

Modern Principles of Surgical Treatment of Colorectal Liver Metastases

Gašper Pilko & Eldar M. Gadžijev

Approximately one half of patients with colorectal cancer will develop liver metastasis at some point in their clinical course. Untreated colorectal liver metastases have a bad prognosis and complete surgical resection is the only treatment that offers a chance of long term survival. In recent years, the survival of patients with colorectal liver metastasis has improved due to several advances in surgical techniques and development of other new methods of treatment. In some studies, 5-year survival is approaching 60%. More than four

lesions, tumors larger than 5 cm, bilobar disease and extrahepatic disease are no longer considered as contraindications for surgery. Nowadays, the eligibility criteria for surgery are feasibility of R0 resection and making sure that at least 20-30% of the liver will remain intact. With careful selection of patients and proper preoperative care, the mortality rate after liver resection is estimated at less than 5%.

Treatment of Patients with Squamous Cell Carcinoma of the Head and Neck with Concomitant Irradiation and Cetuximab

Primož Strojjan & Branko Zakotnik

Contemporary management of locally and regionally advanced squamous cell carcinoma of the head and neck combines simultaneous application of radiotherapy and chemotherapy. With more comprehensive understanding of radiobiological principles of radiotherapy and recent developments in biological drug modeling and technology, more room was provided for improving some other areas of treatment. One of the new promising strategies in the

treatment of head and neck carcinomas is the inhibition of epidermal growth factor receptor (EGFR) signaling using anti-EGFR monoclonal antibodies (e.g. cetuximab, Erbitux®). In this article, we present the first two patients treated at the Institute of Oncology Ljubljana with the combination of irradiation and cetuximab and discuss theoretical background for the new treatment regime and other possible therapeutic indications for cetuximab in head and neck oncology.

The impact of radiotherapy in multimodal management of locally advanced breast cancer

Jasna But Hadžić & Cvetka Bilban-Jakopin

We retrospectively analyzed the data from 55 patients treated for non-inflammatory locally advanced breast cancer (LABC) with neoadjuvant chemotherapy and surgery with or without radiotherapy. The mean follow-up was 55 months. The purpose was to evaluate and compare the impact of postoperative radiotherapy, whether it was indicated on the basis of clinical stage at presentation of the disease or on downstaged pathological disease after initial chemotherapy. The 3-year overall survival (OS) was 74%, disease-free survival (DFS) 73% and relapse-free survival (RFS) 87%. The OS and DFS benefit was seen in

those receiving radiation, with a mean OS of 89 months vs. 68 months ($p=0.029$) and mean DFS of 72 months vs. 54 months ($p=0.029$). Total LRR was 11% (8% vs. 17% in no RT group, $p=0.349$) and mean RFS of 95 months vs. 86 months ($p=0.164$). Significantly lower OS and DFS of the patients who were not treated with radiotherapy suggest that the indication for radiation treatment should be based on clinical pre-chemotherapy stage rather than pathological post-chemotherapy stage for non-inflammatory LABC.

Clinical course of HER-2 positive breast cancer patients

Domen Ribnikar, Špela Fink, Snježana Frković Grazio, Hotimir Lešničar, Aleksander Sadikov & Tanja Čufer

Breast cancer is the most frequent cancer in women. The course and efficiency of breast cancer treatment are influenced by several factors. The expression of HER-2 protein and HER-2 gene is gaining in strength in breast cancer management. The aim of our study was to compare the course of HER-2 positive with HER-2 negative disease. In median time of 2.5 years DFS (disease-free-survival) of patients

with HER-2 positive tumours was 76.1%, and 93.4% for patients with HER-2 negative disease. HER-2 status was the strongest prognostic factor for DFS ($p < 0.001$) in the multivariate model, ranking before nodal status, PR status and age of patients. We may conclude that patients with HER-2 positive disease have worse survival regardless of nodal status.

Superficial and Combined Cervical Plexus Block for Minimally Invasive Parathyroidectomy: Comparison of Their Efficiency and Safety

Tatjana Stopar Pintarič

The use of minimally invasive surgical techniques has, in turn, enhanced the application of minimally invasive anesthetic techniques. Our prospective, randomized and observer-blinded study, conducted at the Institute of Oncology Ljubljana in the years from 2004 to 2006, was performed on 42 patients randomized to receive either a superficial or a combined deep and superficial cervical plexus block (with 0.35 mL/kg of 0.5% levobupivacaine for minimally invasive parathyroidectomy (MIP) to compare anesthetic efficacy, need for intraoperative analgesic

supplementation, time to first postoperative analgesic request, patient satisfaction, complications and side effects.

The results of the present investigation confirmed that the superficial CPB provides sufficient anesthesia for minimally invasive parathyroidectomy with less potential complications and side-effects in comparison with the combined CPB, thus additionally reducing the duration of treatment, hospitalization and treatment expenses.

Delirium in Palliative Medicine. An Undisclosed Companion of Life in Times When It Is Reaching Its Term

Jernej Benedik

Delirium is defined as an altered state of conscience and alertness. It encompasses a wide variety of symptoms from drowsiness to agitated hallucinations. Delirium is very frequent in terminal stage of cancer and is often overlooked. Misinterpretation of its symptoms and overtreatment may aggravate its severity. The causes are multiple and

intertwined. Management of delirium includes non-pharmacological and pharmacological interventions with intent to reorient the patient if feasible, but mostly to prevent further anxiety, stress, and to improve his or her sleep. In some instances sedation of patient is necessary.

