S1. THE ASSOCIATION BETWEEN TAMOXIFEN AND UTERINE CARCINOSARCOMA

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Background: Sarcomas of the uterus have been viewed as rare. Previously known as Malignant Mixed Mesodermal Tumour (MMMT), the preferred term is now carcinosarcoma (CS).
Obesity, unopposed oestrogen exposure and Tamoxifen have all been associated with epithelial endometrial carcinomas. The literature has been scanty in its mention of endometrial carcinosarcomas developing in patients treated with Tamoxifen.
The first National Surgical Adjuvant Breast and Bavel Project (NSABP) report [1] did not make specific mention of an increased incidence of uterine CS in their cohort of patients, although does note an increased incidence of endometrial cancer in patients taking Tamoxifen for breast cancer. The most recent update from the NSABP, looking at more than 17 000 women in a number of NSABP trials [2] does report an increased risk of CS. Bergman again reports only a few cases [3]. There have also been a number of small case series and reports, the largest including 7 cases [4].
Prompted by our own experience and new data emerging regarding the common aetiology of endometrial carcinosarcomas and carcinomas, we decided to review our past four years of experience.
Patients methods: Nearly 100 cases (91) of endometrial /cervical carcinosarcoma, endometrial stromal sarcoma and leiomyosarcoma have been registered with the West of Scotland Gynaecological Cancer Managed Clinical Network (MCN). All newly diagnosed cases are reported to the MCN. We are confident that this represents a very high, if not total, representation of all uterine sarcomas treated in the West of Scotland in the past four years. Basic demographic data were collected on these patients including age. In addition, a previous history of malignancy, or any prior exposure to pelvic irradiation (as might have been used to induce a radiation menopause) was recorded. From this group, 19 patients with a history of breast cancer were identified and their case notes reviewed.
Results: Of these 19 patients, 17 had a history of Tamoxifen exposure and were examined further.
Their average age was 66 years (range 54–78 years) at the time of their breast cancer being diagnosed, and 75 years (range 63–85 years) at the time of their CS being diagnosed. 16 patients had a uterine CS and one cervical. Nine patients had stage 1/2 disease and eight stage 3/ 4.
Average length of time between commencing Tamoxifen and diagnosis of CS (latency period) was 8.8 years (range 2–15 years). The median length of time between stopping Tamoxifen and the diagnosis of CS was 38 months in 12 patients (range 3–72 months), not known in 2 patients, and in 3 patients Tamoxifen was stopped at the time of diagnosis of CS.
Average duration of Tamoxifen use was 6.1 years (range 5–10 years) in 14 patients. One patient had 2 phases of exposure to Tamoxifen. In two patients, precise details were unavailable. All patients received 20 mg of Tamoxifen daily for the duration of their time on it, with the exception of one patient who received varying doses for 8 years. No patient had a history of prior pelvic irradiation. One patient had a previous history of melanoma, but no details were available.
Current follow-up data were available for all patients. One patient is still undergoing treatment, in 16 others; the median length of follow-up was nine months (range 2–22 months). Of these, 12 patients have died (11 of their disease, 1 from causes unclear). 5 are alive; 1 is undergoing palliative chemotherapy, 2 have liver metastases (1 from breast cancer, 1 from CS), and two are disease-free.
The prevalence of other second malignancies in the series of patients with a diagnosis of uterine CS was also noted. 2 patients had a prior history of bladder cancer, 1 ovarian carcinoma, 1 head and neck malignancy, 1 Non-Hodgkin's lymphoma, and one cervical intra-epithelial neoplasia grade 3. One patient had a history of artificial radiation menopause (ARM) 20 years previously for the treatment of menorrhagia.
Discussion: It appears that the association between breast cancer, treatment with Tamoxifen and CS, is perhaps stronger than previously appreciated, and the latency period between starting Tamoxifen and developing CS longer (8.8 years). The importance of clinicians being alert to such diagnoses is thus emphasised and a need for surveillance programmes longer than are currently practiced in most areas is suggested.

References

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