

## CASE REPORT

# Post-Traumatic Basal Cell Carcinoma Associated With Patch Testing

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**Abstract.** Basal cell carcinoma is the most common epithelial skin cancer in humans and usually affects elderly individuals. Although the pathogenesis is directly related to exposure to ultraviolet sunlight, other factors, particularly trauma, may be involved. We present the case of a woman with contact dermatitis due to sensitization to metals. She developed superficial basal cell carcinoma at the same site as a patch test—performed 30 months earlier—that was strongly positive to 1% gold chloride. In the histologic study with a scanning electron microscope, we detected electron-dense particles in the dermis which were subsequently identified as gold.

**Key words:** skin cancer, post-traumatic basal cell carcinoma, contact dermatitis, patch test.

## CARCINOMA BASOCELULAR POSTRAUMÁTICO RELACIONADO CON PRUEBAS EPICUTÁNEAS

**Resumen** El carcinoma basocelular (CBC) es la neoplasia cutánea epitelial más frecuente de la raza humana, que afecta generalmente a personas de edad avanzada. Aunque su patogénesis está directamente relacionada con la exposición a las radiaciones ultravioletas solares, también pueden involucrarse otros factores, entre los que destacamos los traumatismos. Aportamos el caso de una mujer con dermatitis de contacto por sensibilización a metales, que desarrolló un CBC superficial en la misma localización en la que tuvo una prueba epicutánea fuertemente positiva al cloruro de oro 1 %, realizada 30 meses antes del desarrollo del tumor. Realizamos un estudio del corte histológico con el microscopio electrónico de barrido, que nos demostró la presencia de partículas electrón-densas en la dermis, que fueron identificadas definitivamente como oro.

**Palabras clave:** neoplasia cutánea, carcinoma basocelular postraumático, dermatitis de contacto, pruebas epicutáneas.

## Introduction

Nonmelanoma skin cancer is probably the most common malignant tumor among white people and usually appears in fair-skinned individuals. At least 900 000 new cases are diagnosed every year in the United States, of which 80% are basal cell carcinomas (BCC) and the remaining 20% are squamous cell carcinoma.<sup>1</sup>

In Spain BCC is the most common skin tumor and its incidence has increased considerably in recent decades, to the point of becoming a major public health problem.<sup>2,3</sup> Although the tumor is malignant, it grows slowly and rarely metastasizes (around 0.1%), which leads to a low local aggressiveness and low mortality.<sup>4</sup>

## Case Report

A 60-year-old woman, nonsmoker, nonuser of alcohol, and allergic to penicillin and its derivatives, was referred to our outpatient clinic in 1999 for a study of recurrent eyelid eczema. The patient had no sun-induced skin lesions and no family or personal history of skin cancer. She denied regular occupational or recreational sun exposure, had no gold dental work, and had never been treated with gold salts.

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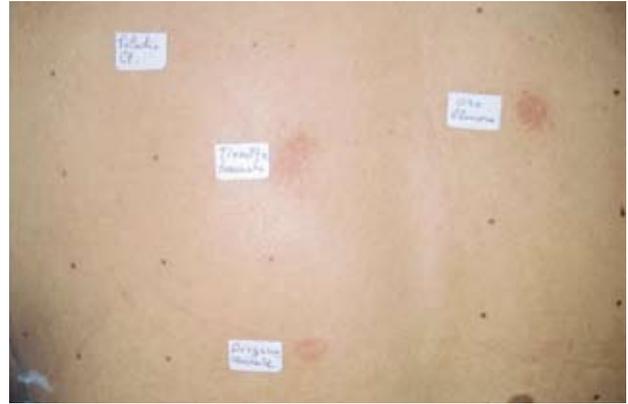
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Additional studies included routine blood tests, protein electrophoresis, thyroid hormones, and immunologic studies (autoantibodies, immunoglobulins, and complement) that were strictly normal. The patient also underwent patch tests with the standard panel of the Spanish Group for Research Into Dermatitis and Skin Allergy (June 1999) and the metal panel (November 1999) with approved allergens supplied by Trolab, Martí Tor, and Chemotechnique Diagnostics. All tests were performed and interpreted according to the recommendations of the International Contact Dermatitis Research Group. The tests showed positive reactions for 5% nickel sulfate (3+), 1% palladium chloride (1+), 0.25% gold sodium thiosulfate (2+), 0.002% potassium dicyanoaurate (2+), and 1% gold chloride (3+) (Figure 1).

The patient was diagnosed with bilateral eyelid eczema due to sensitization to nickel, palladium, and gold metals with positive reactions interpreted as clinically relevant. She was advised to avoid contact with these allergens, and treatment was started with low-potency corticosteroids. The lesions gradually disappeared over 2 weeks and did not recur.

