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Beneficial Effects of Octreotide in a Patient With a Metastatic Paraganglioma

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UPTAKE OF a radiolabelled somatostatin analogue has already been reported in malignant paraganglioma [1, 2], as well as *in vitro* inhibition of catecholamine secretion by octreotide [3].

A 44-year-old man had been treated for a metastatic paraganglioma with several modalities: surgery for adrenal paraganglioma and bone metastases, metaiodobenzylguanidine (MIBG) therapy, chemotherapy and external radiotherapy for bone metastases.

In February 1993, he presented with a low performance status, paraplegia, pseudo-obstruction of the large bowel not responsive to classical treatments, left parotid metastasis measured by ultrasound (45 × 30 × 40 mm), multiple bone metastases and bone marrow involvement with thrombocytopenia (platelets: 16 × 10^9/l) and anaemia (Hb: 8.9 g/100 ml). MIBG uptake was seen in known metastases on scintigraphy, but no hormonal overproduction was found in repeated urinary measurements.

Uptake of a radiolabelled somatostatin analogue (OctreoScan®, Mallinckrodt Medical) was seen in distant metastases on whole body scintigraphy and led us to initiate a treatment with octreotide (500 μg subcutaneously per day). An improvement of the performance status, the normalisation of intestinal function, a decrease of 50% in the size of the parotid metastasis, the normalisation of bone marrow production with an improvement in haematological parameters (platelets: 166 × 10^9/l and Hb: 12.2 g/100 ml) and a decrease of more than 50% in the intensity of metastatic MIBG uptake were noted. No unexpected side-effect was noted. These positive effects lasted for 6 months, after which the disease progressed and the patient died 10 months after initiation of octreotide therapy.

In conclusion, the beneficial effects of octreotide treatment could be quantified by clinical, tumour and scintigraphic criteria, which is rarely the case [4]. These data suggest that octreotide can be useful in the treatment of malignant paraganglioma at a certain stage of the disease.

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Rapid Tumour Lysis Syndrome in a Metastatic Colorectal Cancer Increased by Treatment with Irinotecan (CPT-11)

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TUMOUR LYSIS syndrome (TLS) is usually manifested by hyperuricaemia, hyperkalaemia, hyperphosphataemia and hypocalcaemia and can lead rapidly to an acute nephropathy with renal failure. It is due to massive necrosis of neoplastic cells, sometimes occurring spontaneously but more often after effective cytotoxic therapy. Commonly described in haematopoietic malignancies, it occurs rarely in solid tumours. We report a case of TLS in a patient with metastatic colon carcinoma.

A 42-year-old female underwent a left hemicolectomy in March 1994 for an adenocarcinoma of Dukes' C stage. She subsequently received six courses of adjuvant chemotherapy with 5-fluorouracil (5-FU) and folinic acid. Six months after the end of the treatment, she relapsed with a perirectal disease and multiple liver metastases. She then received pelvic irradiation (60 Gy) and chemotherapy with continuous infusion of 5-FU over 15 days. At the beginning of the treatment, laboratory values revealed elevated uric acid (570 μmol/l), kalaemia (5.4 mmol/l) and phosphataemia (1.43 mmol/l). Lactic dehydrogenase (LDH) was 700 UI/l. Other values including renal function and calcaemia were within the

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normal range. Chemotherapy was stopped after two courses because of metastatic progression in the liver (invading more than 50% of the liver). Uric acid was still elevated (700 μmol/l) without any specific treatment, and phosphataemia was 1.38 mmol/l. Other biological values were normal except a cholestasis with total bilirubinaemia slightly increased up to 25 μM/l and LDH to 1000 UI/l. We decided to treat this patient with irinotecan (compassionate use, Laboratoires Bellon). She received a reduced dose of 300 mg/m^2 because of the cholestasis. At day 8, she was admitted for a profound general deterioration. Laboratory exploration showed severe metabolic anomalies consisting of a major uric acid increase up to 1816 μmol/l, hyperphosphataemia (2.68 mmol/l) with hypocalcaemia (2.0 mmol/l), hyperkalaemia (6.0 mmol/l) with bicarbonates at 21 mmol/l, and renal failure with serum creatinine at 200 μM/l. LDH was 3600 UI/l. Despite forced diuresis, urine alkalinisation and uricolytic therapy, the patient died 48 h later due to renal failure with anuria.

To our knowledge, TLS has never been described as a complication of metastatic colorectal cancer [1]. However, this patient had many common features described in TLS-associated malignancies: bulky tumour, rapid growth, evidence of spontaneous TLS [2]. The rapid progression of the disease and the moderate increase of the lysis with 5-FU reflects the inactivity of this drug. Irinotecan (CPT-11) is a new cytotoxic agent, an inhibitor of the DNA enzyme topoisomerase I, which is effective against advanced and metastatic colorectal cancer, with an 18% response rate in first-line therapy or in tumour resistant to 5-FU [3]. The acute TLS observed in this patient confirms the activity of this agent in a tumour resistant to 5-FU. The principal adverse events of CPT-11 are neutropenia and delayed diarrhoea of secretory mechanism, and are both dose related. None of these effects were observed in our patient. The acute TLS described here is a previously unreported adverse event of CPT-11. Renal failure was probably due to hyperuricaemia combined with hyperphosphataemia. SN 38, the active metabolite of irinotecan, is mainly excreted in the bile and a renal toxicity of irinotecan has never been previously described [4]. This case illustrates that administration of irinotecan for bulky tumours of colorectal origin with rapid doubling time may induce an acute TLS which necessitates frequent laboratory monitoring and prevention by abundant hydration and hypouricaemic treatment.

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Major Interactions Between Radiation Therapy and Systemic Sclerosis: Is There an Optimal Treatment?*

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SYSTEMIC SCLEROSIS (SSc) is a collagen vascular disease characterised by fibrosis, resembling that observed in late radiation damage. An unusually high incidence of complications after radiation therapy (RT) has recently been reported in patients with SSc [1–6]. In these series an excessively severe fibrosis, extending beyond the irradiated fields, rapidly occurred and caused death in a third of patients. However, RT was delivered after surgical removal of the tumour and tumour regression in relation to RT could not be evaluated. We describe here fast and striking tumour regression after reduced RT dose for malignant tumours in 3 patients with severe SSc.

3 patients who had had evolutive SSc for 8–16 years developed inoperable locally advanced cancer and were treated by RT. A total dose of 40–45 Gy in 6 weeks and fraction of 1.8 Gy was delivered with a 4.5 MV photon beam to the tumour. None of the patients was given chemotherapy or a radiosensitiser.

Patient 1

A 54-year-old man with SSc including interstitial pneumonitis and myocarditis presented with T_3 N_2 M_0 epidermoid lung cancer. He received 40 Gy of thoracic RT over 6 weeks. Immediate clinical RT tolerance was excellent, but a 15% decrease in lung diffusing capacity was observed. Evaluated on CT scan, tumour volume reduced by half after a 20 Gy given-dose and by 85% at the end of treatment, thus allowing subsequent surgery. Right pneumonectomy with node dissection was performed 6 weeks later. Pathological examination of the surgical specimen showed a large volume of necrosis without viable tumour cells. The patient died suddenly of respiratory distress syndrome, three days after surgery. Post mortem examination indicated lethal lung fibrosis with haemorrhagic alveolitis compatible with SSc.

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