

Sarcomas: Difficult to tame tumors!

Sarcomas are extremely rare, and consequently, many investigators have been and continue to be deterred from working on these tumors. Their rarity as well as heterogeneity makes them a highly complex entity to diagnose and treat. Fortunately, recent advances in molecular medicine have improved our ability to understand and define these entities resulting in a resurgence of interest in the sarcoma.

A majority of data from the West are generated from multicentric cooperative groups with multidisciplinary expertise, which have led to a greater understanding of these tumors and their management. However, in India, while certain institutions have established specific disease management groups for these tumors, collaborative work across institutions is yet to become a reality. This is also reflected in the nature of published work in India wherein a majority of studies are single institution and retrospective in nature compounding the bias. However, the heartening aspect of data emerging from India is that there is increasing work done on the molecular nature and diagnosis of these diseases. Generation of large retrospective datasets confirming improved survival across various tumors, commensurate with outcomes seen in the West is quite reassuring.

Epidemiological data from registries as well as single institution studies confirm that osteogenic sarcoma (OGS) is the most common bone sarcoma seen in India, followed by Ewing sarcoma (EWS).^[1]

A majority of cancer centers in India use nonmethotrexate-based regimens for OGS – prospective and retrospective data from these centers seem to suggest that this is a viable option for treatment of OGS with seemingly equivalent outcomes to methotrexate-based regimens. The Tata Memorial Hospital (TMH) prospective data (presented at International Society of Pediatric Oncology, unpublished) in 325 patients at a median follow-up of 25 (1–51) months showed an estimated 3 years disease-free survival of 68% in nonmetastatic and 24% in metastatic patients, which is comparable to international standards and high-dose methotrexate (HD-MTX)-based protocols.^[2] This is especially important, considering resource limitation in Indian setting wherein non-HD-MTX-based treatment can be delivered without admissions and complex pharmacokinetic monitoring with acceptable toxicity profile.

Potential prognostic factors and issues of compliance with treatment of OGS have also been addressed and finding that compliance can affect outcome. This emphasizes the importance of doctor–patient relationship (apart from other factors) to improve upon compliant behavior, especially in Indian context, wherein poor understanding in patients due to lack of education, resource-limited settings, and communication gap is prominent and widely prevalent. Studies have looked into alternate methods of prognosticating patients using vascular endothelial growth factor expression, tumor angiogenesis via dynamic contrast-enhanced magnetic resonance imaging and positron emission tomography-computed tomography with interesting results that are hypothesis generating and worth exploring in larger cohorts for validation.

The characterization and accurate diagnosis of EWS have been a focal point of diagnostic work done in India. The studies from TMH suggest that fluorescence *in situ* hybridization is a sensitive test for detecting EWSR1 rearrangements as compared to polymerase chain reaction. Studies from WIA, Adyar, have also conducted research with regard to the analysis of the EWS-FLI1 transcripts and have provisionally suggested a dominant negative biological effect of this fusion. Studies from the All India Institute of Medical Sciences have identified novel prognostic factors (raised white blood cell counts) as well as confirmed previously known factors (tumor volume, location, etc.) in EWS through their retrospective analysis. They have also reported that survival data, which when taking into the consideration the constraints faced by our population, are comparable to Western literature.

The emergence of validated immunohistochemical (IHC) markers has shifted the focus of diagnostic modalities in soft tissue sarcomas (STS). Whereas “spindle cell sarcoma” was the most commonly diagnosed STS previously, and there have been increasing efforts to standardize IHC and its use in this heterogeneous group of tumors. The use of novel IHC markers such as TLE1 and INI1/SMARCB1 has been investigated at TMH with the data generated suggesting a greater role for these markers in the diagnosis of synovial sarcoma.^[3] While there are a few studies with regard to systemic management of STS, a majority of work in the domain of therapeutics in India has come from radiation oncologists. A number of studies have examined the role of brachytherapy as adjuvant or definitive therapy in localized STS with impressive results.

The evaluation of published work from India in the field of sarcomas highlights the daunting obstacles we face in curing sarcoma and suggest a requirement for more active collaboration between the larger cancer centers, a need for randomized control trials with respect to management of these tumors and consensus guidelines regarding management for this rare group of tumors. Every tissue sample of a rare cancer such as “sarcoma” is an invaluable resource. The unique nature of well-defined subsets of tumors will ultimately require personalized treatment. We need to harvest the tissue necessary to characterize the disease.

It is sad that worldwide, only 10% of pediatric patients are on national cooperative group trials and only 2% of adult sarcoma patients have fresh tissue preserved for scientific study. Such low rates of cooperation need urgent remedy by the oncology community at large, and even more specifically in India. A concerted effort should be made to overcome institutional obstacles and personal inertia. Another major concern is the linchpin between bench to bedside - tissue collection. If tissue is collected, translational research will ensue and that will ultimately contribute fruitfully to the lives of all of sarcoma patients.

The most laudable feature of this compilation is that it is timely, points to our collective weakness and prompts us to take action to optimize sarcoma care as a whole.

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Website:

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DOI:

10.4103/2278-330X.187586

How to cite this article: Bajpai J, Patel S. Sarcomas: Difficult to tame tumors!. South Asian J Cancer 2016;5:137-8.