

Breast cancer in young women and pregnancy

Marina Mencinger, Jasna But Hadžić

Breast cancer in young women is a rare occurrence, and successful treatment of this disease offers long survival to the majority of young female patients. Preserving fertility is an important aspect of the quality of life, in particular if bearing in mind that the age at which women have their first child has been increasing. Therefore, young female patients must be aware of the possible negative effects of treatment on fertility already at diagnosis and should be offered counselling. At the gynaecological oncology consilium, patients or

couples are presented the procedures for the storage of genetic material before commencing treatment. In the following article, we present and discuss the newest findings on the association between breast cancer and pregnancy. Moreover, we also present the data collected on pregnancy in very young patients following breast cancer treatment in Slovenia.

Identification of *c-KIT* and *PDGFRA* gene mutations in patients with gastrointestinal stromal tumours

Marina Grgič, Srdjan Novaković

At the Institute of Oncology Ljubljana, the Department of Molecular Diagnostics introduced testing of mutations in the *c-KIT* and *PDGFRA* proto-oncogenes using the direct sequencing method. The use of tyrosine kinase inhibitors to treat patients with gastrointestinal stromal tumours (GIST) enables a more successful treatment. Selection of the most appropriate drug for patients with GIST depends on the activation mutations in the *c-KIT* and *PDGFRA* genes. Mutations in these genes are found in approximately 90% of patients with GIST. The majority of these mutations show a good response to treatment with

tyrosine kinase inhibitors (e.g. imatinib in the first-line treatment), while some mutations cause the patient to become unresponsive to treatment. Secondary mutations are also common, which cause patient's lack of response to the original drug despite the originally good response to treatment with tyrosine kinase inhibitors. In this case, it is necessary to choose a different type of tyrosine kinase inhibitor (e.g. sunitinib, sorafenib, nilotinib). Identification of the *c-KIT* and *PDGFRA* gene mutation status represents important information for the doctor when deciding on the appropriate treatment for individual patients.

The role of a dermatologist in early detection and management of the patient with melanoma

Aleksandra Dugonik

Skin melanoma is one of cancers with the largest annual increase both in the world and Slovenia. Alongside the rapidly increasing incidence, the epidemiological data show stable mortality in the last two decades and a constant share of fatty tumours in male patients aged over 60 years.

Melanoma is a result of a complex interaction between the genotype and environmental factors that also determine the phenotypic characteristics signalling an increased risk of the occurrence of melanoma in one's life.

The role of a dermatologist is to detect melanoma at early stages of the disease, when it is still difficult to recognise it clinically and melanoma can be mistaken for melanocytic nevi or other skin lesions. Early diagnosis of melanoma is based on new diagnostic methods in dermatology, such as dermoscopy, confocal microscopy and teledermatology, as well as on well-organised work which allows

identification and monitoring of individuals with an increased risk for developing melanoma.

In thin melanomas, the dermatologist also performs the therapeutic part, namely tumour excision, while in invasive and metastatic forms of the disease, he decides on the patient's interdisciplinary treatment. Due to an increased risk for the development of a new primary melanoma, management of patients following detection of melanoma also requires lifelong monitoring by the dermatologist.

The dermatological associations design and implement primary and secondary prevention programmes aimed at reducing the risk factors and early detection of melanoma, as well as other forms of skin cancer.

New findings confirm the pathogenic diversity of melanoma, which indicates the need to implement changes and individualise measures aimed at primary and secondary prevention of skin melanoma.

Characteristics of oesophageal and gastric cancers

Vaneja Velenik

According to the Globocan data, a total of 12.7 million people were diagnosed with cancer and 7.6 million people died of this disease in 2008. As many as 56% of new cancer cases and 63% of cancer deaths were recorded in less developed regions of the world. The most common cancers were lung cancer (1.61 million; 12.7% of all cases), breast cancer (1.38 million, 10.9% of all cases) and colorectal cancer (1.23 million, 9.7% of all cases). The leading causes of cancer-related death were lung cancer (1.38 million, 18.2% of all cancer deaths), gastric cancer (738 thousand, 9.7% of all cancer deaths) and liver cancer (696 thousand, 9.2% of all cancer deaths). Projections of the cancer burden are even grimmer. In 2030, a total

of 20.3 million people will be newly diagnosed with cancer, and 13.2 million people will die from this disease. The incidence is thus said to increase by 75% and to almost double in less developed countries compared to 2008. Cancer will become the leading cause of morbidity in every country of the world. Everywhere, we will witness an increase in the share of colorectal cancer, breast cancer and prostate cancer, while the most developed countries will also note an increase in lung cancer in women. The incidence of gastric and cervical cancers will drop, as will the incidence of lung cancer in men in the developed countries (2).

