

## Extravasation of Vincristine

### Extravasación de vincristina

To the Editor:

Extravasation is an infrequent but potentially serious complication of the administration of chemotherapeutic agents. Depending on their capacity to produce tissue damage, cytostatic agents can be classified as: nonaggressive agents, which are harmless, and can even be safely administered intramuscularly; irritants, which cause irritation and minimal necrosis; and vesicants, which cause necrosis if extravasation occurs.<sup>1</sup>

Extravasated vesicants produce a mild initial reaction and, after a few days, a delayed onset of changes characterized by pain, erythema, and necrosis that can affect deep structures. The vesicants include vincristine, an antitumor alkaloid extracted from *Vinca rosea* Linn with a narrow therapeutic range (the minimum effective and toxic plasma levels are similar). Neurotoxicity is the main limiting factor. Vincristine exerts its cytotoxic effects by interfering with the microtubules that form the mitotic spindles during metaphase, thereby interrupting the cell cycle and inducing tissue necrosis. Vincristine must only be administered parenterally. Its indications include acute lymphatic leukemia, Hodgkin disease, and breast cancer.

We report the case of a 62-year-old woman with Hodgkin disease on chemotherapeutic treatment with cyclophosphamide, adriamycin, and vincristine. During vincristine administration, extravasation occurred in the dorsum of her left hand; this was treated immediately by the application of cold, heat, and topical hyaluronic acid. The next day the patient came to our outpatient clinic urgently on account of an erythematous lesion with superficial erosions on the dorsum of the same hand, accompanied by edema of the arm (Figure 1). We prescribed fusidic acid and betamethasone cream, and some improvement was observed after 2 days. A week later the patient returned to the clinic because the lesion on her hand had worsened following the latest infusion in her chemotherapy regimen. Examination revealed significant edema of the patient's left hand with intense erythema on the dorsum of the hand, and a necrotic scab in the center of the lesion. A deep, foul-smelling ulcer with a fibrin-covered base was observed on lifting the crust (Figure 2). Culture of the base was positive for *Pseudomonas aeruginosa*. We prescribed treatment with oral ciprofloxacin and fusidic acid to be applied as a cream once a day. The lesion had almost completely reepithelialized by the next consultation.

Extravasation is a rare complication of the administration of chemotherapeutic agents. Its incidence varies between 0.1% and 6%,<sup>2</sup> and the effects can be potentially serious in some cases. It is important to take preventive measures as follows: avoid using peripheral routes for prolonged infusions; use normal saline to confirm viability of the system before administration; use a method that allows venous return to be observed; avoid the insertion of catheters in areas adjacent to joints; and, naturally, ensure continuous supervision of the patient by specialist staff. Immediate attention is required if extravasation



Figure 1 Erythematous lesion with superficial erosions on the dorsum of the left hand.



Figure 2 Deep ulcer with a fibrin-covered base.

occurs. The European Oncology Nursing Society, in its protocol published in 2007,<sup>3</sup> recommended the following procedure for extravasation of a cytostatic vesicant such as vincristine: stop administration immediately; withdraw the cannula; aspirate the drug; raise the affected limb; mark the site of extravasation; and apply dry heat for 20 minutes, and, if possible, topical or intralesional hyaluronic acid. Surgical debridement should be reserved for cases with confirmed tissue necrosis or persistent pain.<sup>4</sup>

## References

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## Rapid Increase in Incidence of Melanoma In Situ in Girona (Spain), 1994-2005. Effectiveness of Public Education Campaigns About Early Diagnosis

### Rápido incremento de la incidencia del melanoma in situ en Girona (España) 1994-2005. ¿Efectividad de las campañas de diagnóstico precoz?

*To the Editor:*

In recent decades, the incidence of invasive cutaneous melanoma has risen considerably in white populations, with annual increases ranging from 3% to 7%.<sup>1</sup> While Spain still has one of the lowest incidence rates and levels of mortality in Europe for this disease,<sup>2,3</sup> recent studies also reflect an increase in this country.<sup>4</sup> However, there is no epidemiologic data on the incidence in Spain of melanoma restricted to the epidermis, that is, melanoma in situ (MIS).

To obtain more information about the epidemiologic trends and incidence of MIS, we analyzed the data provided by the Girona Cancer Registry, a population-based registry covering the province of Girona with an at-risk population of 687 331 according to the 2006 census.

We calculated crude and age-adjusted incidence rates standardized to the world standard population using the direct method. Using the joinpoint regression model we estimated the annual percentage change (APC) in the incidence of MIS over the 12 years of this study (1994-2005).<sup>5</sup> Differences in MIS trends by sex were studied using the t test for the variable age and the  $\chi^2$  test for the categorical variables.

In total, 688 patients resident in the province of Girona were diagnosed with cutaneous melanoma between 1994 and 2005. The diagnosis was invasive melanoma in 550 cases (79.94%) and MIS in 138 (20.06%). All the cases analyzed were confirmed histologically. Of the 138 patients with MIS, 84 (60.9%) were women (mean age at diagnosis, 62.96 years; range, 22-92 years), while 54 (39.1%) were men (mean age, 61.20 years; range, 25-88 years). There were no statistically significant differences between the sexes. The most common sites were the head and neck (42.8%) followed by the trunk (22.5%). The distribution by sex was not statistically significant ( $P=.20$ ). Histology

results revealed that approximately 60% of cases were lentigo maligna. This group of patients had a mean age at diagnosis of 69.2 years (Table 1), significantly older than the mean age of the other histologic groups (data not shown).

In men, the incidence of MIS increased from 0.54 cases per 100 000 man-years in the period 1994 to 1996 to 1.44 cases per 100 000 man-years in the period 2003 to 2005. This trend was even more marked among women, with an increase from 0.68 cases per 100 000 women-years in the period 1994 to 1996 to 2.23 cases per 100 000 women-years in the period 2003 to 2005. During the 12 years covered by this study, the increase in the incidence of MIS in our region has been much greater than the increase in invasive melanoma.<sup>4</sup> The annual percent change was 11.51% for men (95% confidence interval [CI], 4.61-18.86) and 11.43% for women (95% CI, 2.04-21.69) (Table 2).

Population-based epidemiologic studies on the incidence of MIS are rare, and to date only 4 studies have been published (Sweden 1968-1992,<sup>6</sup> Southern Australia 1981-1992,<sup>7</sup> United States of America [US] 1975-1997,<sup>8</sup> and Queensland [Australia] 1982-2002<sup>9</sup>). All of these studies reported a substantial annual increase in the incidence of MIS (around 10%), a finding consistent with our result (11%).

It is important to highlight the fact that the patients in our population diagnosed with MIS were some 3 years older than the patients with invasive lesions (data not shown), a finding similar to that reported in the US study, in which the age difference was 4 years.<sup>8</sup> The older age at diagnosis of MIS in our population can be explained by the fact that the predominant histologic type of MIS lesion was lentigo maligna, a melanoma that primarily affects exposed areas (head and neck) in older patients.<sup>10,11</sup>

There is no doubt that the public is now better informed about the risks of exposure to the sun. This greater awareness, in conjunction with early detection campaigns (such as Euromelanoma Day started in 2000 by the European Academy of Dermatology<sup>12</sup>), improved access to health care, and the more frequent excision of suspicious pigmented lesions,<sup>13</sup> may have contributed to the increase in the incidence of MIS.

Monitoring trends in melanoma by stage will make it possible in the future to evaluate the effectiveness of cutaneous melanoma prevention campaigns in Spain. Consequently, there is a need to include more information concerning the diagnostic characteristics of the cases of cutaneous melanoma in Spanish population-based cancer registries.