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Case Reports

Case reports are accepted under this heading. These reports should be short and concise and contain a minimum of figures, tables and references.

BREAST ANGIOSARCOMA AFTER RADIATION THERAPY

Angiosarcoma after radiation therapy for breast-conserving treatment of breast carcinoma is a rare primary breast malignancy, with only 16 cases reported to date (1, 2). We here describe a new case of breast angiosarcoma, previously treated with tylectomy and radiation therapy.

Case report. A 73-year-old woman underwent tylectomy of a carcinoma of left breast and axillary lymphadenectomy in August 1986. The tumor measured 2 cm at its greatest diameter and one lymph node of the 9 removed was affected. The tumor tissue presented high levels of estrogen receptors.

Postoperative radiotherapy was delivered to the left breast and to supraclavicular, axillary and internal mammary lymph nodes, with 15-mV photon beams using a lineal accelerator, until a total dose of 40 Gy was reached over the described areas. Electron-beam irradiation was continued over the same fields until a dose of 50 Gy was reached. Once therapy was completed, a boost of 10 Gy was administered over the primary breast site, using a direct anterior field of 9-meV electrons.

The patient's course continued without evidence of tumor until November 1992, when a mass filling almost the entire left breast, accompanied by skin thickening, was detected. Moderately differentiated angiosarcoma with a low mitotic rate was seen at biopsy. Radical surgical extirpation was ruled out, and the patient received four courses of chemotherapy combining iphosphamide and VP-16. The treatment achieved an important reduction of angiosarcoma size, and simple mastectomy was performed in May 1993. In November 1993, a recurrence over the mastectomy scar was evidenced, and the patient underwent en bloc excision (major pectoral muscle, lower third of sternum and 8th, 9th and 10th ribs).

The patient died in August 1994, with metastatic spread including skin recurrence over the aforementioned area.

Discussion. Since 1987, when Body described the first case of breast angiosarcoma after radiation therapy for invasive ductal carcinoma, 16 more cases have been published (1–3). Those authors who have studied the relation of total radiation dose, orthovoltage or megavoltage radiation and dose per fraction to the frequency of appearance, have found no significant differences (4).

The interval between the start of radiation therapy for a first tumor and the diagnosis of a postirradiation sarcoma is about 12 to 13 years. Differences have been reported in the median interval depending on the type of radiation received by the patients, viz. 15.9 years for orthovoltage radiation and 7.4 years for megavoltage radiation (5). Among the patients with postirradiation angiosarcoma described to date, the latency period was 6.1 years (2.5 to 12.6) (4).

The median age at presentation of this tumor is 64.5 years. The cause of its failure to appear in younger patients is unknown, despite the great number of patients that receive radiation therapy at early ages after partial surgical breast resection (6).

We think that it is important to study histologically every lesion suspected of being associated with recurrence after breast-conserving treatment to determine the exact incidence of this second primary tumor, taking it in consideration prior to radiation therapy in elderly patients.

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ACUTE RENAL INSUFFICIENCY DUE TO VIRAL INFECTION CAUSED BY CYTOMEGALOVIRUS (CMV) DURING TREATMENT WITH METHOTREXATE

In October 1993, a 65-year-old man was admitted to the Department of Oncology of Helsinki University Central Hospital for treatment of large B-cell malignant lymphoma involving the sigmoideal part of the large bowel. This local and only tumour found after examinations including whole body computer tomography was radically excised. Adjuvant treatment with three BACOD-M courses (bleomycin, doxorubicin, vincristine, cyclophosphamide, dexamethasone, and high-dose methotrexate (HDMTX)) was initiated. Two BACOD and the first HDMTX were given without complication. The second HDMTX was given as planned 5.6 g on day 15 after BACOD, in December 1993. The patient did not complain of any symptoms and all laboratory values, including creatinine, were normal. On day 2 after HDMTX, the patient had fever up to 39°C. Serum concentration of methotrexate (MTX) was 1.45 Umol/l, creatinine was 85 Umol/l, and C-reactive protein (CRP) 40 g/l. The patient had no other sign of infection, and blood culture tests were negative. On day 3 after HDMTX, creatinine rose to 227 Umol/l and serum concentration of MTX decreased to an acceptable value of 0.24 Umol/l. CRP was 28 g/l. Diminution of urine secretion was noticed. Control creatinine was 356 Umol/l on day 4. Renography demonstrated decreased renal function in both kidneys. Intensive diuresis

and continuous administration of leukovorin rescue (100 mg/m^2 every three hours), with maintenance of pH $\geq$ 7 were initiated. In subsequent examinations, cytomegalovirus (CMV) titer was high, 3 200. No other micro-organisms were found. On day 6 after MTX, creatinine value continued to increase up to 441 Umol/l, but the patient's general condition remained excellent, and intensive therapy for renal insufficiency was maintained. Creatinine value started to decrease on day 7 and normalized (98 Umol/l) only after two months, in February 1994. Serum IGM for CMV antibodies was then 3.7 g/l, i.e. higher than in October 1993 (0.6 g/l). In our department, laboratory examinations for viral infection are systematically performed on all patients with malignant lymphoma. The patient is being followed up and he has no recurrence of malignant lymphoma nor other sequelae of the viral infection.

