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LETTERS TO THE EDITOR

Irinotecan and cisplatin vs. cyclophosphamide, doxorubicin, and vincristine as second-line treatment after platinum and etoposide in small-cell lung cancer

Dear Editor,

Second-line chemotherapy for small-cell lung cancer (SCLC) has lowest effectiveness and it is important to respond the question over which regimen to use in patients with relapsed or refractory SCLC. We reviewed the medical records of 21 cases with SCLC who had received second-line chemotherapy at the department of Oncology. Eleven of them had been treated with vincristine (2 mg flat dose), doxorubicin (50 mg/m^2) and cyclophosphamide (1000 mg/m^2) (VAC), all administered i.v. on day 1; the remaining 10 had received irinotecan (60 mg/m^2, days 1,8 and 15) and cisplatin (60 mg/m^2, day 1) every 4 weeks. Six of these patients were refractory and the remaining had relapsed after first-line chemotherapy with cisplatin plus etoposide.

Chemotherapy response was evaluated according to the World Health Organization criteria. The hematological and non-hematological toxicities were assessed according to the National Cancer Institute Common Toxicity Criteria.

Eighteen patients had died (10 in the VAC group and 8 in the irinotecan-cisplatin group). Two complete responses (CRs) and 2 partial responses (PRs) were observed in the irinotecan-cisplatin group, while 1 case with stable disease (SD) was documented in the VAC group. One VAC patient died of febrile neutropenic septicemia. Grade 3 or 4 diarrhea was higher in the irinotecan-cisplatin group than in the VAC group. Other toxicities were similar in both groups. Overall median survival was 11.3 weeks for VAC patients and 13.3 weeks for irinotecan-cisplatin patients (p=0.513). The median progression-free survival was 7.8 weeks for the VAC group and 10.7 weeks for the irinotecan-cisplatin group (p=0.120). Three irinotecan-cisplatin patients (2 CRs and 1 PR) achieved long-term progression-free survival (median 44 weeks, range 38-52).

Previous studies [1-5] have shown good antitumor activity for VAC and irinotecan-cisplatin regimens in first- and second-line chemotherapy of SCLC. However, these two chemotherapy protocols have not been compared with each other in SCLC second-line chemotherapy after cisplatin-etoposide treatment.

In our patients, overall survival and progression-free survival were slightly longer in the irinotecan-cisplatin group compared to the VAC group, however the difference between the two groups did not reach statistical significance.

In conclusion, our preliminary study demonstrated that irinotecan plus cisplatin combination chemotherapy is an effective and safe treatment option in second-line chemotherapy of SCLC patients. Further studies with larger numbers of patients are needed to confirm our results.

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New intraoperative gamma camera for the sentinel lymph node localization in breast cancer. From radio to TV?

Dear Editor,

Sentinel node biopsy (SNB) has become the standard of care for the axillary staging of breast cancer patients. The identification of the sentinel lymph node (SLN) is currently achieved with the simultaneous use of blue dye and radiocolloids, a combination which provides a good identification rate and reduces the false negative biopsies to as low as 5% [1].

The addition of radiocolloids to the dye-only technique of SNB has offered several advantages [2,3]. The identification of a "hot and blue" node is technically easier than a "blue only" node, requiring less surgical exposure; furthermore, radiocolloids are sufficiently retained in the SLN, offering a wider time window for the completion of the biopsy.

The greatest disadvantage of lymphoscintigraphy, however, is that it cannot be performed in real time and the surgeon is dependent on the preoperative imaging. Furthermore, the intraoperative widely used hand-held Geiger probes cannot visualize the whole axillary area simultaneously (cannot "map" the axilla) and depend on the arbitrary 10% rule: after removing the "hottest" lymph node, the surgeon should search for further "hot" or "warm" lymph nodes until the remaining radioactivity is less than 10% of the initial.

The emergence of mobile mini gamma cameras, able to perform small- field scintigraphy intraoperatively, can potentially overcome these problems [4]: the ever so important scintigraphy can now take place in real time and the search for "warm" lymph nodes is not dependent on a blind scan but can be accurately directed. After the initial use of the MiniCam II (Euro medical, France) at our institution (Figures 1 and 2) several advantages and disadvantages became apparent and are briefly listed below:

- Large field of view with simultaneous visualization of the total axillary area in a single window (actual axillary "mapping").
- Real time imaging
- Easy orientation of the field of view and planning of the primary incision
- Identification of more than one nodes of different radioactivity ("hot" and "warm") simultaneously
- Semi-quantitative view of the radioactive structures with graded color imaging, based on the number of counts/sec
- Easy semi-quantitative investigation for background radioactivity after the removal of the "hot" node
- Easy set up
- Easily data transfer and storage.

