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# Fatal Toxic Epidermal Necrolysis during Suramin Therapy

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SURAMIN IS under investigation as a treatment of advanced malignancy, such as metastatic prostate cancer, relapsed nodular lymphoma and adrenocortical carcinoma [1–4].

Armand [5] stated that "although the activity of suramin is shortlived and mainly biochemical, it is encouraging evidence of the development of a new approach to cancer therapy". However, a limiting factor in treatment is toxicity, a narrow therapeutic window and a highly variable individual response.

We report the case of a 53-year-old woman who developed toxic epidermal necrolysis shortly after introduction of suramin therapy. The patient was referred to our hospital with metastatic adrenocortical carcinoma. At diagnosis 3 months earlier, the primary tumour had a diameter of 12 cm, and there were metastatic lesions in the liver and enlarged para-aortic lymph nodes. Testosterone and cortisol were elevated and not suppressible by dexamethasone. Primary treatment consisted of resection of the tumour mass together with the involved lymph nodes. Radiotherapy was not used. The patient received aminoglutethemide for 1 month, then mitotane. However, the disease progressed.

On referral, the patient was in good condition. A suramin loading-dose of 9.6 g was given over the next 16 days. A transient erythematous rash and a mild sterile phlebitis at the injection site on the left arm were observed. Laboratory results were normal and the patient was discharged. As an outpatient she received weekly maintenance therapy with 700 mg/m$^2$ suramin as intravenous infusion. Suramin concentrations were between 179 and 246 μg/ml. During the third week of maintenance therapy, she developed an extensive rash and was re-admitted to our hospital. The onset was sudden, with eruption of urticarial plaques and erythema of the neck. Clear bullae appeared and became confluent with extreme congestive erythema and purpura. The epidermis came off in large sheets. The day after admission, the patient developed acute respiratory distress due to a mucous plug in the upper airways and cardiopulmonary resuscitation was necessary. Orotracheal intubation was difficult because of extremely oedematous mucous membranes. The patient died the same day in cardiac arrest. The drug implicated as a causative agent was most probably suramin, since the permanent medication consisting of nifedipine, clonidine and captopril had not been changed for years.

Low-grade fever, keratopathy, leukocytopenia and lymphocytopenia, thrombocytopenia, severe neurotoxicity, kidney toxicity, liver dysfunction, adrenal insufficiency and coagulation problems have been described after suramin administration. A transient erythematous rash is commonly observed. Non-fatal exfoliative dermatitis has been described in 3 patients treated for trypanosomiasis [6]. Measurement of plasma suramin levels during treatment, aiming at concentrations between 200 and 300 μg/ml, have been recommended to limit toxic effects [7].

Our case highlights the toxic potential of suramin, since even therapeutic plasma levels did not prevent the fatal outcome. Suramin should only be used within well documented, prospective trials. Patient eligibiltiy must be restricted to cases of advanced malignancy after conventional treatment has failed.

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# Terminal Stages of Breast Cancer: Changes in Clinical Practice

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PREVIOUSLY we reported the extent of diagnostic examinations and treatment of all breast cancer patients who were residents of the Tampere University Central Hospital District and who were near death [1]. The frequency remained the same for examination, but increased for treatment of terminal patients compared to patients with recurrent disease, but not, however, in actual terminal stages. We concluded that the patient's quality of life would improve and resources would be conserved with less frequent examinations and treatment, without shortening the patient's life. Here we report on the change in clinical practice after the results of the previous study were published [2] in the central hospital oncology clinic where most of the resident patients were followed up.

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Four groups of patients were compared—group A: death in September 1987–1988 and last visit less than a week before death; group B: death in September 1987–1988 and last visit more than a week before death; group C: death in 1977–1985 and last visit less than a week before death; and group D: death in 1977–1985 and last visit more than a week before death.

Among the patients who died in 1987–1988 more than a week after the last visit (Group B), the type and intensity of examinations was similar to the earlier period (Group D). Substantially fewer examinations were made on patients who died in 1987–1988 a week or less after the last visit (Group A). The decrease (Group A vs. C) in both roentgenological examinations and clinical tests was statistically significant (Table 1).