Acute renal insufficiency caused by concomitant use of HDMTX and other agents such as non-steroidal anti-inflammatory drugs has been reported previously (1). Since then renal complications due to MTX have been avoided in our department. It has been reported that viral infection could cause renal failure in patients with cancer (2), and administration of immunosuppressive medications could result in increased frequency and severity of viral infections, especially when cell-mediated and humoral immunity are impaired. It is known that in such cases, even vaccination with live vaccines is contraindicated because it may lead to renal failure (3).

In the present case, viral infection probably caused renal insufficiency during antineoplastic treatment. This possibility should always be considered when no other causes are found. Fortunately for the present patient, CMV developed when the plasma concentration of MTX was quite low and rapidly decreasing (1.45–0.24 Umol/l). This perhaps permitted the relative rapidity and reversibility of the renal insufficiency. Higher MTX plasma concentration could have caused more serious renal complication. Immediate initiation of intensive supportive treatment with increased diuresis, leukovorin rescue and maintenance of pH at 7 definitely played an important part in normalising the general condition of the patient and his renal function.

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AGGRESSIVE HEPATIC LEIOMYOSARCOMA—AN IMMUNOHISTOCHEMICAL EVALUATION OF MALIGNANT POTENTIAL USING MONOCLONAL ANTIBODY MIB-1

The rarity of leiomyosarcoma of the liver is well appreciated. This tumor has been reported to be slowly progressive and late metastatic (1–3). In the present report we describe a rapidly growing leiomyosarcoma of the liver, which recurred with multiple metastases one year after surgical resection. This is the first case with bone metastases. For these lesions multimodal treatments, including irradiation, chemotherapy and tumor necrosis factor therapy (4, 5), were introduced. In order to clarify the malignant potential of this tumor, an immunohistochemical evaluation of mitotic activity using monoclonal antibody MIB-1 (6, 7) was performed.

Case report. A 39-year-old, previously healthy, woman was admitted to our hospital in October 1990. The patient was completely asymptomatic, although a tumor was discovered by an abdominal ultrasound scan during a routine physical examination. Imaging studies revealed a single 7 cm mass in the medial segment of the liver. A needle biopsy of the tumor was interpreted as leiomyosarcoma. An elective laparatomy disclosed a tumor in the left hepatic lobe without evidence of intraabdominal metastases. No other primary lesions were found. An extended left hepatectomy was performed. The liver mass was well circumscribed, measured 7 × 6 cm, and on sectioning appeared creamy white. Histopathological findings showed interlacing spindle-shaped cells that revealed frequent mitotic activity of 37 mitoses per 10 high power fields. Immunohistochemical staining for vimentin and desmin were positive. With prior microwave treatment monoclonal antibody MIB-1 immunostaining was performed of formalin-fixed and paraffin-embedded tissues, using the avidin-biotin-peroxidase complex method as described elsewhere (6, 7). MIB-1 staining was positive in tumor cells showing mitotic figures. Venous invasion was also recognized in some areas. One month after surgery, chemotherapy treatment was started, consisting of 3 weekly administrations of 4 mg mitomycin C and 10^6 units of recombinant tumor necrosis factor -S (r-TNF-S) (4, 5) intravenously. One month after completion of the chemotherapy treatment, the patient was discharged. She then remained in total remission for a period of one year, but subsequently multiple nodular liver metastases were discovered in the right lobe. Chemotherapy with doxorubicin 20 mg, and mitomycin C 10 mg was started through an intraarterial infusion port and 500 mg 5-FU (5-fluorouracil) was added to the protocol for 2 subsequent weekly infusions. Two weeks later adrenal and pancreatic metastases were discovered. After another eight weeks, the patient developed additional bone metastases (left frontal, costae) and radiation therapy was begun. However, the tumors responded poorly to these treatments and the patient died 2 years after surgery. No autopsy was performed.

Discussion. Primary leiomyosarcoma of the liver is rarely recognized and because of their rarity, the biological behavior of these tumors is not well understood. In general, tumors of this type are slow-growing (1–3). However, as evidenced in the present report, this is not always true. Recently others have reported the correlation between metastatic potential and mitotic activity (8), and low mitotic activity may yield a long survival period (9). However, correlation with the clinical course is not absolute (10). There is presently no widely accepted objective mitotic index for diagnosis of malignancy in primary smooth muscle tumors of the liver. MIB-1 staining allows a much better measurement of mitotic activity and discriminate clearly positive tumor cells from negative cells. In our case, the tumor revealed high mitotic activity as evaluated by MIB-1 staining, possibly contributing to its clinical behavior. Thus, MIB-1 staining is useful as a means of detecting rapid growth patterns in aggressive leiomyosarcoma with high malignant potential.

In light of this and previous reports, surgical treatment seems to offer the sole hope for a cure (1, 11). In this case, even after a successful tumor resection, lesions recurred and grew rapidly in a