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Squamous cell carcinoma antigen elevation in cervical cancer follow-up: the forest hiding the tree

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Summary

Background: The measurement of squamous cell carcinoma antigen (SCC) levels is part of usual follow-up in epidermal cancers, such as epidermal cervical cancers of the uterus. Numerous benign and malign diseases and particularly skin disorders can also create an elevation of SCC. *Objective:* In this article the authors describe benign diseases leading to an SCC elevation, being able to mislead the physician during follow-up of a patient with a history of epidermal carcinoma. *Materials and Methods:* The authors describe two cases of patients having suffered a cervical cancer being suspected to have a recurrence after finding elevated SCC-levels. Both patients presented a personal history of psoriasis. *Results:* Thanks to PET-scan, a recurrence could be ruled out. Several skin disorders have been described to induce an elevation of SCC levels, particularly those affecting the skin-barrier, for example psoriasis. A common criterion is a marked erythema, which may allow an increased penetration of SCC into the blood. *Conclusion:* In case of SCC-elevation in patients followed for a cervical cancer, dermatological disorders such as psoriasis should be excluded.

Key words: Cervical cancer; Parakeratosis; Psoriasis; SCC; Tumor marker.

Introduction

Tumor markers are frequently used to follow cancer patients. While they are often useful, they might sometimes be misleading as they have high sensitivity and low specificity. While pitfalls of tumor markers have been described, the finding of elevated tumor makers during follow-up after primary treatment usually leads to multiple investigations to rule out a recurrence. These investigations beside their cost generate high anxiety in patients and their family. Squamous cell carcinoma antigen (SCC) measurement is used in the follow-up of epidermal cervical cancers. Here the authors describe two cases of cervical cancers presenting with increased SCC: investigation were undertaken to rule out a recurring disease, while the cause of SCC elevation was indeed obvious.

Case Report

Case 1: A 50-year-old female first diagnosed with a FIGO 2A epidermoid carcinoma of the uterine cervix. The patient underwent para-aortic lymphadenectomy for staging and subsequent chemoradiation and brachytherapy. The following radical hysterectomy demonstrated no tumor residue. A year after completion of treatment, SCC antigen was found to be elevated (3.3 µg/l for normal level < 1.5 µg/l). This prompted thorough clinical examination and PET-CT: no abnormality was found. After the routine examinations were performed, the authors noticed that the patient complained about an increase of her already known psoriasis. She had discontinued methotrexate due to elevation of liver enzymes (Figure 1). The psoriasis was treated by UV-therapy and acitretin (retinoid): SCC subsequently returned to normal. The patient has been lost to follow-up for her psoriasis and she interrupted treatment. When seen for her gynaecological follow-up, she presented important psoriatic lesions and again an elevation of the SCC antigen. The last gynaecological examination was normal and there were no signs of recurrence. The last PET-CT showed no metastatic lesions.

Case 2: The second patient is a 57-year-old woman with a FIGO IIB epidermoid cervical cancer. The patient underwent para-aortic lymphadenectomy for staging and subsequent chemoradiation and brachytherapy. No tumor residue was found in the uterus following radical hysterectomy. At six-years' follow up, SCC was found to be increased (2.1 µg/l). The patient's clinical and PET-CT investigation did not show any sign of recurrence. Interestingly she also presented active psoriasis lesions at the moment of the SCC-control (Figure 2).

The patient refused the possible treatments proposed by the dermatologist. An annual control of the SCC antigen and PET-CT were therefore performed. Last SCC control was 1.6 µg/l and therefore slightly above normal. Further controls will be performed.

Discussion

SCC has first been extracted in 1977 from SCCss of the uterine cervix by Kato and Torigoe [1]. This antigen has been observed to increase in SCCs in particular in case of metastatic disease. Sixty-six percent of the patients with

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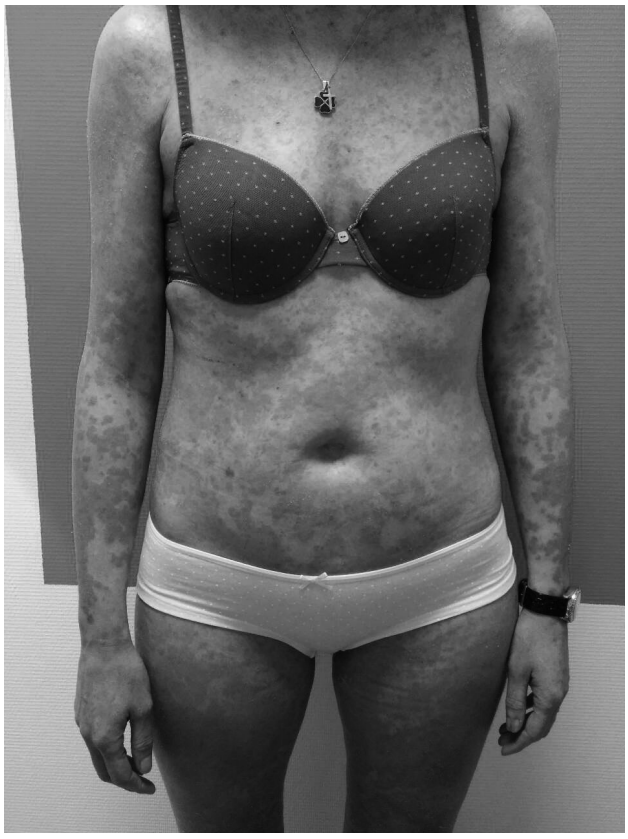

Figure 1. — Active psoriasis in a 50-year-old patient (case 1).

