too restrictive a parameter. Indeed, severe SOS can be identified macroscopically (Figure 1) or histologically in preoperative frozen sections. By making the surgeon aware of this lesion, a large resection can be avoided or more extensive portal embolisation can be used before surgery to reduce the risk of post-operative liver failure.

Since the recent publication of our paper we have become aware of several cases of patients developing complications (with long hospitalisations in intensive care unit) because of the delay in liver regeneration and liver insufficiency after limited hepatectomy (unpublished data). A patient has developed acute fatal portal hypertension after oxaliplatin-based adjuvant chemotherapy for colorectal carcinoma [2]. The publication of such observations in the near future will support the concept that SOS is a real and relevant clinical entity in oxaliplatin-based chemotherapy.

In our experience, oxaliplatin is a very useful drug that yields excellent responses in hepatic colorectal metastases, and we believe that its use will continue to increase. Therefore, far from intending to question the efficacy of oxaliplatin in the treatment of colorectal metastasis, we suggest that the occurrence of clinically significant secondary effects on the liver need to be recognised to increase the safety of liver surgery. The scope of these observations may further expand as oxaliplatin is becoming used as adjuvant therapy in the treatment of several other malignancies.

L. Rubbia-Brandt[1]*, G. Mentha[2], B. Dousset[3] & B. Terris[4]

[1]Division of Clinical Pathology and [2]Division of Digestive Surgery, University Hospital, Geneva, Switzerland; [3]Service of Surgery, Hôpital Cochin, Paris, France; [4]Service d'Anatomie Pathologique, Hôpital Cochin, Paris, France (*E-mail: laura.rubbiarandt@hcuge.ch)

References

1. DeLeve LD, Shulman HM, McDonald GB. Toxic injury to hepatic sinusoids: sinusoidal obstruction syndrome (veno-occlusive disease). Semin Liver Dis 2002; 22(1): 27–42.
2. Tisman G, MacDonald D, Shindell N et al. Oxaliplatin toxicity masquerading as recurrent colon cancer. J Clin Oncol 2004; 22(15): 3202–3204.

doi:10.1093/annonc/mdi038

Obesity may decrease the amenorrhea associated with chemotherapy in premenopausal breast cancer patients

We read with great interest the article by Berclaz et al. [1], which stated that body mass index (BMI) is an independent prognostic factor for overall survival in patients with breast cancer, especially among pre-/perimenopausal patients treated with chemotherapy without endocrine therapy. These authors proposed different explanations for this association. We would like to mention another explanation.

Amenorrhea is also an important prognostic factor for predicting the efficacy of chemotherapy in premenopausal patients [2]. It is known that obese women have a longer reproductive life and that longer exposure to estrogen increases breast cancer risk. Although there were insufficient data to demonstrate that chemotherapy is associated with a decreased incidence of amenorrhea in obese patients compared with lean counterparts, Mehta et al. [3] showed that 71% of obese patients develop amenorrhea after receiving chemotherapy, compared with 80% of non-obese breast cancer patients. In light of the above information, we propose that obesity itself, by suppressing the amenorrhea associated with chemotherapy, may result in poorer prognosis in premenopausal breast cancer patients with a high BMI.

K. Altundag[1]*, O. Altundag[1], P. Morandi[2] & M. Gunduz[3]

[1]Department of Medical Oncology, Hacettepe University Faculty of Medicine, Ankara, Turkey; [2]Department of Medical Oncology, S. Bortolo General Hospital, Vicenza, Italy; [3]Department of Oral Pathology and Medicine, Graduate School of Medicine and Dentistry, Okayama University, Japan (*E-mail: drkadri@usa.net)

References

1. Berclaz G, Li S, Price KN et al. Body mass index as a prognostic feature in operable breast cancer: the International Breast Cancer Study Group experience. Ann Oncol 2004; 15: 875–884.
2. Poikonen P, Saarto T, Elomaa I et al. Prognostic effect of amenorrhea and elevated serum gonadotropin levels induced by adjuvant chemotherapy in premenopausal node-positive breast cancer patients. Eur J Cancer 2000; 36: 43–48.
3. Mehta RR, Beattie CW, Das Gupta TK. Endocrine profile in breast cancer patients receiving chemotherapy. Breast Cancer Res Treat 1992; 20: 125–132.

doi:10.1093/annonc/mdi044

Reply to the Letter to the Editor on "Obesity may decrease the amenorrhea associated with chemotherapy in premenopausal breast cancer patients", by K. Altundag et al. (Ann Oncol 2005; 16: 333)

Altundag and colleagues suggest that obese women have an increased breast cancer risk due to a longer reproductive life.

A meta-analysis of 23 studies providing information on body mass index incidence in premenopausal breast cancer

has shown an inverse association between obesity and breast cancer [1]. These results have been confirmed in the large US female nurses cohort [2].