Biphosphonates in the Treatment of Breast Cancer Patients

Simona Borštnar

Cancer patients suffering from bone metastases are at increased risk for skeletal complications, which contributes to increased morbidity and have a negative effect on patients' quality of life. Bisphosphonates prevent, reduce, and delay cancer-related skeletal complications in patients, and have substantially decreased the prevalence of

such events since their introduction. In addition, the results of clinical trials investigating the efficacy of bisphosphonates in cancer-treatment bone loss have been recently published. Today, a broad range of bisphosphonates with differences in potency, efficacy, dosing, and administration as well as approved indications is available.

National Cervical cancer Screening Program ZORA: Answers to Questions Most Frequently Asked by Women

Mojca Florjančič, Marjetka Uršič Vrščaj & Maja Primic Žakelj

The Slovenian national cervical cancer screening program ZORA was established in 2003. The Screening Registry of the ZORA program at the Institute of Oncology Ljubljana is in charge of sending invitations to women to attend for screening, of running high quality database, coordinating the work process with the external associates, making analyses, and promoting and implementing the program. One of the major tasks of the Registry is to establish contacts with the users of this program, i.e. with the women and young girls who are

addressing the Registry by e-mail or phone to get more information about the program. The staff involved in the program implementation has therefore made a list of the most frequent questions and also supplied the answers to these questions, and classified both into groups by subject matter, hoping that such a list will serve as a key to better understanding of the program and provide immediate and accurate answers.

Molecular Diagnosis of Lymphomas

Ira Koković & Srdjan Novaković

Demonstration of clonality and detection of specific genetic abnormalities enable distinguishing between neoplastic lesions and reactive processes and, thus, have an important value in the diagnosis of lymphoid neoplasms. A clonal population of lymphoid cells can be detected by PCR amplification of rearranged genes encoding B- and T-cell receptors. Furthermore, chromosomal translocations specific for certain lymphomas can also be detected by PCR. We have introdu-

ced PCR-based assays for clonality analysis, and for the detection of t(11;14) and t(14;18) chromosome translocations in mantle-cell and follicular lymphoma, respectively. Assays are simple and fast and can be applied on small amounts of blood and tissue samples. Detection rates of our PCR assays are in agreement with reported data. We have been using molecular techniques as additional methods in the diagnosis of lymphoproliferative disorders since 1997.

Screening for Mutations in Tp53 Tumor Suppressor Gene using DGGE and Sequencing

Alenka Ličar & Srdjan Novaković

Mutations in the T53 gene have been detected in more than 50% of different malignancies. The development of many of these diseases is directly associated with the mutations in the Tp53 gene. The aim of this

article is to provide information about new methods that have been introduced into our Department of Molecular Diagnostics at the Institute of Oncology Ljubljana for scanning mutations in the Tp53 gene.

Screening for melanoma susceptibility gene mutations in patients with familial cutaneous melanoma

Petra Cerkovnik, Barbara Perić, Marko Hočevar & Srdjan Novaković

At the Institute of Oncology Ljubljana, Department of Molecular Diagnostics, genetic testing for familial cutaneous melanoma (CM) was started in 2005. The patients are selected according to the guidelines of genetic counseling for CM. The screening for melanoma susceptibility genes is performed in the patients and their healthy relatives from the families with at least two affected family members and in the patients with multiple primary CM without family history. The mutation screening for melanoma susceptibility genes – *CDK-*

N2A, *CDK4* and *MC1R* is performed by direct sequencing. Altogether 70 patients and their healthy relatives (40 patients or their relatives selected from 28 families after considering their on family history and 30 patients with multiple primary CM) have been tested so far. Our results showed high prevalence of *CDKN2A p16^{INK4a}* mutations in the patients with familial CM. In *CDKN2A p14^{ARF}* and *CDK4*, no mutations were detected in Slovenian patients.

Polymorphisms and *MLH1* and *MSH2* Gene Mutations in Non-Polyposis Colorectal Cancer

Vida Stegel & Srdjan Novaković

Colorectal cancer affects approximately 1200 individuals in Slovenia every year. Hereditary colorectal cancer (hereditary non-polyposis colorectal cancer - HNPCC and familial adenomatous polyposis - FAP) accounts for around 10% of all colorectal cancers. Thirty-two colorectal patients were screened for DNA variations in *MLH1* and *MSH2* genes (miss-match repair genes- MMR genes). All patients were screened using high resolution melting (HRM). The exons of *MLH1* and *MSH2* genes were amplified using PCR (polymerase chain

reaction). Amplified double stranded products were stained with intercalating dye and dissociated by heating. The melting curves of the tested samples were compared to the melting curve of the control and all PCR products, showing different melting curve than that of the control, were sequenced. We found 5 different mutations, 2 UVs (unclassified variants), 13 polymorphisms. Among mutations, 1 deletion, 2 splice-site mutations, and 2 missense mutations were found.

Vascular Disrupting Effect of Electrochemotherapy

Gregor Serša, Maja Čemažar & Marko Snoj

The therapeutic potential of targeting the tumor blood supply is now well acknowledged. Vascular targeted therapies target tumor blood vessels. The research and development have resulted in a variety of investigational agents, among which many are currently being clinically tested. Two distinct groups of vascular targeted therapies have evolved, anti-angiogenic and vascular-disrupting approach. They differ in several aspects: their physiological target, the type and extent of the disease which is likely to be susceptible to one or the

other group of therapies, and their treatment scheduling. Besides the direct cytotoxic effect of electrochemotherapy on tumor cells, recent discoveries have detected also its vascular-disrupting effect. Due to vascular damage, abrogation of tumor blood flow, and consequently, of tumor ischemia, a cascade of tumor-cell deaths is induced. Therefore, electrochemotherapy is effective in the treatment of bleeding metastases due to its vascular disrupting effect; it quickly stops bleeding and reduces tumor burden