Most of the treatment was cancer-related and only relatively seldom was there recorded any treatment for physical discomfort related to the patient herself. In the more recent period, the overall treatment intensity was somewhat less than earlier. A statistically significant decrease occurred in the prescription of chemotherapy for the patients who died a week or less after the last visit (group A vs. C) (Table 1). This decrease was partially compensated for by an increase in palliative treatment for relief of discomfort of the patient such as aspiration of ascites or fluid from the pleural cavity.

It can be argued that rare incidences of prolonged survival in selected patients and the unpredictability of the terminal stages of cancer motivate frequent examinations and treatment.

We found earlier that only 3 of the 54 patients who died a week or less after the last visit were likely to benefit from the examinations [1]. Chemotherapy is known to frequently cause side-effects, and it will not prolong average survival time at this stage [3–5]. All patients suffer from side-effects, and if some patients have their lives prolonged, others must have theirs shortened in order to leave the average unchanged. Therefore, the hope of prolongation is not based on well-established evidence, and any policy based on such a hope will not counterbalance the detrimental effects of chemotherapy.

No major changes occurred in the distribution of treatment among patients who died more than a week after the last visit (Groups B and D). However, there was a change from chemotherapy to other treatment aimed at relief of discomfort among patients who died a week or less after the last visit (Group A vs. C). Also, examinations at the terminal stage became fewer. The results therefore demonstrate that the terminal stages of breast cancer were adequately predictable.

The results also demonstrate that there are grounds for substantial and rapid changes in clinical practice. The reasons for such changes can not be fully identified. The results of the previous study were originally reported in Finnish in August 1987 [2]. The report itself obviously stirred some discussion on diagnostic procedures and treatment practices. In 1987–1988 Finland's first hospice was designed and built in Tampere. The general idea of the hospice may have changed general attitudes. The hospice itself did not directly influence the results: only 3 patients died in the hospice, all surviving more than a week after admission.

The instigation of treatment which proves unsuccessful may be the wish of the patient, relatives, nurse, doctor or other physicians, or it may be a consequence of a threat of legal action [6]. Reduction in the use of high technology in medicine has been proposed on the basis of economic constraints [7, 8]. No critical new scientific evidence on survival of patients with metastatic breast cancer appeared within this period, nor were there any changes in resources or economic constraints in the clinic. The changes in clinical practice are probably attributable mainly to changes in value judgements of the doctors responsible for the treatment of the terminal patients.

*Table 1. Number (%) of examinations and treatments measured at the last follow-up visit of patients who died from breast cancer at the Tampere University Hospital in 1977–1985 and in 1987–1988*

| | Death ≤7 days after visit | | Death >7 days after visit | |
|---|---|---|---|---|
| | Group A 1987–88 ($n$ = 24) | Group C 1977–85 ($n$ = 50) | Group B 1987–88 ($n$ = 22) | Group D 1977–85 ($n$ = 94) |
| Diagnostic examinations | | | | |
| X-rays | 7 (29) | 37 (74) | 14 (64) | 63 (67) |
| Clinical tests | 14 (58) | 46 (92) | 18 (82) | 78 (83) |
| Isotopes | – (–) | 2 (4) | 1 (5) | 4 (4) |
| Other | 1 (4) | – (–) | 1 (5) | 6 (6) |
| Treatment for cancer and physical discomfort | | | | |
| Chemotherapy | 1 (4) | 17 (34) | 5 (23) | 28 (30) |
| Hormonal therapy | 19 (79) | 41 (82) | 13 (59) | 72 (77) |
| Surgery | – (–) | – (–) | – (–) | 4 (4) |
| Radiotherapy | 1 (4) | 1 (2) | 3 (14) | 12 (13) |
| Physical discomfort | 8 (33) | 9 (18) | 4 (18) | 15 (16) |


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# Correction

**Fotemustine with or without dacarbazine for brain metastases of malignant melanoma.**— In this article by Dr O. Merimsky *et al.* (Vol. 27, 1066), references 3–4 were omitted from the reference list. They are:


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