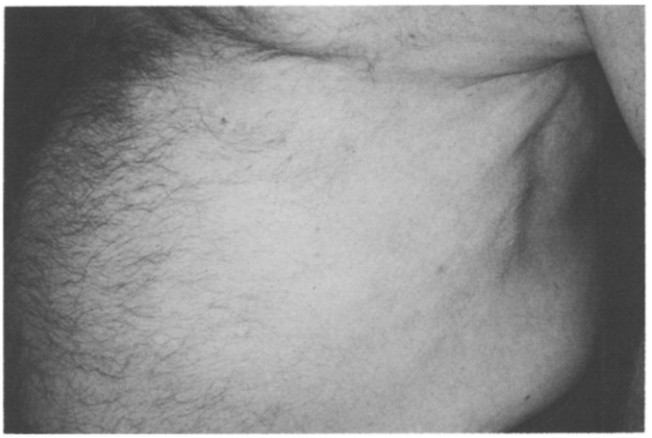

Fig. 2. Complete remission after intralesional rIFN-α2a (January 1993).

used in the treatment of cutaneous T-cell lymphomas (CTCL) systemically [5, 8]. Intralesional rIFN-α also has a beneficial effect in early plaque stage CTCL (mycosis fungoides) [8, 9]. More recently, intralesional rIFN-γ and rIL-2 have been reported to be effective in CTCL [8, 10]. B cell neoplasms are also potential targets for IFN [7], and our case demonstrates the efficacy of local rIFN-α2a in CBCL. In the study of 83 CBCL of Santucci and colleagues [3], 1 case of PR after rIFN-α2b has been reported.

Our case also illustrates the problem of differentiation between pseudolymphoma (such as lymphocytoma cutis and Jessner's lymphocytic infiltration) and malignant skin infiltrates [1, 3]. In the literature, CR of a B cell cutaneous pseudolymphoma treated with intralesional IFN-α has been reported [11].

The lack of extracutaneous spread of CBCL justifies the choice of non-aggressive therapy [2]. Remissions can usually be achieved repeatedly with local irradiation. EBRT proved to be the most suitable treatment for both initial lesions and relapse to the skin [2, 3]. Intralesional administration of rIFN-α may be given safely and can lead to a remission of CBCL in heavily pretreated patients, if local EBRT is not more possible. Large series and longer follow-up are required to confirm the precise role of IFN-α in CBCL.

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Escape Phenomenon After Successful Bromocriptine and Octreotide Treatment in Thyroid Stimulating Hormone Secreting Pituitary Adenoma Residual Tissue

G. De Rosa, A. Testa, D. Giacomini and C. Carrozza

WE REPORT the case of a 63-year-old male with thyroid stimulating hormone (TSH) secreting pituitary adenoma in which bromocriptine and octreotide were temporarily effective.

The patient had a goiter and hyperthyroidism and was treated with thyrostatics from 1965 to 1979 without improvement.

In 1979, laboratory data confirmed thyrotoxicosis with radioimmuno assay (RIA) TSH levels ranging from 5.2 to 16.7 μU/ml. Skull tomography revealed a hypophyseal adenoma, with invasion of the sphenoidal area, which was removed transphenoidally.

TSH levels stabilised around 3 μU/ml but thyrotoxicosis persisted and thyroidectomy followed by radioiodine was performed. The patient was euthyroidal with oral levothyroxine (L-T4) (1.8 μg/kg/day) but TSH did not fall below 8 μU/ml. Bromocriptine was administered with success but an escape phenomenon arose after 3 months (TSH 16 μU/ml). Cranial computerised tomography (CT) (magnetic resonance imaging was impossible because of metal clips attached after surgery) revealed tissue in the sphenoidal area. A 24-h TSH assay demonstrated an absence of cyclicity with high night levels and no inhibition after triiodothyronine (T3). The α subunit/TSH ratio (10.2) was elevated. A single 0.1 mg subcutaneous (s.c.) dose of octreotide followed by TSH immunoradiometric assay (IRMA) every hour for 8 hours showed a decrease in TSH levels from 13.9 to 9.7 μU/ml. Continuous adminstration (0.1 mg s.c./8 h for 5 days) produced a decrease in TSH levels from 13.9 to 0.7 μU/ml.