In May 2002 the patient consulted again for a moderately pruritic lesion on her back. Her husband insisted that the lesion was at exactly the same site as the positive patch test reaction to 1% gold chloride in 1999; that reaction lasted longer than 1 month and subsequently she complained of discomfort and slight itching at the site. Physical examination revealed an erythematous lesion with pearly borders and telangiectases and an approximate diameter of 1 cm (Figure 2). We made a clinical diagnosis of superficial BCC and proceeded to its complete resection; the diagnosis was confirmed histologically (Figure 3). General examination showed no solar lentigines, actinic keratosis, or other sun-induced lesions in exposed areas.

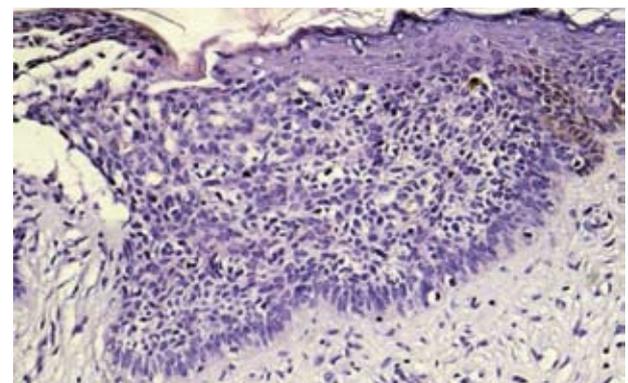
Because the patient had a history of trauma (patch test) and developed a tumor (superficial BCC) and because some studies have reported the presence of gold in the skin of rheumatoid arthritis patients treated with gold salts,<sup>5,6</sup> the histologic specimen was examined under polarized light microscopy (LEICA DM RXP), observing numerous electron-dense areas with an approximate diameter of 1  $\mu$  (Figure 4). X-ray microanalysis (LINK QX-2000) using an electron probe to identify elements according to their specific frequency emission pattern confirmed that the particles in the dermis were gold residues (Figures 5A and 5B); however, no gold precipitate residues were observed in histologic sections taken from the edges of the BCC. The specimen showed a characteristic orange-red birefringence under polarized light, but this could not be photographed.



**Figure 1.** Results of patch tests with the metal panel showing a positive reaction to 1% gold chloride (3+).



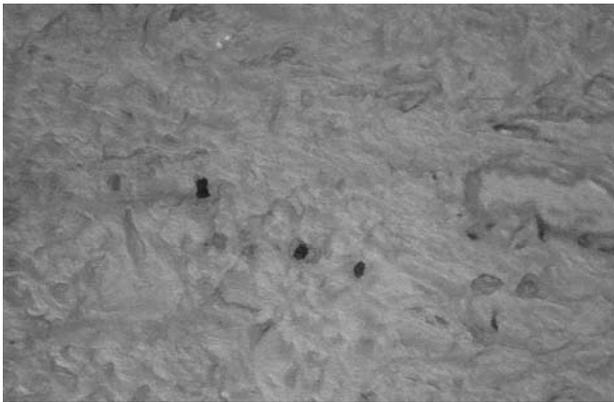
**Figure 2.** Superficial basal cell carcinoma: erythematous lesion with pearly borders and superficial telangiectases. Note that it coincides precisely with the patch application area (the presence of an intradermal melanocytic nevus below the patch area and the basal cell carcinoma is taken as a reference).



**Figure 3.** Nests of basaloid cells originating in the epidermis and arranged in palisade, but with no dermal infiltration (hematoxylin-eosin  $\times 40$ ).

## Discussion

Although the incidence of BCC is high, its etiology is still not clear. The tumor is directly related to ultraviolet radiation (UV) exposure (particularly UVB radiation between 290 and 320 nm), which is presently considered the most important etiologic factor because the cancer is usually found in exposed areas (85% of tumors are found on the head and neck).<sup>7,8</sup> Nonetheless, this does not appear to be the only factor influencing its development.

