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Pediatric Surgery International

Professional forum

A common language for childhood liver tumours

Introduction

As a follow-up to the recommendations of the liver tumour workshop held in Berne in February 1990 [1], the CELTIC (Childhood Epithelial Liver Tumours – International Criteria) group was convened at St. Bartholomew's Hospital, London, in September 1990. Representatives from the International Society of Paediatric Oncology (SIOP), the German Paediatric Oncology Group (GPOG), the Japanese Liver Study, and Canada were present[1]. In order to compare outcomes across studies using differing treatment philosophies, common definitions are mandatory. The aim of the meeting was, therefore, to achieve a consensus on (a) histopathologic definitions of childhood hepatocellular tumors, (b) criteria for assigning pre-treatment extent of disease, and (c) definitions of response to treatment.

Histopathology

The definitions were generated by a pathology working group[2]. Hepatoblastoma was defined as an embryonal tumour, containing hepatic epithelial parenchyma, divisible into four subtypes, which most frequently are intermixed. The subtypes are: (1) fetal; (2) embryonal; (3) macrotrabecular; and (4) small-cell undifferentiated. These histologic subtypes may have prognostic significance.

Hepatocellular carcinoma in childhood is similar in gross and microscopic features to its counterpart in adults. Fibrolamellar carcinoma constitutes a distinct subtype.

Criteria for assigning pretreatment extent of disease

No common system for defining the extent of disease prior to treatment exists. The pretreatment grouping system used in the SIOP study, known as SIOPEL 1, based on the number of liver sectors free of tumour, the presence of venous involvement, extrahepatic extension, and metastatic spread, (Fig. 1) was accepted as a reasonable basis for data collection. This grouping system is not synonymous with a conventional staging classification.

Each co-operative study will collect this data in parallel with the data required for their current studies. It is hoped

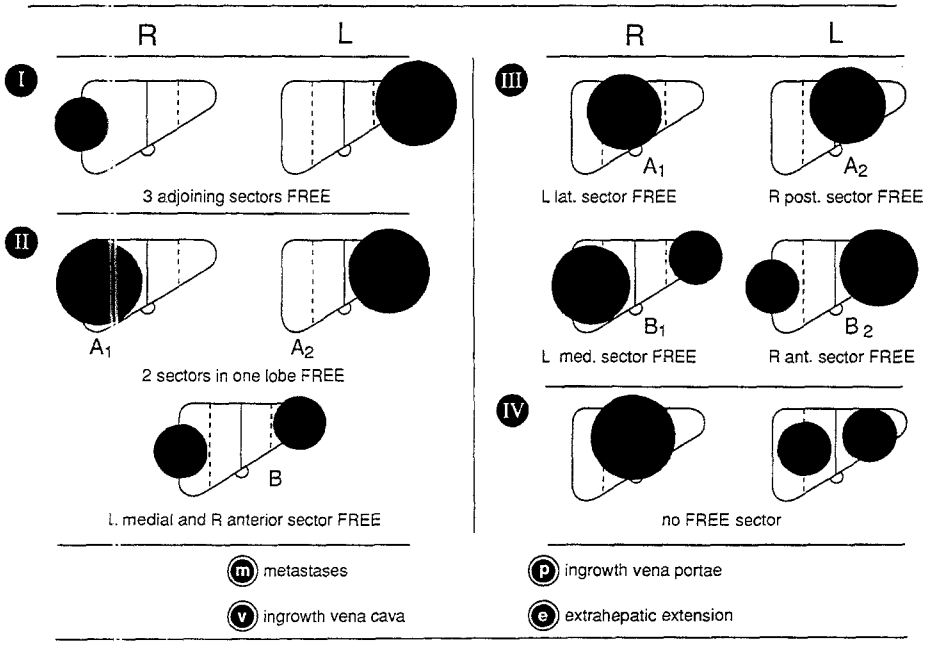

Fig. 1. SIOPEL 1 pretreatment grouping system

For footnotes see page 326

that the wider application of this grouping system will validate its use and encourage its application in future studies by other groups.

Response criteria

Definition of response is inconsistent between studies. It was agreed that response criteria must include serum alpha-fetoprotein levels and imaging studies of the primary tumour and of any metastatic lesions. Serum alpha-fetoprotein level may be the most sensitive indicator of disease status. All groups agreed to monitor and record alpha-fetoprotein levels, ideally weekly, and to standardise imaging by utilising CT scanning or MR imaging for evaluation of response. Response will be assessed to pre-operative chemotherapy and overall response and disease status will be reassessed on completion of all treatment. Application of these common definitions and criteria to patients included in other studies will enable a comparison of different therapeutic regimens.
We would be happy to receive enquiries from any group or individual wishing to join the study or requiring additional information.

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Reference

1. Participants on a Liver Tumor Workshop (1991) Letter to the Editor. Med Pediatr Oncol 19: 149–150

[1] B. de Camargo (Brazil), H. Costa (Brazil), C. Dicks-Mireaux (UK), M. Greenberg (Canada), T. Hasumi (Japan), Y. Hata (Japan), J. Kingston (UK), G. MacKinlay (UK), G. Perilongo (Italy), J. Plaschkes (Switzerland), J. Pritchard (UK), E. Shafford (UK), N. S. Silva (Brazil), J. Uchino (Japan), D. von Schweinitz (Germany)

[2] J. Haas, J. Keeling, D. Schmidt, F. Gonzalez-Crussi, M. Finegold, A. Weinberg

[3] B. de Camargo (Brazil), H. G. de Campos Costa (Brazil), M. H. Chang (Taiwan), C. Dicks-Mireaux (UK), M. Greenberg (Canada), R. Grundy (UK), H. Hamada (Japan), Y. Hata (Japan), S. Kellie (Australia), J. Keeling (UK), H. Kosmidis (Greece), G. MacKinlay (UK), I. Marky (Sweden), N. Pal (Sweden), G. Perilongo (Italy), A. Phillips (UK), J. Plaschkes (Switzerland), L. Richard (Argentina), E. Shafford (UK), N. S. da Silva (Brazil), I. Toogood (Australia), D. von Schweinitz (Germany), A. Vos (Holland)

Addendum. The Celtic Group[3] reconvened in Athens on September 28–29, 1991 in an attempt to finalise the common definitions for histopathology, pre-treatment extent of disease and response. Representatives from the International Society of Paediatric Oncology (SIOP), the German Paediatric Oncology Group (GPOG), the Japanese Liver Study, Canada and Taiwan were present.

Histopathology

The histopathological definitions generated by the Pathology Working Group were accepted at the last meeting. The classification has been put into practice and found to be satisfactory. The prognostic value of this classification however remains to be seen.

Pre-treatment Extent of Disease

The preliminary findings are that the pre-operative grouping system described above, based on the number of liver sectors free of tumour, has proved accurate in predicting the findings at surgery so each group has agreed to continue to collect prospectively this data in parallel with data required for their current studies.

Response

All groups agreed to use tumour shrinkage and change in serum alpha fetoprotein levels as parameters to assess response. In an ongoing clinical study it is not possible to change definitions of response but analysis of the results of the present studies may introduce an objectivity into response assessment which has not hitherto been possible. There are currently a number of clinical trials in childhood liver cancer throughout the world so our efforts to develop a common language seem particularly justified.