On the other hand:

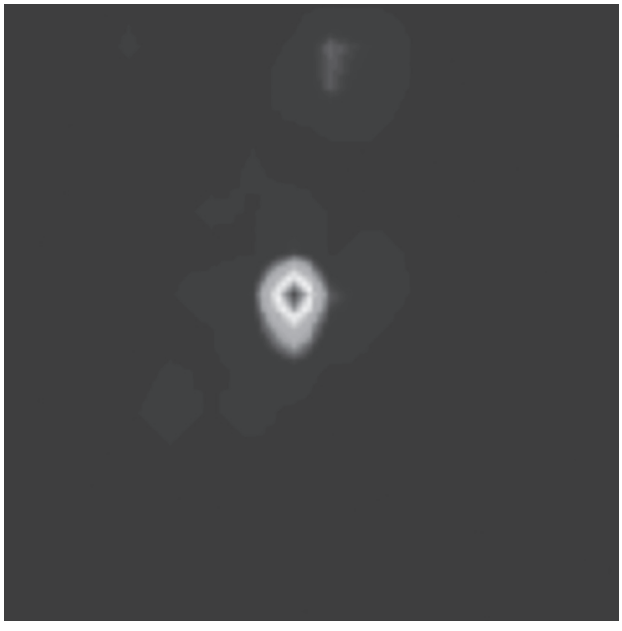

Figure 1. Mini camera displays a straightforward single "hot" node.

Figure 2. Mini camera shows two hot spots, possibly representing two different sentinel nodes. This can facilitate the planning of the incision and direct the surgical dissection to the hot areas.

- Bulky and heavy hand-held component
- Occasional failure of recognition of the deep-sitting radioactive nodes, as, because of its size, it cannot be pressed against the axillary tissue and minimize the distance between a "hot" node and the sensor
- Semi-quantitative and not quantitative imaging or numeric indications. The 10% rule cannot be applied
- Sensitive to the movement with long image acquisition time.

In conclusion, the intraoperative MiniCam cannot at the moment replace the hand-held Geiger probe. The development of a smaller hand-held component and the ability to display quantitative indications will significantly improve its competitiveness in the SNB.

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Recurrent chylothorax in a patient with mediastinal and abdominal paragangliomas

Dear Editor,

The thoracic duct collects and transports chyle into the circulation and its damage leads to leakage of chyle into the pleural cavity (chylothorax). This condition is rather uncommon. We describe a case of a patient with paragangliomas and chylothorax.

A 38-year-old white female, who had no remarkable medical history, was admitted to the hospital with gradual onset of dyspnea and anterior chest pain. The symptoms had started 15 days before her admission. The patient had been smoking 1 package of cigarettes per day for 10 years and quit 9 years before her admission. Family history was noncontributory. Physical examination showed remarkable degradation of respiratory sounds of the left lung.

The laboratory workup revealed elevation of serum CA-125 and the aspirated pleural fluid was chylous in appearance. Chest X-ray (CXR) examination revealed left pleural effusion and ipsilateral diffuse interstitial infiltrates. A computed tomography (CT) scan showed multiple prevascular and smaller paratracheal lymph nodes (≤ 3 cm), left pleural effusion accompanied by ipsilateral pleural thickening and pneumothorax. From the pulmonary parenchyma there was segmental atelectasis and alveolar infiltrates at the left lung base as well as ipsilateral diffuse microcystic fibrosis with interstitial infiltrates. The right lung was normal. There was also an abdominal cystic mass located in front of the inferior vena cava, extending from the renal hila to the aortic bifurcation.

Biopsies from mediastinal lymph nodes and the abdominal cystic mass were taken and the patient underwent lymphangiography which showed cystic dilatations of the lymph vessels at the level of cisterna chyli and leakage of lymph to the left hemithorax at the T5 level. The biopsies revealed paraganglioma, the patient underwent talc pleurodesis and was discharged.

