Treating Pediatric Liver Tumors in India: A Challenging Proposition

We read with interest the recent article on status of hepatoblastoma in India [1] . In this context, we wish to share our experience of hepatic tumors and highlight certain pertinent points.

Of 825 pediatric malignancies diagnosed at our institution between 2005 and 2012, 13 (1.6%) had primary liver tumors. The median age was 4 years (2 mo - 15 yrs), 9 males. In 12 cases (92.3%), a malignant primary was present of which hepatoblastoma was the commonest, seen in 8(67%) cases. Hepatocellular carcinoma (HCC) was diagnosed in 3(25%) and undifferentiated embryonal sarcoma(UES) in 1(8%). Mesenchymal hamartoma was identified in 1 child. For hepatoblastoma and HCC risk stratification was done according to PRETEXT criteria and SIOPEL-3 chemotherapy protocol was used [2]. Serum alfa-fetoprotein (AFP) was measured in all cases and serially monitored.

Only eight children (61.5%) opted for therapy (6 hepatoblastoma, 1 UES and 1 mesenchymal hamartoma) of which 5 are alive and well at a median follow-up of 30 months. Two with PRETEXT IV disease underwent orthotopic liver transplant (OLT). Five had complete excision of the involved lobe/s and 1 with harmatoma had partial excision. Three relapsed and died (2 hepatoblastoma and 1 UES). Of the relapsed hepatoblastoma patients, 1 was high risk and had undergone OLT. The other did not show expected decline in his AFP levels post complete surgical resection and later relapsed in lungs and bone. There were no deaths in peri-operative period and none due to sepsis or cardiotoxicity. Five (30.7%) abandoned therapy soon after diagnosis (HCC-3 and Hepatoblastoma-2).

AFP monitoring is vital in management of hepatic tumors. Both very high and low levels of AFP are associated with a poor outcome. Failure of AFP to decline to age appropriate levels with therapy is associated with a high risk of relapse/disease progression [3]. Interestingly, in two patients of hepatoblastoma we found a maternal history of colon cancer. Association of hepatic tumors with inherited syndromes such as familial adenomatous polyposis is well known [4] and must be searched for. Treatment abandonment is a major hurdle in improving outcome of pediatric liver tumors. However, reasonably good outcomes can be achieved if patient comply with therapy.

SATYA PRAKASH YADAV AND NIVEDITA DHINGRA
Pediatric Hematology Oncology and BMT Unit, Department of Pediatrics, Sir Ganga Ram Hospital, Delhi 110 060, India.
satya_1026@hotmail.com

REFERENCES

1. Arora RS. Outcomes of hepatoblastoma in the Indian context. Indian Pediatr. 2012;49:307-9.
2. Zsíros J, Maibach R, Shafford E, Brugieres L, Brock P, Czauderna P, *et al*. Successful treatment of childhood high-risk hepatoblastoma with dose-intensive multiagent chemotherapy and surgery: final results of the SIOPEL-3HR study. J Clin Oncol. 2010;28:2584-90.
3. Van Tornout JM, Buckley JD, Quinn JJ, Feusner JH, Krailo MD, King DR, *et al*. Timing and magnitude of decline in alpha-fetoprotein levels in treated children with unresectable or metastatic hepatoblastoma are predictors of outcome: a report from the Children's Cancer Group. J Clin Oncol. 1997;15:1190-7.
4. Lynch HT, Lynch JF, Shaw TG. Hereditary gastrointestinal cancer syndromes. Gastrointest Cancer Res. 2011;4: S9-S17.

Good Outcome with ATG in Aplastic Anemia: Welcome News, Though Thought-provoking!

We read with interest the article by Nair, *et al.* [1] on immunosuppressive therapy (IST) in children with aplastic. It is encouraging that authors have shared their experience and reported good results. A uniform dose and preparation of anti-thymocyte globulin was administered to all patients. There are a few points that we would like to highlight.

The response rate reported in earlier studies from India is nearly half as compared to reported by Nair et al. The difference is difficult to explain from better supportive care alone, as the patients dying from infections during first 3-months of therapy were excluded from analysis in earlier Indian studies [2-5]. Additional causes for the better response could be lower number of children with very severe aplastic anemia (VSAA) and a

lower symptom-to-IST interval.