In a prospective evaluation about relative weight on the occurrence of natural menopause, no association could be demonstrated between obesity and a delayed menopause [3].

We agree with Altundag and colleagues that the role of obesity in the development of amenorrhea after chemotherapy needs to be evaluated in larger studies as in the quoted publication of Mehta et al. [4], in which the number of patients [37 of 46 (80%) non-obese and 17 of 24 (71%) obese women became amenorrheic] was much too small to draw any conclusions ($P = 0.84$).

G. Berclaz* On behalf of the IBCSG

Frauenklinik des Inselspitals, Schanzeneckstr. 1, 3012 Berne, Switzerland (*E-mail: gilles.berclaz@insel.ch)

References

1. Ursin G, Longnecker MP, Haile RW, Greenland S. A meta-analysis of body mass index and risk of premenopausal breast cancer. Epidemiology 1995; 6: 137–141.
2. Huang Z, Hankinson SE, Colditz GA et al. Dual effects of weight and weight gain on breast cancer risk. JAMA 1997; 278: 1448–1449.
3. Willett W, Stampfer MJ, Bain C et al. Cigarette smoking, relative weight, and menopause. Am J Epidemiol 1983; 117: 651–658.
4. Mehta RR, Beattie CW, Das Gupta TK. Endocrine profile in breast cancer patients receiving chemotherapy. Breast Cancer Res Treat 1992; 20: 125–132.

doi:10.1093/annonc/mdi045

Intra-arterial hepatic chemotherapy in heavily pretreated patients with epithelial ovarian cancer

Ovarian cancer is the fifth leading cause of cancer-related death among women, and is the most lethal of the gynaecologic malignancies [1, 2]. The standard first-line treatment is cytoreductive surgery and combination chemotherapy [3]. Relapsed ovarian cancer is generally incurable and patients who relapse will die of their disease. The most common site of recurrence is the peritoneal cavity, while liver metastases are very rare. Patients who develop liver involvement often have refractory disease to systemic chemotherapy and carry a very poor prognosis [4].

Systemic melphalan has been widely used, from oral administration to high-dose chemotherapy, in a strategy of blood and marrow transplantation [5, 6]. The intra-arterial route is not documented. From March 2002 to December 2003, four patients with histologically confirmed liver metastases and peritoneal involvement from ovarian cancer entered this study. Median liver involvement was more than 50% and ascites was observed in three patients. All patients had platinum-resistant disease and they progressed after systemic chemotherapy with taxanes, topotecan and pegylated liposomal doxorubicin. The median age was 53 years; performance status (WHO criteria) was 2 in one patient and 1 in three. Abdominal pain was present in all patients, with a median visual analogue scale (VAS) value of 5.3. In three patients, CA125 level was high (median 12.5 U/ml).

Melphalan was infused bolus by angiographic catheter introduced in the proper hepatic artery using the Seldinger technique at a dosage of 20 mg/m^2 on day 1, every 4 weeks; after each administration the CA125 catheter was removed. The response was evaluated according to WHO criteria and toxicity was graded according to the National Cancer Institute Common Toxicity Criteria.

Fifteen cycles were administered; no side-effects related to the angiographic procedure were observed. Mild haematological toxicity occurred: one case of grade 3 leukopaenia and one case of grade 3 thrombocytopaenia were observed. Three patients showed a reduction of liver metastases of more than 50%, but one showed disease progression after one cycle. In two patients we observed a significant reduction of ascites and an impressive reduction in CA125 level in the other two cases. The responders showed an improvement in performance status and a marked pain reduction (median VAS of 2.3).

After a median follow-up of 15 months (range 5–21) three patients were dead, with a median survival of 13 months from intra-arterial chemotherapy. The time taken to respond to chemotherapy was 3 weeks and the time taken to ascertain failure of the treatment was 4.5 months. The live patient is a responder and showed a liver and pleural progression of the disease after 5 months.

This novel therapeutic approach appears very well tolerated and feasible in heavily pretreated patients with liver metastases from platinum-resistant epithelial ovarian cancer. This approach showed an interesting activity and a significantly rapid clinical improvement.

Further studies are warranted to verify these preliminary results.

A. Mambrini[1], R. Caudana[2], D. Zamagni[3], C. Rabbi[3], A. Del Freo[1], F. Sanguinetti[4], G. Fiorentini[1] & M. Cantore[1]*

Departments of [1]Oncology and [2]Radiology, City Hospital, Carrara; Departments of [3]Oncology and [4]Radiology, "C. Poma" General Hospital, Mantova, Italy (*E-mail: mauriziocantore@hotmail.com])

References

1. Hensley ML. Epithelial ovarian cancer. Curr Treat Options Oncol 2002; 3: 131–141.
2. Sherman ME, Mink PJ, Curtis R et al. Survival among women with borderline ovarian tumors and ovarian carcinoma: a population-based analysis. Cancer 2004; 100: 1045–1052.