Sustained complete remission of metastatic oesophageal adenocarcinoma using long-term therapy with 5-fluorouracil

Patients with liver metastases of oesophageal cancer have a median survival of <1 year [1], while 5-year survival is anecdotal. We report a 7-year disease-free survival in a patient with histologically confirmed liver metastases of oesophageal adenocarcinoma treated with chemotherapy for 30 months. A 70-year-old man was diagnosed in 1995 with a focally poorly differentiated adenocarcinoma of the lower oesophagus. History included myocardial infarction in 1991 and gastro-oesophageal reflux disease. World Health Organization performance status at the time of diagnosis was 1. Serum creatinine was elevated (155 μmol/l) due to nephroangiosclerosis. Carcinoembryonic antigen serum level was normal. Owing to a computed tomography finding of enlarged paraaortic/paratracheal lymph nodes, without evidence of systemic metastatic spread, neo-adjuvant chemotherapy with 5-fluorouracil (5-FU) as a continuous infusion (c.i.) for 5 days, combined with doxorubicin on day 1, in a 3-week schedule was started. Response to therapy was documented and the patient underwent radical oesophagectomy. Disease was classified as pT2pN0M0 according to tumour–node–metastasis classification (TNM Classification of Malignant Tumours, UICC, Sixth Edition 2002). Postoperative complications consisted of renal failure requiring transient dialysis, bilateral pneumonia and complex cardiac arrhythmia, which were all successfully managed. In the following year the patient underwent several endoscopic dilatations of benign anastomotic strictures without evidence of cancer. In March 1996, an abdominal ultrasound revealed two hepatic lesions, both in segment V, which were confirmed on biopsy to be metastases. Old age and cardiac and renal co-morbidities were the reasons for treatment choice: low dose 5-FU c.i. with folinic acid given 14 out of 28 days. In November 1996, liver imaging disclosed the disappearance of all liver lesions (Figure 1). Therapy was continued as 5-day 5-FU infusion every 4–6 weeks until November 1998. The patient is still alive in complete remission (CR), with excellent quality of life despite regular peritoneal dialysis recently introduced for a worsening of the renal failure. Chemotherapy may offer palliation and prolongation of survival in patients with advanced oesophageal cancer. Cisplatin in combination with 5-FU, taxanes or irinotecan yield objective response rates of 30–50% [2], but the impact of response on survival and on quality of life is unclear due to the lack of information from comparative trials of chemotherapy versus supportive care alone. On the other hand, CRs are rare, and the duration of any response is typically short. Despite the sub-optimal chemotherapy administered, the patient achieved a sustained CR persisting 5 years beyond completion of treatment. A similar favourable course of oesophageal cancer has been described only anecdotically in subjects with metastatic Barrett’s adenocarcinoma [3] or squamous cell carcinoma [4].

Treatment outcome and prognosis in the case of an oesophageal carcinoma depends on both patient and disease characteristics. In advanced disease, performance status, extent of disease and lactate dehydrogenase are independent prognostic factors [5]. The median survival for patients with none of these variables is estimated to be 12 months, compared with 4 months for those who have all the unfavourable characteristics. We consider this case as the illustration of a possible, albeit extremely rare, cure of metastatic oesophageal cancer with prolonged use of chemotherapy. The particular role of the drug or the schedule used can only be speculated.

Figure 1. Representative abdominal CT scan images showing the disappearance of liver metastases.
Early subcutaneous wash-out in acute extravasations

Schrijvers [1] has published a review article on extravasation injuries and their treatment. The paper gives guidelines of prevention, and conservative and late operative treatment. However, the early treatment option of subcutaneous wash-out [2, 3] is neither mentioned nor referenced.

Despite this the technique is very successful in our experience, possibly due to an early reduction in concentration of the highly toxic chemotherapeutic, and especially when it is performed within 6 h of extravasation injury [3]. Under regional anesthesia we position two to three incisions, thereby providing sufficient access to the affected subcutaneous tissue (Figure 1). With an infiltration canula, which is commonly used in liposuction, isotonic NaCl solution is infiltrated and may be flushed out through the other incisions. In a second step the infiltrated fluid is removed by careful suction with a small liposuction canula. This procedure is repeated until 300–500 ml of wash-out solution has been used. Eight patients with full extravasation injury of vinca alkaloids or anthracyclines have been treated with this technique, out of a larger series with other, less toxic extravasation injuries. All patients healed without soft tissue defect and in none of the patients was a secondary surgical procedure necessary. No patient experienced any loss in the range of motion of the joints in the hand.

Schrijvers [1] presents a typical case of conservatively treated extravasation of highly toxic doxorubicin, where the opportunity for early subcutaneous wash-out was missed and skin necrosis developed, with exposure of the muscles and ligaments. Despite all precautions, the tissue toxicity of the drug possibly led to lacerations of the fragile vascular wall, with all the consequences of extravasations. However, a surgical treatment was considered only 24 h after injury, which in our experience is too late for subcutaneous wash-out. Follow-up showed that 6 weeks after treatment a skin graft was enough to cover the defect, which is surprising from a surgical point of view: when ligaments or tendons are exposed a flap is usually needed. However, nothing was reported concerning the result in terms of hand function, which is often highly deficient and multiple operations may be needed for restorage. Reduced hand function and severely prolonged hospitalization may be disastrous, especially for a tumor patient. At the end of the case report the author mentions that the patient sued the department for medical fault. This highlights a further aspect of early subcutaneous wash-out, which may diminish legal consequences. On the other hand, additional medico-legal problems may arise when this treatment is not considered by the treating oncologist or surgeon.

In conclusion, early subcutaneous wash-out in acute extravasation injuries is a safe and simple procedure. We consider the technique a further option in the armament of extravasation treatment that helps to reduce the severe sequelae of highly toxic drug extravasation for the patient and that deserves more attention. Every review or monograph on extravasation injury should at least mention and discuss the technique to provide complete information to readers.

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