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Second Primary Rhabdomyosarcoma in Nonhereditary Unilateral Retinoblastoma Not Treated with Radiotherapy

Dear Editor,

Hereditary retinoblastoma (RBL) survivors are known to have 0.5% to 1.0% increased risk of second malignancy per year, according to cumulative studies, but in contrast, nonhereditary RBL does not [1]. Therefore, second malignancy occurrence is rare in nonhereditary RBL, especially without radiotherapy [1].

Herein we present a case of an 11-year-old girl with nonhereditary unilateral RBL who developed second malignancy, rhabdomyosarcoma (RMS), 7 years after chemotherapy post-enucleation without radiotherapy.

Eleven-year-old girl presented with papillomatous mass on her right upper eyelid. She had been diagnosed with sporadic unilateral (right) RBL at the age of 2 and underwent enucleation followed by systemic adjuvant chemotherapy (cyclophosphamide, vincristine, Adriamycin, methotrexate). Pathologic findings were compatible to RBL endophytic type, involving 50% of retina, optic disc and nerve, and lamina cribrosa. Resection margins were clear.

Six years and eight months after completion of chemotherapy, papillomatous mass was developed on her right upper eyelid (Fig. 1A). Excision under the impression of granuloma was done without biopsy. Seven months later, right upper eyelid mass reappeared at previous excision site (Fig. 1B). Biopsy confirmed features consistent with RMS. Hematoxylin and eosin stained sections revealed sheets of primitive spindled mesenchymal cells with myxoid stroma in dermis. Immunostaining demonstrated neoplastic cells positive for desmin and myogenin (focal positive), and also vimentin, Ki-67 (10% positive), neuron specific enolase (focal weak positive), and CD56 (focal positive) (Fig. 1C-1E). For further evaluation, F-18 fluorodeoxyglucose-positron emission tomography, chest computed tomography, abdominopelvic computed tomography, brain magnetic resonance imaging, and bone marrow biopsy were done and didn't reveal any malignancies. Wide local excision with 3-mm margins was performed followed by eyelid reconstruction with Tenzel semicircular rotational flap. Final specimen confirmed RMS. Chemotherapy (vincristine, dactinomycin) under the impression of low risk RMS was done. She received regular follow-up of 1 to 3 months and is free from tumor to date.

Pure eyelid RMS is extremely rare and can easily be misdiagnosed as benign [2]. Shields et al. [2] reported that of 33 primary ocular RMS, there was only one pure eyelid form. Our patient presented a simple eyelid margin mass without prominent ocular symptoms which grew slowly over a 7-month period. Therefore, suspecting malignancies, such as eyelid confined RMS, is important when diagnosing recurrent eyelid masses.

According to Turaka et al. [3], among 245 RBL patients treated with chemotherapy (vincristine, carboplatin, +/– etoposide), 4% of hereditary patients (total of 187 hereditary RBL patients) developed second malignancy at a mean of 11 years and none in nonhereditary patients. One hereditary bilateral RBL patient developed RMS at temporal fossa but the patient had also been treated with external beam radiotherapy [3]. Our patient had nonhereditary unilateral RBL and developed RMS 7 years after adjuvant chemotherapy, without any radiotherapy treatment. It can be inferred that there is a possible relationship between chemotherapy and the development of RMS in RBL patients.

Araki et al. [4] also revealed moderate relevance between RBL patients treated with chemotherapy and occurrence of second malignancies, such as myelogenous leukemia, but there has not been any report affirming definite relationship between chemotherapy alone and the development of second malignancy.

Suttie et al. [5] compared latency periods of occurrence of sarcoma between radiotherapy with chemotherapy and radiotherapy alone, and revealed a mean of 5 years, 14.5 years, respectively. The authors emphasized that chemotherapy shorten latency periods of radiation induced sarcoma [5]. Though our case is irrelevant to radiotherapy, chemotherapy history provides sufficient possibilities of inducing RMS.

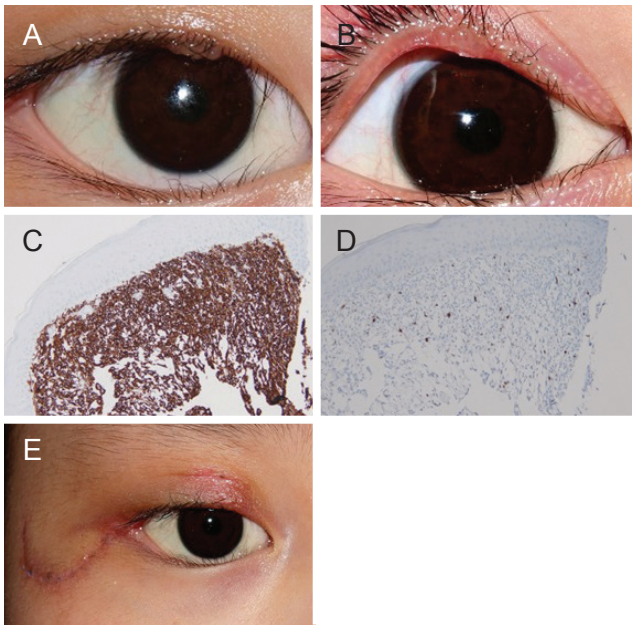

Fig. 1. A papillomatous mass lesion on her right upper eyelid which was confirmed as rhabdomyosarcoma. First papillomatous mass at eyelid margin before first excision (A). Recurred papillomatous eyelid margin mass (B). Immunohistochemically, the neoplastic cells were diffuse positive for desmin (original magnification ×200, 1 : 200 dilution of clone D33 [Dako, Glostrup, Denmark] (C) and focally positive for myogenin (original magnification ×100, 1 : 500 dilution of clone F5D [Dako] (D). Postoperative eyelid photo after wide excision and eyelid reconstruction with Tenzel semicircular rotational flap (E).

In conclusion, we report an unusual presentation of second malignancy, RMS, in a nonhereditary RBL patient treated with enucleation and adjuvant chemotherapy without radiotherapy. Another unusual aspect is that second primary RMS, grew slowly confined to the eyelid margin. Further studies are warranted to elucidate a relationship between chemotherapy and RMS development, or second malignancy after RBL. Further gene studies to reveal more relevant mutations, other than *RB* gene mutation, in nonhereditary RBL involved in developing second malignancy are also required. Finally, when evaluating eyelid mass without prior radiotherapy in nonhereditary unilateral RBL patients, second malignancy, including eyelid confined RMS, should be considered.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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