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Letters to the editor

Radiation pneumonitis after local-regional radiotherapy following autologous stem-cell transplant for high-risk breast cancer

We have read the article by Moore et al. [1] regarding the toxicity and outcome of high-dose chemotherapy with stem-cell support followed by local and regional radiotherapy in a cohort of 103 patients with high-risk breast cancer. Radiation therapy to the breast (or chest wall) plus regional lymph node areas is aimed at decreasing the unacceptably high rate of loco-regional relapses (33% in Peter's report [2]) seen in patients with metastasis to >10 axillary lymph nodes after surgery plus high-dose chemotherapy. Indeed, it significantly decreases the rate of loco-regional relapses in this patient population, as shown by Moore et al. [1]. However this is achieved at the cost of substantial toxicity for some patients.

We have recently analyzed the toxicities of local-regional radiotherapy following high dose chemotherapy with carboplatin, tiothepa and cyclophosphamide [3] with autologous stem-cell transplant in a cohort of 31 patients with high-risk breast cancer (>10 axillary nodes: 7 patients; 4–9 nodes: 7 patients or stage III: 17 patients). All patients received the scheduled dose of radiation (electron beam: 5500 cGy to the breast or chest wall, and 4500 cGy to the axillary, supraclavicular and internal mammary lymph node areas) relatively early after transplant (median time from stem-cell infusion to initiation of radiotherapy: 49 days, range 19–84 days; median duration of radiotherapy: 43 days, range 36–54 days), and only five patients (16%) required temporary discontinuation of radiation for one to two weeks following mild fever of unknown origin (3 patients) and acute pneumonitis (2 patients). Radiation pneumonitis was a frequent toxicity in this series. Ten patients (32%) had acute pneumonitis. Dry cough and fever were the presenting symptoms. Most patients underwent an unsuccessful work-up for infectious pneumonia often including admission. The symptoms subsided with corticosteroid therapy.

We feel it should be emphasized that radiation pneumonia is a frequent cause of fever in patients with high-risk breast cancer undergoing local-regional radiation therapy after high-dose chemotherapy with stem-cell support.

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References

1. Moore HCF, Mick R, Solin LJ et al. Autologous stem-cell transplant after conventional dose adjuvant chemotherapy for high-risk breast cancer: Impact on the delivery of local-regional radiation therapy. Ann Oncol 1999; 10: 929–36.
2. Peters WP, Ross M, Wredenburgh JJ et al. High-dose chemotherapy and autologous bone marrow support as consolidation after standard-dose adjuvant therapy for high-risk primary breast cancer. J Clin Oncol 1993; 11. 1132–43.
3. Antman K, Ayash L, Elias A et al. A phase II study of high-dose cyclophosphamide, thiotepa, and carboplatin with autologous marrow support in women with measurable advanced breast cancer responding to standard-dose therapy. J Clin Oncol 1992; 10: 102.

Urinary bladder cancer death rates in Europe

Several risk factors have been associated with bladder cancer risk, including cigarette smoking, occupational exposure to aromatic amines and other chemicals, bladder infections, selected aspects of diet, and the use of some drugs such as phenacetine-containing analgesics, chlornaphazine and cyclophosphamide [1]. In the US [2], Britain [3] and Italy [4] 50%–70% of bladder cancers in men, and 20%–35% in women were attributable to cigarette smoking, and 5%–10% to occupational exposures. Changes in exposure to these two major risk factors, therefore, may largely explain trends registered in mortality from the disease, mostly for males.

In 1990–1994, most of the age-adjusted (world standard population) mortality rates for men in Europe ranged between 5 and 8 per 100,000. Only Denmark (8.9), Spain and Italy (8.6), and Hungary (8.1) had rates over 8/100,000. Sweden and other Nordic countries had low rates. Rates for women were between 1 and 3/100,000 in most European countries [5, 6]. An age-period and cohort model showed that in most western Europe mortality increased up to the generations born around 1920 to 1940, and declined thereafter [7]. In the United States, the declines had started earlier, and bladder cancer mortality has been declining in white and black populations of both sexes since the late 1970s [8].