Gastric cancer surgery

Mirko Omejc

Although the incidence of gastric cancer has been decreasing in the world and in Slovenia, it is still a major cause of cancer mortality. The prognosis is poor, since the disease is often detected at an advanced stage. Treatment results can be improved only by early detection. A multidisciplinary approach is a very important part of treatment,

but the main role is still played by surgery. We describe the current principles of surgical treatment: the extent of resection in all three dimensions (on the organ itself, on neighbouring structures and organs or their parts), the extent of lymphadenectomy and the reconstruction methods.

The role of endoluminal stenting during neoadjuvant treatment of oesophageal carcinomas

Anton Crnjac, Boris Greif, Aljaž Hojski

The first goals of treatment of symptomatic malignomas of the oesophagus include maintenance of the nutritional path and prevention of haemorrhage and pain. All patients require a multidisciplinary assessment in order to get the appropriate regular multi-modal therapy. Definition of the most appropriate nutritional support for the oesophageal cancer patient must be individual. Treatment depends on the disease stage, symptoms, the available technology and experience of the attending doctor.

We present our method for treating dysphagia with the help of intraluminal oesophageal stents. In our practice, the intraluminal oesophageal stent has proven to be a very effective and the most patient-friendly method for optimal delivery of nutrients before and during neoadjuvant therapy. There are few complications, and insertions do not have a negative impact on the perioperative outcomes.

The radiation therapy practitioner's view of oesophageal cancer treatment

Franc Anderluh

Oesophageal carcinoma is a disease with an increasing incidence in the world, and the prognosis of which is generally still poor, despite the progress achieved in oncology in the last years. In 2010, a revised TNM classification for oesophageal carcinomas was published, which is currently still applicable and takes better account of the natural

course of the disease and biological characteristics of squamous cell carcinomas compared to adenocarcinomas. Radiation plays an important part in the treatment of patients with oesophageal carcinoma, both in the scope of preoperative treatments (with concurrent chemotherapy) as well as in non-operative treatment methods.

Treatment of oesophageal cancer from the medical oncologists' point of view

Martina Reberšek, Tanja Mesti, Marko Boc

The incidence of carcinoma of the oesophagus in Slovenia is small and has not changed in years. The prognosis of patients with metastatic carcinoma of the oesophagus is poor, with less than 10% 5-year survival. In the early stages of the disease, we recommend surgical treatment in combination with neoadjuvant chemoradiation for squamous cell carcinoma or perioperative systemic chemotherapy for adenocarcinoma of the gastroesophageal junction. In locoregionally advanced carcinoma, we recommend neoadjuvant chemoradiation. In the case of cervical carcinoma of the oesophagus or in high-risk patients not fit for surgery, we recommend definitive chemoradiation. The most optimal systemic therapy for metastatic disease is selected based on the general state of the patient, his concurrent diseases, the expected toxicity of systemic therapy, and HER2 status in patients

with adenocarcinoma. For first-line treatment, we recommend doublet chemotherapy, mainly due to a better toxicity profile. In the case of HER2-positive adenocarcinoma, doublet may be combined with trastuzumab. In patients who are in good general condition, we can try with a combination of three cytostatics. For patients in poor general condition, only palliative supportive care is recommended, since the benefit of such treatment outweighs the potential treatment complications. We are eagerly awaiting the results of the ongoing clinical trials of new combinations of cytostatics and targeted drugs, hoping for more effective combinations of drugs that would enable us to treat patients with metastatic carcinoma of the oesophagus and gastroesophageal junction more effectively.

The radiation therapy oncologist's view of oesophageal cancer treatment

Irena Oblak

Gastric cancer is associated with a poor prognosis. At diagnosis, approximately 50% of patients have a non-resectable disease. In patients who underwent radical resection, the disease recurs in as many as 75%, of which 40-64% are local and/or regional recurrences (2-4). Despite this fact, we are observing that survival of patients has improved over the years. According to the SLORE data, relative

5-year survival was 14.7% in 1985, 17.8% in 1995, 22.1% in 2000 and 25.6% in 2005 (5).