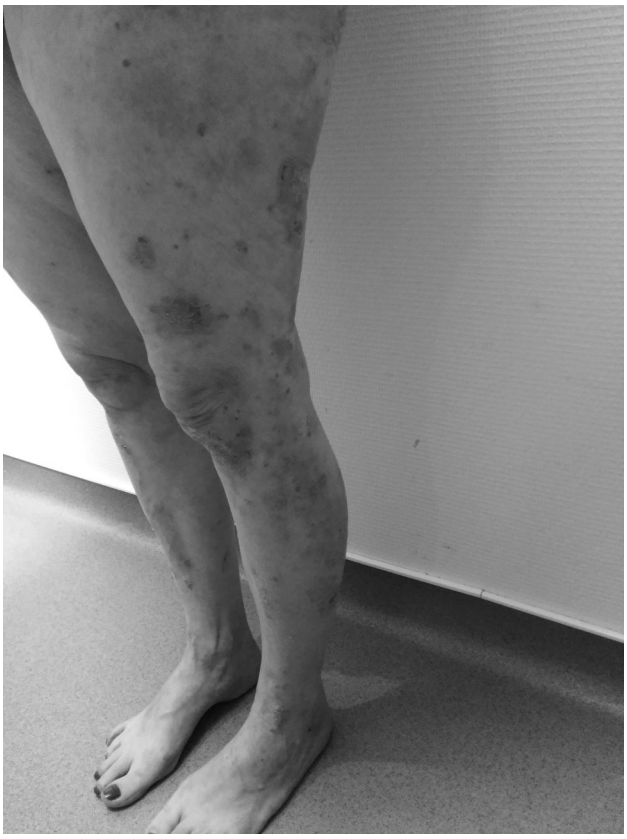

Figure 2. — A 57-year old patient with active psoriasis as described in case 2.

Table 1. — *Diseases causing an SCCA elevation [5].*

Malign diseases
Lung cancer
Esophageal cancer
Cancer of vulva and vaginal areas
Cancers of urothelium and anal canal
Benign diseases
Kidney failure
Dermatologic disorders (atopic dermatitis, psoriasis, pemphigus, erythrodermic dermatitis)
Pulmonary diseases (tuberculosis, bronchogenic cyst, pulmonary infiltration with eosinophilia, sarcoidosis, adult respiratory distress syndrome (ARDS)

cervical cancer showed elevated SCC levels at diagnosis; in 75% of the patients with recurrence, elevated SCC level were found [2].

The detection of SCC-levels is primarily used for the follow-up of epidermoid cancers of the uterine cervix. In 46% to 92% of the cases its elevation seems to precede the clinical diagnosis of recurrence [3]. Following French recommendations, PET-CT is used for restaging in case of a suspected recurrence.

There are other possible sites of epidermoid cancer causing an SCC-elevation, such as the lung, head and neck, and skin cancers [4, 5] (Table 1). There have been studies proving that an SCC elevation is also possible in non-tumoral skin-diseases: an elevation of the SCC in psoriatic patients has first been described in 1977 [6]. SCC is a marker for skin barrier function [7, 8]. The SCC belongs to the serpin-family and two different types are distinguished: SCC 1 and SCC 2. In psoriatic skin we normally find hyperkeratosis and parakeratosis (the persistence of nuclei in the cells of the stratum corneum, the upper skin level) [8]. Katagiri *et al.* found that SCC 1 is always present in parakeratotic skin while it is hardly detectable in normal skin. They suggest that an up-regulation of SCC 1 in inflammatory skin causes a down-regulation of the skin barrier presenting as main feature the parakeratosis.

Benign skin diseases are able to cause an elevation of the SCC level if more than 2% of the skin surface is affected [5]. The SCC levels rise proportionally to the extent of the skin disorder, although they do not seem correlate to the severity of the disease [5, 9]. Nevertheless, more recent studies do find a correlation between the SCC level and the

severity of the skin disorder [10, 11]. Patients with acute inflammatory psoriasis, acutely exacerbated atopic dermatitis due to bacterial infection or with erythrodermic atopic dermatitis, showed markedly high SCC levels [1]. These three skin disorders have as a common finding a marked erythema. The increased blood supply in these tissues may allow a higher SCC-absorption, which can explain the markedly high blood levels. Some authors describe the SCC elevation as a sign of psoriatic disease activity [1]. Interestingly it has been described that SCC levels in patients with psoriasis do decrease when the acute inflammation regresses, but never return to normal values [1].

In the two earlier presented cases, the diagnosis of psoriasis was obvious when SCC was measured. However comprehensive clinical and preclinical examinations was performed to rule out recurrence. While it may be difficult to avoid these examinations, an obvious finding such as psoriasis could help reassure the patients.

Conclusion

Patients having suffered a cervical cancer should continue usual follow-up, including SCC determination and PET-CT scan if a suspicion of recurrence exists. In case of a negative PET-CT scan and an unexplained SCC elevation, there a numerous other disorders to be ruled out. A detailed patient history eliminating any dermatological or pulmonary diseases is fundamental.

In conclusion, it should be remembered that a SCC level determination is not a reliable follow-up of cervical cancers in patients suffering from a skin disorder.

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