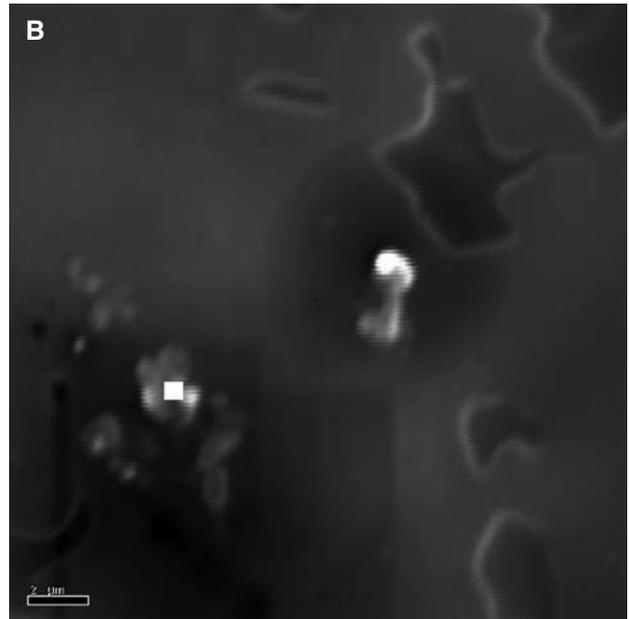
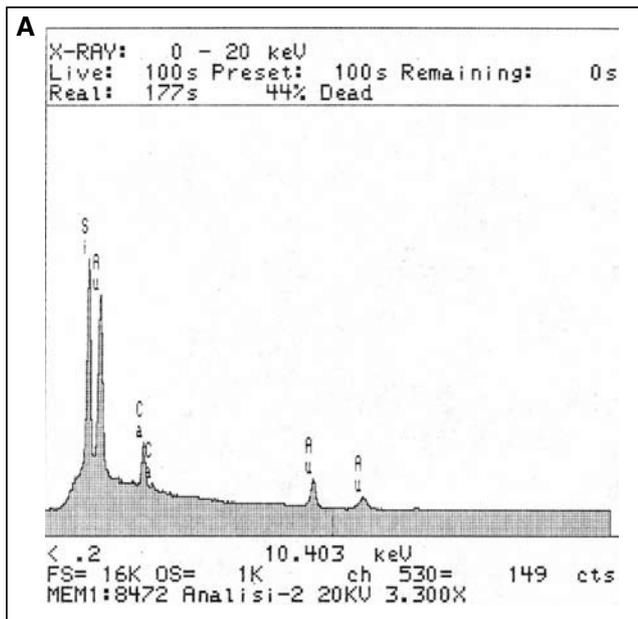


**Figure 4.** Black particles of gold deposited in the dermis of the superficial basal cell carcinoma, seen under polarizing optical microscopy (LEICA DM RXP  $\times 20$ ).

Although excessive sun exposure during childhood and adolescence and a family history of skin cancer are currently considered the main risk factors for this tumor, many environmental factors (in particular, traumatic injuries) also play a key role in the genesis of the tumor.<sup>9,10</sup> BCC has been reported to develop on lupus vulgaris scars,<sup>11</sup> smallpox vaccination sites,<sup>12</sup> chronic radiodermatitis, and thermal burns,<sup>13</sup> although squamous cell carcinoma is more common in these cases (1:3 ratio).

The causal relationship between a traumatic injury and skin cancer was first proposed in 1863 by Virchow; however, it continues to be a subject of debate. Years later, in 1935, Ewing<sup>14</sup> proposed criteria to relate the presence of an isolated trauma and the subsequent appearance of a neoplasm at the same site. Those criteria were modified by Stoll and Crissey<sup>15</sup> and are presently a major aid in making a definitive diagnosis of post-traumatic BCC (Table). Recent studies<sup>16</sup> also report the relationship between traumatic injury and the development of a BCC and conclude that injuries can be considered an additional etiologic agent.

In our case, the patient and her husband insisted that the tumor had developed in the same area as 1 of the positive patches and mentioned the persistence of mild itching in the region, which led us to consider the diagnosis. The positive reaction to 1% gold chloride was interpreted as an allergic and irritative reaction, given the high concentration of the allergen, and 30 months later, the patient presented a superficial BCC in the area



**Figure 5.** A and B, x-ray microanalysis showing that the electron-dense particles are gold deposits (SEM-JSM-820 and LINK-QX 2000).

with a border that coincided precisely with the patch application.

In our patient, we felt that the patch test was obviously related to the development of BCC. The gold salt applied in the patch is percutaneously absorbed by the dermis, where it remains and causes an acute immunologic inflammatory response in a sensitized patient. Its presence in the dermis more than 2 years after the tests supports our hypothesis that gold not only influenced the induction phase of skin carcinogenesis, but also the promotion phase. The induction of oncogenesis in this case could be explained by various mechanisms: *a)* gold as a metal deposited in the dermis that caused a foreign-body reaction, *b)* intense toxic and allergic immunologic reactions caused by this metal, *c)* intense nonspecific inflammatory response that occurred during the allergy test, and *d)* all of these factors acting together.

