al-Zahrani AA, Kamal BA, Eldarawani HM, Hashim TM. Leiomyosarcoma of the bladder in a 16-year-old girl with a history of cyclophosphamide therapy for bilateral retinoblastoma during infancy. Saudi Med J 2006;27:531-3.

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