After 2 months of octreotide administration IRMA TSH levels became persistently high (4 μU/ml). The voluntary suspension of therapy by the patient brought TSH levels back to the initial concentrations (23 μU/ml). We resumed octreotide therapy but the TSH levels remained high.

Euthyroidism obtained with L-T4 and no TSH suppression with T3 administration exclude elevated TSH levels as compen-

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sation of hypothyroidism. The following evidence supports a neoplastic TSH origin: (a) an elevated α subunit level [1]; (b) residual intrasphenoidal tumour; (c) absence of 24 h TSH cycle.

Cases of TSH-secreting adenoma, in which bromocriptine or octreotide produce a persistant decrease in TSH and α subunit secretion, have been reported [2–7]. The octreotide escape phenomenon has been reported in cases with ectopic adrenocorticotropic hormone [8]. In our case, the escape phenomenon could be due to the disappearance of sensitive receptors present on the TSH-secreting adenoma [9,10] or to the presence of different cell clones with a different sensitivity to inhibition by somatostatin and/or bromocriptine.

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Mitoxantrone, 5-Fluorouracil and Levo-leucovorin as Salvage Treatment in Advanced Breast Cancer Patients

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THE USE of combination chemotherapy in the treatment of advanced breast cancer produces objective responses in 60–80% of patients, with complete remission in fewer than 30% [1].

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The probability of obtaining objective responses with second-line treatment ranges from 10 to 35% [2]. At present, optimal therapy for most patients consists of maximising response rate while limiting drug-induced toxicity.

We report the results of a phase II study with mitoxantrone, fluorouracil and leucovorin in 49 patients with metastatic breast carcinoma [3–6].

Eligibility criteria included ECOG performance status ≤ 2, adequate white blood cell and platelet cell count, adequate cardiac, renal and hepatic function and expected survival of longer than 12 weeks. Chemotherapy consisted of mitoxantrone 10 mg/m^2 intravenously (i.v.) on day 1, levo-leucovorin 250 mg/m^2 administered over 2 h and 5-fluorouracil 500 mg/m^2 i.v. push after the first hour of leucovorin infusion on days 15 and 16, i.e. the period of presumed neoplastic repopulation. This combination could emphasise the potential additive effects of the agents while avoiding overlapping toxicities. Courses were repeated every 28 days. Informed written consent was obtained from all patients.

Patients who received at least three cycles of treatment were evaluable for response. All patients were analysed for toxicity. 48 patients completed three or more courses of treatment and were assessable for response and toxicity. The remaining patient received only two cycles of therapy and refused further treatment; this patient was not evaluable for response. Patients' characteristics are shown in Table 1; it is noteworthy that 22/49 (44.9%) patients were aged more than 65 years. 20 patients received prior adjuvant therapy; 23 patients received mitoxantrone, leucovorin and 5-fluorouracil as the front-line regimen while 25 were pretreated with antracycline- based chemotherapy for metastatic disease.

A median number of six courses (range 2–11) were administered. Objective responses were observed in 18/48 patients (38%), in particular, 1 patient with soft tissue metastases achieved complete response and she is currently disease-free; 22/48 patients (46%) had stable disease while 8 (16%) progressed. Response rate was analysed according to prior treatment with or without anthracyclines. No difference was observed between the two groups.

Median response duration was 8 months (range 2–28); median survival was 13 months (range 3–33); to date, 23 patients have died, 1 of these without evidence of disease. The regimen was well tolerated with only 1 patient presenting with grade III leucopenia who did not require hospitalisation. No grade III–IV non-haematological toxicities were recorded.

Our results are comparable to the response rate reported in the literature with second-line regimens [2], although Hainsworth and Jones [7, 8], using the same drugs with different schedules, observed better results. Perhaps patient selection may explain the difference in response rates achieved in these trials. The present study suggests the use of this safe and well-tolerated combination as second-line treatment in metastatic breast carcinoma.

Table 1. Patients' characteristics

No. of patients	49
Median age (years)	63 (range 42–79)
Median performance status	0 (range 0–2)
Site of metastases	
Soft tissue	25
Bone	31
Viscera	29