Figure 1 gives trends in age-standardized (world standard) all age and truncated 35–64 years bladder cancer mortality from 1955 to 1994 in the European Union, derived from the World Health Organisation database [9, 10]. Overall age-standardized rates in males increased from 4.5/100,000 in

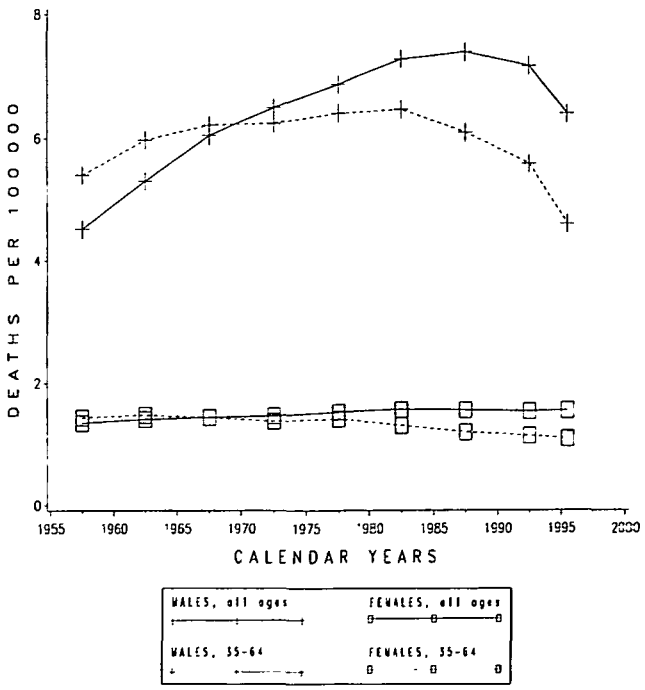

Figure 1. Trends in age-standardized (per 100,000, world standard) mortality rates from bladder cancer in the 15 countries of the European Union, 1955–1996.

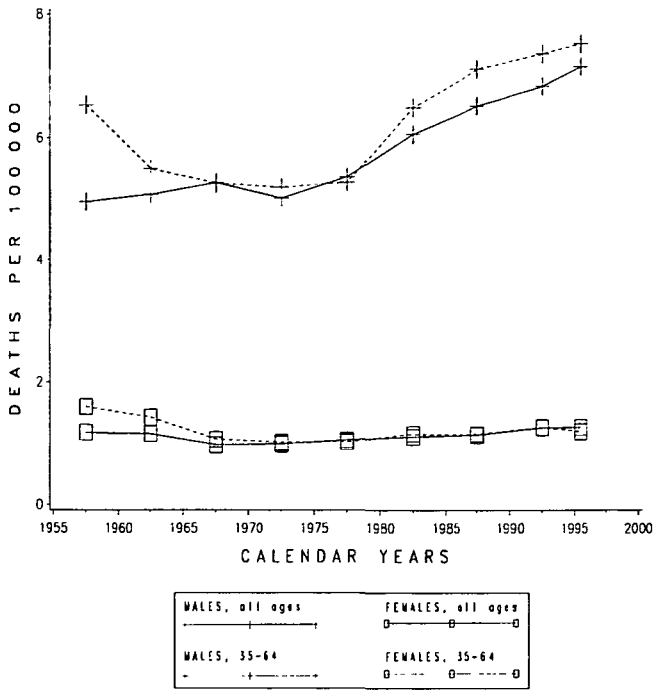

Figure 2 Trends in age-standardized (per 100,000, world standard) mortality rates from bladder cancer in six eastern European countries, 1955–1996

1955–1959 to 7.4 in 1985–1989, and levelled off thereafter to 6.4/100,000 in 1995–1996. Truncated rates were 5.4/100,000 males in 1955–1959, peaked at 6.5 in 1980–1984, and declined to 4.6/100,000 males in 1995–1996. For females, overall rates increased from 1.4/100,000 in 1955–1959 to 1.6 in 1985–1989, and remained approximately stable thereafter. Truncated rates in females remained around 1.4/100,000 between 1955 and 1980, and declined thereafter to reach 1.1/100,000 in 1995–1996.

