Ewing’s Sarcoma as Second Malignant Neoplasm after Retinoblastoma: A Case Report

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Introduction

Retinoblastoma (RB) is the most common form of malignant eye tumour found among children. It could develop due to hereditary and non-hereditary reasons. Patients who suffer from the hereditary type have a germ line mutation of the \textit{RB1} gene, present at an early age and usually have bilateral disease, while children without germ line mutation of the \textit{RB1} gene present at a later age and develop unilateral disease. Children with the hereditary form of RB are prone to second malignant neoplasms (SMNs). These second malignancies are usually in the form of bone or soft-tissue sarcomas, which may or may not be related to radiation therapy. Children with a germ line mutation of the \textit{RB1} gene and who receive radiation therapy as part of their treatment for RB are at the risk of developing SMNs \cite{1}.

We report the case of a child with the hereditary form of unilateral RB, who developed Ewing’s sarcoma of the right fibula 3 years after the enucleation of the right eye.

Case Report

Based on a family photograph, which showed a yellow reflex in the right eye (cat’s eye reflex) the patient, aged 9 months, was taken to the eye centre and was found to have RB of an advanced stage. He was fully investigated and found to have locally advanced RB with bone marrow involvement (Reese-Ellsworth stage IVA). Enucleation was recommended to the family, but they refused. The patient received chemotherapy and diode laser thermotherapy in Kuwait and the UK. He had a local relapse after 11 months and subsequently underwent enucleation of the right eye. After 3 years, he was investigated for a small swelling in his right lower leg. After extensive investigations, it was reported as Ewing’s sarcoma. He was treated with chemotherapy, surgery (complete excision of the fibula) and high-dose chemotherapy followed by autologous stem cell transplantation. The child is now nearly 2 years after completing the treatment and is disease free.

Conclusions

This case confirms the increased risk of a second malignant neoplasm (SMN) in children with hereditary RB. These children need a very close follow-up for the early diagnosis of SMNs or even subsequent malignancies.
started on the carboplatin, vincristine and etoposide chemothera-
py protocol. After receiving 5 courses he was taken to the UK where he
received a further 2 courses of chemotherapy and 2 sittings of
diode laser thermotherapy. He achieved partial remission (more
than 50% reduction in tumour size). A year later, he relapsed and
subsequently underwent enucleation of the right eye and was fol-
lowed up by the ophthalmic surgeon. Three years later, he present-
ed with a small swelling over the right lower leg. An X-ray of the leg
revealed a lytic lesion in the mid shaft of the right fibula. A bone
scan was positive. Fine-needle aspiration cytology from the lesion
reported it to be a small round cell tumour and he underwent exci-
dion biopsy of the lesion. Initially it had been reported as metastat-
ic RB, but after extensive immunohistochemistry it was reported
as Ewing’s sarcoma. The family took him to M.D. Anderson Hospi-
tal, Houston, Tex., USA, where he was treated with chemothera-
pthy, followed by surgery (complete excision of the fibula), another
round of high-dose chemotherapy and finally autologous stem cell
transplantation. Fluorescent in situ hybridization analysis of the
tissue sample of the fibula biopsy taken from Kuwait confirmed the
presence of chromosomal translocation consistent with the diag-
nosis of Ewing’s sarcoma. Genetic tests on the original RB speci-
men confirmed the presence of translocation involving the RB1
gene [46 XY, t (4;13)(p14;q14)]. His left eye has not shown signs of
disease activity, and his vision in that eye is normal. Two years
later on, he is in complete clinical and radiological remission.

These SMNs can present in a variety of histologies, most commonly being osteosarcoma [2–5]. Ewing's sar-
coma as SMN is quite uncommon [6, 7] as in our case.

The SMNs after RB usually occur in radiation fields,
but can also occur in non-irradiated fields most com-
monly in the extremities [2–5, 8] as in our patient.

In the majority of cases, SMNs develop in children
with bilateral RB [8–11], but it can occur in children with
unilateral retinoblastoma [9] as in the present case. The
clinical outcome of the children who develop SMN de-
deps upon the location and response of the second tu-
mour to treatment, requiring aggressive chemotherapy
with adjuvant radiotherapy [3–5]. In a number of studies,
children with SMNs who were aggressively treated with
multimodality therapy survived longer than those with-
out aggressive treatment [3–5, 12]. Our patient who un-
derwent very aggressive treatment, which included in-
duction chemotherapy, surgery and high-dose chemo-
therapy followed by autologous stem cell transplantation,
is surviving and is being followed up very closely.

Discussion

SMNs are not uncommon in patients with RB, who
have germ line mutation of the RB1 gene as previously
reported [2, 3]. Our patient developed SMN 4.3 years af-
after the initial diagnosis of RB; however, this period is
much shorter than previous reports of 14.2 years [2] or 18
years (range 10–32 years) [3–5].

Conclusions

This report confirms that patients suffering from RB
with germ line mutation are at an increased risk of devel-
oping SMNs, which can occur as late as 30 years or even
later after the initial treatment for RB. These patients re-
quire a very close follow-up with specific instructions to
look for any evidence of SMNs. Once diagnosed as having
secondary neoplasms, they need aggressive treatment to
achieve a second cure.

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