After 2 years, the patient was readmitted with similar symptoms and left chylothorax was diagnosed. The pulmonary findings from CXR and CT scan were reviewed, showing diffuse pulmonary interstitial infiltrates involving both lungs. A left talc pleurodesis was performed and the patient was discharged.

The presence of pleural effusion on CXR is usually the initial finding of a chylothorax. CT scan of the chest is helpful when examining for tumors in cases with a chylothorax of non-traumatic etiology, as was the case in our patient [1]. Definitive diagnosis of whether an effusion is a chylothorax is made by laboratory analysis of the pleural fluid. The aetiology of chylothorax in adults with a negative history of iatrogenic and non-

iatrogenic trauma includes neoplasms, infections, pancreatitis, hypothyroidism, nephrotic syndrome and miscellaneous rarer causes like lymphangioleiomyomatosis and lymphangiomatosis [2-4].

To our knowledge, this is the first reported case of paragangliomas in association with a chylous pleural effusion. Paragangliomas are rare tumors that arise from extra-adrenal paraganglia [5]. Most of the patients present with mass-effect symptoms and do not have documented catecholamine hypersecretion. Although very rare, paraganglioma must be considered in the differential diagnosis of chylothorax of non-traumatic origin.

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Skin metastasis of ovarian cancer: a rare entity

Dear Editor,

A 38-year-old woman was admitted to the hospital with vesicular and pustular lesions on the chest and abdominal skin and subcutaneous nodules in both breasts 5 years after the diagnosis of ovarian cancer. She had initially undergone total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, appendectomy, lymph node dissection and low rectal resection for stage IIIC serous papillary adenocarcinoma of the ovary. Postoperatively, she had received 6 cycles of paclitaxel and carboplatin (PC). Relapse occurred at the perirectal tissue 14 months after the end of chemotherapy. She was treated again with 4 cycles of cisplatin and paclitaxel without response. Laparotomy was then performed during which disease deposits involving peritoneal surfaces, liver and spleen were observed. Only multiple biopsies were taken, revealing again serous papillary ovarian adenocarcinoma. She was then given 8 cycles of 3-weekly liposomal doxorubicin with disease stabilization. Due to disease progression therapy was switched to weekly topotecan (total 48 weeks). However, 3 months after stopping topotecan serum CA-125 levels increased to 50 U/ml and abdominal CT scan showed progression of intraabdominal metastases. Four cycles of single-agent gemcitabine were administered. A lump was observed in her right breast one month after the last administration of gemcitabine. Pathological examination of the mass revealed metastatic papillary ovarian adenocarcinoma. Then, she was given oral etoposide for about 9 months until malignant pleural effusion occurred bilaterally. Cytology of the effusion was again consistent with ovarian adenocarcinoma and oral cyclophosphamide and methotrexate (CM) were subsequently administered. After 3 cycles of CM serum CA-125 levels increased to 413 U/ml with progression of the pleural effusion. Weekly melphalan p.o. was initiated and after 3 cycles of this treatment the patient was admitted to the hospital with vesicular skin lesions on the chest and abdominal skin and subcutaneous nodules in both breasts and worsening dyspnea. Serum CA-125 level was 614 U/ml. Punch biopsy of the skin lesions and trucut biopsy of the subcutaneous breast nodules revealed metastases of serous ovarian papillary adenocarcinoma. Weekly paclitaxel was planned for the patient, but she couldn't take it because of poor performance status. The patient died after 2 months from the occurrence of skin metastases.

Skin metastasis is rarely seen in ovarian carcino-

ma (2-4%) but when occurring it heralds poor prognosis [1]. Skin metastasis can mimic various types of dermatological lesions such as herpetic, nodular, infectious-like or cicatricial plaques. It occurs generally in the skin of lower abdominal wall, usually from surgical or interventional puncture sites [2]. However, chest wall, breast, buttocks and sometimes -as in our case- whole anterior trunk might be involved [3]. Scalp metastasis was also reported in a case [4]. Systemic therapeutic choices were not shown to be beneficial for palliating symptoms or improving survival. Treatment of skin metastasis is generally with local modalities. If single or a few number of nodular metastases are present, surgical resection might be performed. However, it will not be practical in case of diffusely involved skin. Electron beam therapy, electrocoagulation and hematoporphyrin derivative injection with infrared phototherapy might offer palliation [5]. Local or systemic analgesics and antibiotics might also be helpful for palliation of pain and also prevention or treatment of infections.

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