Corresponding values for six eastern European countries providing data (Bulgaria, Hungary, Poland, Romania, Czech Republic, Slovakia, i.e., former Czechoslovakia) are given in Figure 2. Overall bladder cancer rates for males in eastern European countries rose from 4.9 in 1955–1959 to 7.1/100,000 in 1995–1996. Truncated rates declined from 6.5/100,000 in 1955–1959 to 5.2/100,000 in 1970–1974, but steadily increased thereafter to reach 7.5/100,000 in 1995–1996. In females, overall rates slightly increased from the early 1970s (1.0/100,000) to reach 1.3/100,000 in the mid-1990s. Truncated rates, after a decline between the mid 1950s (1.6/100,000 females) and the early 1970s (1.0/100,000), remained around 1.2/100,000 until the mid 1990s.

The present figures indicate that bladder cancer mortality has started to decline for males in the European Union about ten years later than in the United States. In Eastern Europe, in contrast, bladder cancer mortality is still appreciably upwards in males, is now higher than in the European Union, and has started to rise in females, too. This indicates that there were substantial delays in controlling major risk factors for bladder cancer in these countries, mainly tobacco and occupational exposure to carcinogens [9, 10].

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References

1. La Vecchia C, Airoldi L. Human bladder cancer: Epidemiological, pathological and mechanistic aspects. In Draper CC, Dybing E, Rice JM, Wilboum JD (eds)· Species Differences in Thyroid, Kidney and Urinary Bladder Carcinogenesis. IARC Scientific Publication No. 147. Lyon: International Agency for Research on Cancer 1999; 139–57.
2. Hartge P, Silverman D, Hoover R et al. Changing cigarette habits and bladder cancer risk: A case-control study. J Natl Cancer Inst 1987; 78: 1119–25
3. Moolgavkar SH, Stevens RG Smoking and cancer of bladder and pancreas: Risks and temporal trends. J Natl Cancer Inst 1981; 67: 15–23.
4. D'Avanzo B, La Vecchia C, Negri E et al. Attributable risks for bladder cancer in northern Italy. Ann Epidemiol 1995; 5: 427–31.
5. Levi F, Lucchini F, Boyle P et al. Cancer incidence and mortality in Europe, 1988–1992. J Epidemiol Biostat 1998; 3: 295–373.
6. Levi F, Lucchini F, Negri E, La Vecchia C. Worldwide patterns of cancer mortality, 1990–1994. Eur J Cancer Prev 1999; 8: 381–400.
7. La Vecchia C, Negri E, Levi F et al. Cancer mortality in Europe· Effects of age, cohort of birth and period of death. Eur J Cancer 1998; 34: 118–41.
8. Anonymous. Stat Bite. US urinary bladder cancer death rates. J Natl Cancer Inst 1999; 91: 1362.
9. Levi F, Lucchini F, Negri E et al. Cancer mortality in Europe, 1990–1994, and an overview of trends from 1955–1994. Eur J Cancer 1999; 35: 1477–516.
10. Levi F, Lucchini F, La Vecchia C, Negri E. Trends in mortality from cancer in the European Union, 1955–1994. Lancet 1999; 354: 742–3.

Elevation of urinary porphyrin levels following gemcitabine administration

A 67-year-old man with a diagnosis of porphyria cutanea tarda (PCT) and HCV-positive well compensated (Child-Pugh A) liver cirrhosis came to our institution because of ultrasonographic evidence of a 4 cm liver lesion, discovered during a routine examination. Cytologic examination of a fine-needle biopsy (FNAB) of this lesion was suggestive of adenocarcinoma. A laparotomy showed diffuse abdominal adenomegalies. Histologic examination of an intraoperatory liver mass biopsy and a resected retroperitoneal lymph node showed the presence of a metastatic cholangiocarcinoma. After an uneventful postoperative recovery, the patient agreed to participate in an investigational protocol with gemcitabine that was administered at the dosage of 1.000 mg/m^2 on days 1, 8 and 15, repeated every 28 days. Twenty-four to seventy-two hours after each administration, the patient noticed dark urine. Urine examination was negative for the presence of blood or biliary pigments. Before the second chemotherapy cycle, the assay for total urinary porphyrins was within normal values (78 µg/l, normal range 50–200 µg/l). A new assay performed on urine collected 48 hours after the first administration of the second