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Leptomeningeal Relapse of Embryonal Rhabdomyosarcoma after 15 years

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Abstract

Aim
Rhabdomyosarcoma (RMS) is the most common malignant soft tissue tumour of childhood. We present the case of a late relapse of RMS to the leptomeninges after 15 years.
Methods
A 20 year old male presented with a 3 week history of headaches and nausea. He previously had RMS of his right ear diagnosed at age 5 years which was treated with concurrent chemoradiotherapy. An MRI Brain and Spine confirmed extensive leptomeningeal disease and CSF analysis confirmed the presence of recurrent embryonal RMS.
Results
He completed two cycles of cyclophosphamide and topotecan followed by 45Gy/25Fr of craniospinal radiotherapy.
Conclusion
Late relapses beyond five years can be seen in up to 9% of patients, however very late recurrences (>10 years) are exceedingly rare. Molecular based methods such as gene expression profiling can aid risk stratification and survivorship clinics may become increasingly useful in following patients with high risk features.

Introduction

Rhabdomyosarcoma (RMS) is the most common malignant soft tissue tumour of childhood, albeit accounting for only 3-4% of all childhood cancers. Embryonal RMS accounts for around 60% of all RMS cases, usually occurs in children less than 5 years of age and commonly originates from the head, neck or urogenital system. Alveolar RMS is responsible for about 21% of cases and tends to affect the trunk and limbs. Other less common subtypes include botyroid and spindle cell RMS.[1]

The introduction of a combined modality treatment approach has resulted in improved patient outcomes, with over 70% of patients with localised RMS cured of their disease.[2] Disease relapse tends to happen early and is associated with a poor prognosis, but late relapse is poorly studied and understood. We present the case of a very late relapse of RMS in an unusual location.

Case Report

A 20-year old male presented to the oncology OPD as a GP referral with a 3 week history of headaches and nausea. Physical examination revealed ataxia, nystagmus and convergent strabismus of the left eye. His background was significant for intermediate risk embryonal RMS of his right ear with mastoid and nasopharyngeal extension diagnosed at age 5 years. At that time he completed a six-drug trial chemotherapy regimen of ifosfamide, vincristine, actinomycin D, carboplatin, epirubicin, and etoposide following the MMT95 study protocol, with concurrent radiation of 40Gy/22Fr.[3] Treatment was successfully completed with a complete remission obtained.

A magnetic resonance imaging (MRI) brain and spine revealed diffuse spinal leptomeningeal disease. Restaging scans showed no local or extracranial recurrence. While recurrent RMS was included in the initial differential diagnoses, this was felt to be extremely unlikely given the long interval of 15 years and a new haematopoietic or lymphoproliferative process was initially favoured. A lumbar puncture was performed and cytology confirmed the presence of recurrent embryonal RMS. He completed two cycles of cyclophosphamide and topotecan followed by 45 Gy/25Fr of craniospinal radiotherapy. The patient unfortunately had progressive decline and passed away six months after his relapse diagnosis.

Discussion

The majority of RMS patients present with localized disease, and treatment intent is curative. The Children's Oncology Group (COG) risk stratification for RMS is based on pretreatment staging, a clinical grouping system and histology. Poor prognostic factors for late relapse include alveolar subtype and advanced disease at diagnosis.[4] Up to 30% of patients will relapse, the majority (90%) of which will be diagnosed within 2 years of completing primary therapy.[5]

Prognosis for patients with relapsed RMS is poor, with reported 5-year survival rates of only 17- 36%.[6] Very late recurrences (>10 years) are exceedingly rare, and have only been described in isolated case reports.[7-9] To our knowledge this represents one of the longest time periods from completion of primary treatment to relapse in the reported literature.

The alveolar RMS subtype is associated with chromosomal translocations known as *PAX-FOXO1* fusions which are an unfavourable prognostic factor. Molecular testing for these target genes and a weighted scoring system allows estimation of the success of salvage therapy in a patient with relapsed RMS.[10]

In summary, a high level of suspicion for new symptoms, even 15 years after completion of primary therapy is essential. Survivorship clinics may also become increasingly useful in following patients with high risk features, and molecular based methods such as gene expression profiling may aid risk stratification for relapse.

Declaration of Conflicts of Interest:
The authors have no conflicts of interest to declare.

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