- The number of children with VSAA is much lower as compared to earlier studies from India (12% *vs.* 27-45%) [2-4]. The data from western countries is conflicting on response of VSAA to IST. Chandra, *et al.*[2], and Sharma, *et al.*[3], have reported lower response rates in VSAA as compared to SAA (33% *vs.* 54.5% and 25% *vs.* 68.7%), respectively. Similarly, children with higher neutrophil count were found to have superior response by Gupta, *et al.* [4].
- The median *symptom-to-IST* interval in the study was 2.5 months. This interval is nearly the same or less than *diagnosis-to-IST* interval in earlier Indian studies, except the one from Varanasi [2,4-5]. A quicker referral and early administration of IST in armed forces hospitals, as compared to 'civilian institutions' is possibly another reason for the superior outcome. Recent studies have documented that a shorter diagnosis-to-IST interval predicts better response by preventing irreversible damage to hematopoietic progenitor cells from auto-reactivated T cells.

The relapse rate observed (3%) is significantly less as compared to several Indian/Western pediatric series (10-33%). Although relapses can occur several years following IST, the median time to relapse in majority of the reports is 18-30 months. A prolonged duration and slow tapering of cyclosporine has been reported to be associated with a lower relapse rate. Although, the authors have mentioned the cyclosporine schedule in the treatment protocol, the median duration of administration of cyclosporine and cyclosporine dependence has not been cited. This information may help to explain the lower relapse rate.

It would be interesting to learn if such good results are replicated from other centers in India in the future.

SAPNA OBEROI AND DEEPAK BANSAL
Hematology-Oncology Unit,
Department of Pediatrics, Advanced Pediatric Center,
Post Graduate Institute of Medical Education and Research,
Chandigarh, India.
deepakritu@yahoo.com

REFERENCES

1. Nair V, Sondhi V, Sharma A, Das S, Sharma S. Survival after immunosuppressive therapy in children with aplastic anemia. Indian Pediatr. 2012;49:371-6.
2. Chandra J, Naithani R, Ravi R, Singh V, Narayan S, Sharma S, *et al*. Antithymocyte globulin and cyclosporin in children with acquired aplastic anemia. Indian J Pediatr. 2008;75:229-33.
3. Sharma R, Chandra J, Sharma S, Pemde H, Singh V. Antithymocyte globulin and cyclosporine in children with aplastic anemia: a developing country experience. J Pediatr Hematol Oncol. 2012;34:93-5.
4. Gupta V, Kumar A, Tilak V, Saini I, Bhatia B. Immunosuppressive therapy in aplastic anemia. Indian J Pediatr. 2012 Jan 25. [Epub ahead of print]
5. George B, Mathews V, Viswabandya A, Lakshmi KM, Srivastava A, Chandy M. Allogeneic hematopoietic stem cell transplantation is superior to immunosuppressive therapy in Indian children with aplastic anemia—a single-center analysis of 100 patients. Pediatr Hematol Oncol. 2010;27:122-31.6.

Eyelid Myoclonia with Absence Seizure: Precipitated by Carbamazepine Therapy

Jeavons syndrome (eyelid myoclonia with absence seizure) is a rare type of idiopathic generalized epilepsy [1]. We report a young girl who presented with this disorder after introduction of carbamazepine.

A nine year old girl, presented with two episodes of unprovoked seizures during sleep characterized by deviation of eyes and head to right and tonic clonic movement of all four limbs during sleep for two weeks before presentation. Antenatal and birth histories were uneventful. Maternal uncle had history of generalized seizures. Patient was a developmentally normal child. Physical examination was noncontributory. MRI brain showed no abnormality. Her first EEG showed generalized discharges. She was already on carbamazepine (CBZ) started by some private physician. CBZ was continued. Over next two months her academic performance deteriorated and she felt giddy on looking at television or sun. After three months, she presented with continuous eye blinking for three days. EEG showed absence status. She was diagnosed as having eyelid myoclonia with absence seizure. Status was controlled by intravenous benzodiazepines and sodium valproate. CBZ was stopped. Seizures stopped within 48 hours. She was discharged on sodium valproate and clonazepam. Only two brief episodes of eyelid myoclonia occurred in first