Allergic contact dermatitis to gold is extremely rare, and a clinical suspicion should be confirmed by patch testing. The test allergens consisted of several gold preparations, such as 0.002% potassium dicyanoaurate in water, 0.5% to 2.0% gold sodium thiomalate, gold trichloride at concentrations between 0.02% and 2% (which is an irritant), and 1% gold chloride. On occasions, positive gold reactions can occur that persist for weeks or months with histopathologic changes that include an inflammatory infiltrate; use is therefore not advisable.

The characteristics of our patient suggested post-traumatic BCC for the following reasons:

1. The very intense allergic and irritative positive reaction in the patch test (1% gold chloride) and the presence of gold particles in the dermis induced a foreign-body inflammatory response that could have triggered carcinogenesis.
2. The patient had no photoinduced lesions on her back, and the site of the superficial BCC coincided precisely with the positive reaction to 1% gold chloride.
3. The cancer lesion was confirmed by histopathology.
4. The tumor appeared more than 1 year after the patch test.
5. The patient had no family or personal history of skin cancer and no habit of regular sun exposure; she also denied sunburns during childhood or adolescence.

We have found no reports of skin tumors as possible complications of patch tests. This could be explained by the fact that it is extremely rare and because the latency period for clinical manifestations of the tumor is prolonged, often making it difficult to suspect or establish a relationship with patch tests. Nevertheless, the possibility of a rare fortuitous coincidence should be considered.

**Table 1.** Diagnostic Criteria for Post-traumatic Skin Cancer

Existence and severity of the previous trauma
Prior skin integrity of the anatomic region affected
Emergence of tumor in the area of trauma
Histologic confirmation of the tumor
Reasonable time limit between the injury and the appearance of the tumor, which may be up to 20 years

## Acknowledgements

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## Conflicts of Interest

The authors declare no conflicts of interest.

## References

1. Miller DL, Weinstock MA. Nonmelanoma skin cancer in the United States: incidence. *J Am Acad Dermatol.* 1994;30:774-8.
2. Festa F, Kumar R, Sanyal S, Unden B, Nordfors L, Lindholm B, et al. Basal cell carcinoma and variants in genes coding for immune response, DNA repair, folate and iron metabolism. *Mutat Res.* 2005;574:105-11.
3. Gallagher RP, Ma B, McLean DI, Yang CP, Ho V, Carruthers JA, et al. Trends in basal cell carcinoma, squamous cell carcinoma, and melanoma of the skin from 1973 through 1987. *J Am Acad Dermatol.* 1990;23:413-21.
4. Von Domarus H, Steven PJ. Metastatic basal cell carcinoma; report of five cases and review of 170 cases in the literature. *J Am Acad Dermatol.* 1984;10:1043-60.
5. Cox AJ, Kenneth WM. Gold in the dermis following gold therapy for rheumatoid arthritis. *Arch Dermatol.* 1973;108:655-7.
6. Keen CE, Brady K, Kirkham N, Levison DA. Gold in the dermis following chrysotherapy: histopathology and microanalysis. *Histopathology.* 1993;23:355-60.
7. Kopf AW. Computer analysis of 3531 basal-cell carcinomas of the skin. *J Dermatol.* 1979;6:267-81.
8. Hussein MR. Ultraviolet radiation and skin cancer: molecular mechanisms. *J Cutan Pathol.* 2005;32:191-205.
9. Rustin MH, Chambers TJ, Munro DD. Post-traumatic basal cell carcinomas. *Clin Exp Dermatol.* 1984;9:379-83.
10. Wilkin JK, Strobel D. Basal cell carcinoma arising at the site of venipuncture. *Cutis.* 1985;36:297-8.
11. Orfuss AJ. Lupus vulgaris and superimposed basal cell epitheliomas. *Arch Dermatol.* 1971;103:555.
12. Rich JD, Shesol BF, Horne DW 3rd. Basal cell carcinoma arising in a smallpox vaccination site. *J Clin Pathol.* 1980;33:134-5.

13. Kantor I, Berger BW, Wilentz JM. Basal cell epithelioma in a thermal burn scar. *J Occup Med.* 1970;12:170-2.
14. Ewing J. Modern attitude toward traumatic cancer. *Arch Pathol.* 1935;19:690-728.
15. Stoll HL Jr, Crissey JT. Epithelioma from single trauma. *NY State J Med.* 1962;62:496-500.
16. Ozyazgan I, Kontas O. Previous injuries or scars as risk factors for the development of basal cell carcinoma. *Scand J Plast Reconstr Hand Surg.* 2004;38:11-5.