Surgical resection of the tumour and regional lymph nodes is the method of choice for treating gastric cancer with no distant metastases. Until 2000, it was also the only treatment method.

The internist oncologist's view of gastric cancer treatment

Janja Ocvirk

After resection, a large number of patients with gastric carcinoma (GC) and carcinoma of gastroesophageal junction (GEJ) have recurrences. Recurrences are local or with distant metastases, or a combination of both. Adjuvant chemotherapy can improve overall survival in some types of solid tumours primarily by minimising the residues of micro-metastases. While the importance of adjuvant chemotherapy in GC and GEJ is not entirely clear, adjuvant radio-chemotherapy significantly prolongs the disease-free period and overall survival. Perioperative treatment with ECF chemotherapy significantly improves disease-free and overall survival. ECF chemotherapy or its other regimens, namely EOF, ECX or EOX, are the standard treatment for patients with advanced gastric carcinoma (GC) or GEJ. Treatment with taxans in combination with 5-FU and cisplatin (TCF) is also effective. New combinations of cytostatics and the introduction of new cytostatics have improved the median

survival of patients with gastric carcinoma and GEJ. Target drugs have also been introduced for the treatment of metastatic GC and GEJ. Determination of biomarkers and introduction of target treatment in combination with chemotherapy has opened a new era of patient-adapted treatment, also for patients with advanced gastric carcinoma and GEJ.

After resection, a large number of patients with gastric carcinoma (GC) and carcinoma of gastroesophageal junction (GEJ) have recurrences. Recurrences are local or with distant metastases, or a combination of both. In Europe and the USA, locoregional recurrences are more common and most frequently occur in the abdominal region, regional lymph nodes or at the anastomosis. The most common systemic extensions are liver metastases and metastases to peritoneum. GEJ carcinoma can often metastasise also to the lungs.

Do target drugs have its place in radiochemotherapy of gastrointestinal tumours?

Vaneja Velenik

In the last decade, we have been witnessing a rapid development of the understanding of tumour biology and immunology of gastrointestinal cancers. Simultaneously, there have been great improvements in radiation techniques, which have subsequently improved local disease control by enabling a larger dose on the tumour and reducing toxicity on healthy tissues. However, a high share of the occurrence of distant metastases remains of great concern, since it indicates

the need for an even more aggressive multi-modal treatment. The expected benefit of target drugs in non-metastatic gastrointestinal cancers is still subject to clinical research. It is necessary to identify the right population of patients and include them in research, regardless of the histology or localisation of the tumours but based on specific molecular and genetic abnormalities, thus based on their specific genetic profile.

Palliative care

Maja Ebert Moltara

Palliative care (PC) is an important, indispensable and integral part of medical care of patients with incurable diseases, and it is performed at all levels of healthcare system. Comprehensive care of palliative patients is provided by a multi-professional team, which resolves

physical, psychological, social and spiritual problems faced by palliative patients and their families. The main goal is to ensure the best possible quality of life. PC recognises life and death as natural processes.

Nutritional support for a cancer patient

Nada Rotovnik Kozjek

Oesophageal cancer patients very frequently lose their body weight, which leads to malnutrition and accelerates the development of cachexia. Weight loss and development of malnutrition accelerate the development of cachexia and deteriorate the functional state of patients and their quality of life. Functional state and quality of life of patients thus become worse. This also results in poorer tumour response to treatment, which is accompanied by adverse events and decreased survival.

There are numerous causes of weight loss and development of malnutrition in patients with gastrointestinal tumours, which often develop already at the onset of the disease. Therefore, the diagnosis

of cachexia and nutritional management of the patient should be undertaken at the same time as treatment of the cancerous disease. They are performed in the same manner as any other medical therapy. Nutritional intervention, as the basic measure for preventing malnutrition and development of cachexia, must be started early enough to prevent and/or minimise further loss of body cell mass. The energy needs of cancer patients are comparable to those of patients who do not have cancer. Protein requirements are 1.2-2.0 g/kg of body weight/day. In patients with cachexia, we can use modulation of metabolism by omega-3 fatty acids.

