

## Breast carcinoma and primary skin carcinomas of the vulva and the back: a possible association with arsenicism

AMOS PINES<sup>1</sup>, MD, EHUD J. MARGALIOH<sup>2</sup>, MD, ENRIQUE Z. FISMAN<sup>1</sup>, MD

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**Unitermos:** Mama — Câncer. Pele — Câncer. Vulva — Câncer. Arsenismo

**SUMMARY** — Various cancers of the skin might develop following chronic ingestion of arsenical medications. The possible association of malignancies of internal organs with chronic arsenicism has also been discussed in the literature. We report a woman who was treated by Fowler's solution when young and 20 years later suffered from 3 different carcinomata — invasive ductal carcinoma of the breast, metastatic squamous cell carcinoma of the vulva and intraepidermal carcinoma of the back. To the best of our knowledge, breast carcinoma has never been reported in this context and there has been only one other description of carcinoma of the vulva related to chronic arsenicism.

### INTRODUCTION

Fowler's solution, an arsenic medication [potassium arsenite,  $KAsO_2$ ], has been used extensively up to the middle of this century in the treatment of various pulmonary, hematologic and neurologic disorders<sup>(9)</sup>. Particularly it was prescribed for the treatment of cutaneous diseases such as psoriasis and lichen planus<sup>(3)</sup>. The first report of the association between arsenicals and skin cancer was published 150 years ago and this was reconfirmed by Hutchinson some 100 years ago<sup>(8)</sup>. Since then, a large number of patients have supported these observations, that chronic arsenical ingestion leads to the development of precancerous as well as malignant skin tumors<sup>(18)</sup>. Recently, a possible association with internal malignancies was suggested as well<sup>(3)</sup>. We hereby describe a patient who was treated at youth with Fowler's solution, and some 20 years

later suffered from three different tumors—metastatic squamous cell carcinoma of the vulva, intraepidermal carcinoma (Bowen's disease) of the back and breast carcinoma.

### CASE REPORT

A 41 year old woman was admitted for biopsy of vulvar skin lesion. When young she had been suffering from severe asthma, and had been treated with Fowler's solution for more than two years. At the age of 40 years the patient underwent right radical mastectomy because of invasive duct carcinoma. A year later an intraepidermal carcinoma (Bowen's disease) was excised from her back. At the same time, another skin lesion was observed by the patient on her labia majora, but no actions were taken by the patient to identify its nature.

Except for a reddish ulceration, measuring 5mm in diameter, which was located on the left labia majora, there were no other abnormal findings on physical examination. Routine blood tests, chest radiogram, intravenous pyelogram, liver and bone scans — were all nonrevealing. Biopsy of the lesion demonstrated squamous cell carcinoma. The patient refused radical vulvectomy, thus a wide excision of the tumor and dissection of the local lymph nodes was performed. Metastatic well differentiated squa-

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1. The Department of Medicine F, Sheba Medical Center and Sackler School of Medicine, Tel Aviv University.
2. The Department of Obstetrics and Gynecology, Hadassah University Hospital, Jerusalem.

Correspondence to: Amos Pines, MD, Department of Medicine F, Sheba Medical Center, Tel Hashomer 52621, Israel.

mous cell carcinoma was identified in enlarged inguinal nodes only 3 months after operation. The area was irradiated and currently the patient is under the surveillance of the oncologists.

## DISCUSSION

Arsenic may enter the body in several ways<sup>(3)</sup>: (a) through contaminated well-waters in endemic areas<sup>(18)</sup>; (b) environmental pollution [paint and dye industries, pesticides, rat poisons]<sup>(10,11)</sup>; (c) therapeutic or malicious use of arsenic medications. Continuous ingestion of small doses of arsenicals for long periods may cause signs of poisoning. The skin is usually the first to be involved. The dermal manifestations of chronic arsenicism include dryness of the skin, dermatitis, pigmentation, keratinization, loss of hair and nails and various forms of skin cancers. A total dose of Fowler's solution (potassium arsenite) exceeding 400ml provoked keratoses in about 50% of subjects, who were using this quantity of the drug<sup>(4)</sup>. On the other hand, a smaller dose of 75ml was reported to be the cause of skin cancer<sup>(4)</sup>. The latent period for the development of cancer is usually 20 to 30 years or more. The arsenical cancers of the skin are usually located on unexposed parts of the body<sup>(18)</sup>, in contrast with ordinary skin cancers which mainly involve the exposed areas, such as the face, lips, neck and dorsal aspects of hands and forearms.

Individual susceptibility to the arsenical carcinogenic effect was suggested by many authors and may give reason to the relatively early age at which the vulvar lesion appeared in our patient. Bettley and O'Shea<sup>(2)</sup> hypothesized that patients with arsenic induced skin cancer remove the arsenic more rapidly from the blood and store it in certain tissues, mainly in the skin.

Intraepidermal carcinoma (carcinoma in situ, Bowen's disease) is the most typical arsenical induced skin cancer. In fact, arsenical exposure is definitely the cause of many cases of Bowen's disease. Only 5% of these lesions become invasive and 2% metastasize; therefore

one of the following possibilities has to be considered regarding our patient: either she suffered from 2 different histologic types of skin cancer from the beginning or that she had Bowen's disease at the vulva which later transformed into metastatic squamous cell carcinoma. Arsenical induced cancer of the vulva is rare. In the survey of Yeh, How and Lin<sup>(18)</sup>, in a total of 238 arsenical skin cancers in 153 patients, there was only one woman with squamous cell carcinoma of the vulva.

The association of Bowen's disease and tumors of internal organs was well documented<sup>(6,12)</sup>. In fact, Bowen's disease is regarded as a risk factor for the future development of various malignancies. Despite the close relation between Bowen's disease and arsenicals, the possible association between arsenical exposure and carcinomata of internal organs is somewhat less convincing. There have been some reports upon higher incidence of lung cancers in areas with airborne pollution of inorganic arsenicals<sup>(5)</sup>, and there were also single case reports on liver<sup>(15)</sup>, nasopharyngeal<sup>(13)</sup>, colonic<sup>(17)</sup>, bladder<sup>(1)</sup>, lymphatic tissue<sup>(17)</sup>, and lung<sup>(7,16)</sup> tumors in patients who had been treated by Fowler's solution. To the best of our knowledge, our case is the first report of breast carcinoma related to arsenicals.

It should be mentioned, however, that the statistical significance of the presumed link between arsenicals and non-dermal tumors was challenged in two large studies<sup>(3,14)</sup>. Nevertheless, those patients who actually developed arsenical keratoses and other skin lesions, did have a higher risk of contracting cancers of internal organs.

Although common statistics suggest that in 2-4% of all patients who have one cancer, a second unrelated malignancy may develop, but we presume that the breast carcinoma and the multiple skin cancers were associated with past history of prolonged use of arsenicals.

The possible grave prognosis of these arsenical late effects stresses the need for careful periodical examinations in each subject with a history of chronic arsenicism.

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