Cancer Science 2020: Small Round Blue Cell Tumors, management dilemma. A case report on Alveolar Rhabdomyosarcoma in a four year old child, Pakistan

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Rhabdomyosarcoma is one of the small round blue cell tumors, and though rare, it is the most common soft tissue sarcoma in children. Similar microscopic appearance and similar histochemistry makes differentiation and diagnosis very difficult in these lesions. Here we report a case of a 4 year old boy, who presented with an abdominal mass. Initial investigations confirmed presence of heterogeneously enhancing pelvic mass with no metastasis or local extension. It was confirmed to be Rhabdomyosarcoma on ultrasound guided biopsies, though further differentiation was not possible. Patient responded well to initial treatment in the form neo adjuvant chemotherapy with significant reduction in size of tumor. After subsequent surgical resection, the child had a relapse of disease while he was still on adjuvant chemotherapy. The aim to report this case is to highlight the problems associated with diagnosis and management of this rare disease.

Small round blue cell tumours of childhood include neuroblastoma (NB), rhabdomyosarcoma, non-Hodgkin's lymphoma, Ewing's sarcoma and the closely related primitive neuroectodermal tumour (PNET) and the blastemic component of Wilms' tumour. The tumours have similar appearance by light microscopy and are often indistinguishable by common immunocytochemical markers. Moreover, diagnosis, which is often based on the clinical features of the tumours, may be difficult for those presenting in an unusual clinical context.

For differential diagnosis a panel of antibodies that recognize various tumour-associated markers is currently used. These include neuron-specific enolase (NSE) and GD2, which are present in NB and sometimes in osteosarcomas and rhabdomyosarcomas; CD99 expressed by Ewing's sarcoma and by some PNETs; NB84 expressed by NB cells and sporadically by Ewing's and PNETs; and desmin and cytokeratin present in desmoplastic tumours. However, none of these markers has, by itself, clinical utility in unambiguously differentiating small round blue cell tumours.

We recently isolated a novel monoclonal antibody termed 5B14, which specifically recognizes a surface glycoprotein termed B7-H3. This molecule is an additional member of the B7 family, which also includes B7-1 (CD80) and B7-2 (CD86). Unlike most B7 members, whose receptors have been identified, B7-H3 represents an orphan ligand. On the other hand, functional data suggest that T and natural killer (NK) lymphocytes express specific receptor(s) displaying either an inhibitory or co-stimulatory function. In particular, B7-H3 expressed at the tumour cell surface exerts a protective role in NK-mediated lysis. Notably, the mAb selectively stains NB cells infiltrating the bone marrow of stage 4 patients.

Differentiating a blue cell tumour from others is a diagnostic challenge when considering that both treatment and prognosis vary greatly among these tumours. In this study we evaluated the potential use of 5B14 mAb for diagnostic and/or prognostic purposes. We analysed the expression of B7-H3 in a large number of paraffin-embedded small round blue cell tumours. Tumour specimens included lymphoblastic and Burkitt's lymphomas, blastemic component of Wilms' tumour, primary NB, rhabdomyosarcomas and medulloblastomas.

One hundred and one previously diagnosed small round blue cell paraffin-embedded tumours, stored in the Department of Pathology of the Gaslini Institute, were analysed. These included seven lymphoblastic lymphomas, 11 Burkitt's lymphomas, eight Wilms' tumours, six PNET/Ewing's sarcomas, nine rhabdomyosarcomas, seven medulloblastomas and 53 NB. All NB tumours were schwannian stroma poor with different differentiation grades and different mitotic karyoretic indices (MKI); 15 were stage 1, 11 stage 2, one stage 3, 20 stage 4 and six stage 4s, as assessed according to International Neuroblastoma Staging System criteria. Only four of the 53 NB specimens were Myc-N amplified.