Treatment of locoregionally advanced oesophageal carcinoma – a case report

Jasna But Hadžić, Marko Bitenc

In this article, we present a case of a 67-year-old patient with advanced stage T3 N2-3M0 carcinoma of the middle third of the oesophagus which is spreading to the upper and lower thirds. Despite the extensiveness of the disease, the patient received optimal treat-

ment with pre-operative radiochemotherapy and surgery. Successful treatment was a result of an individual approach, close collaboration of all branches of oncology and use of new radiation techniques.

A clinical case of a patient with metastatic squamous cell carcinoma of the oesophagus

Marko Boc, Tanja Mesti, Martina Reberšek

The incidence of oesophageal cancer has not changed in the last years, neither in the world nor in Slovenia. According to the 2012 Cancer Registry of Slovenia, a total of 87 patients were diagnosed with oesophageal cancer in 2009, of which 74 were males and 13 were females. The most common histological type was squamous cell carcinoma; in 2009, there were 60 such patients, while adenocarcinoma, which is the second most common type, was found in 19 patients.

Patients with oesophageal cancer have a poor prognosis. A half of these patients have advanced disease already at diagnosis. Median survival with advanced disease is eight to ten months, while 5-year

survival is merely 5-17%. When the disease is operable, patients are treated surgically, and if the disease is limited locoregionally, the patients are treated with pre-operative chemoradiotherapy and surgery. However, despite such primary treatment, the disease recurs in approximately 65% of patients in the first five years, either in a form of metastases or as a local recurrence (2, 3, 4, 5, 6).

In this article, we present a patient with squamous cell carcinoma of the middle third of the oesophagus which has started to spread to the upper and lower thirds six months after primary treatment and effective first-line systemic treatment.

Pre-operative irradiation in a gastric cancer patient

Ajra Ščeroč Ermenc

In patients with unresectable or borderline resectable gastric cancer with no spreading of the disease, we recommend pre-operative radiochemotherapy, which may reduce the tumour and thus increase the likelihood of complete removal (R0 resection). The article presents a case of a female patient with clinical stage T4 N1 M0 gastric cancer

treated with pre-operative chemotherapy followed by total gastrectomy. Pre-operative treatment showed a very good response. After surgery, the patient received complementary chemotherapy and had no recurrence of the disease five years after treatment.

Primary spread of adenocarcinoma of gastroesophageal junction to the brain

Tanja Mesti, Marko Boc, Martina Reberšek

In the last years, we have noted a decline in the incidence of gastric adenocarcinoma but at the same time also an increase in the incidence of adenocarcinoma of gastroesophageal (GE) junction (1). According to the 2012 Cancer Registry of Slovenia data, a total of 55 patients were diagnosed with gastric cancer in 2009, of which 363 were men and 192 were women (2). Generally, gastric cancer patients have a poor prognosis, especially

in the case of primarily metastatic disease. Gastric cancer most commonly spreads to peritoneum, which is followed by lymph nodes, bones, lungs and liver (3-5). Metastases in the central nervous system mostly represent a late or rare manifestation (< 4%) (6). In the article, we present a patient with adenocarcinoma of GE junction with primary spread of the disease to the brain, who was treated with two lines of systemic therapy.

Secondary malignant tumour of the colon after childhood cancer treatment - a case report

Lorna Zadavec Zaletel, Miroslav Vujasinović, Marko Boc, Berta Jeréb

The risk of developing secondary colon cancer is larger in patients treated for childhood cancer than in the general population, and it is rapidly increasing with observation time and increased radiation dose to the abdominal area. A patient, who was successfully treated for Hodgkin's disease at the age of 12 with chemotherapy and radiation of the affected regions, including para-aortic lymph nodes, was diagnosed with microcytic hypochromic anaemia 27 years after treatment. A suspicion that this is gastrointestinal haemorrhage was not confirmed by a single-stool examination. Half a year later, the patient was found with metastatic adenocarcinoma of the colon and was treated operatively with systemic treatment and palliative

radiation of spinal and brain metastases. A year and a half after the start of treatment of secondary tumour, the patient died at the age of 40 years. Patients treated for childhood cancer experience several late consequences. Secondary malignant tumours are the second most common cause of death, right after disease recurrence. Therefore, timely detection and appropriate treatment are of utmost importance. Since 2014, the international guidelines recommend that patients receiving 30 Gy or more to the abdominal region are monitored by colonoscopy. A single-stool examination for occult blood and US of the abdomen are not reliable methods for detecting colon cancer.

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