Syringomas are benign adnexal tumors of eccrine ductal origin, characterized by small, firm, flesh-colored or yellowish papules located on the eyelids, anterior region of the neck, trunk, or abdomen. The highly characteristic histology consists of an epithelial growth in the form of tubules or nests made up of 2 flat cell layers; these structures develop a “tadpole-shaped” tail. The most widely used treatment is ultrapulsed CO₂ laser, although no studies have confirmed its efficacy. These lesions are rarely self-limiting, and recurrences are common.

We describe a 25-year-old woman with no relevant history who consulted for asymptomatic, flesh-colored papules of 1-2 mm, distributed on the anterior area of the neck and neckline (Figure 1). The symptoms started 10 years earlier on the lower eyelids, gradually spreading to the abdomen, neck, and neckline, with outbreaks after periods of sun exposure.

Histological study with hematoxylin-eosin showed an epithelial growth in the superficial and middle dermis, composed of cells with a pale eosinophilic cytoplasm and rounded, monomorphous nuclei. The cells were arranged in tubules and solid nests, some with a tadpole shape. The neoplasm showed a sclerotic stroma (Figure 2).

The diagnosis based on clinical presentation and pathology was generalized syringomas. The patient was informed of the possible therapeutic options, initially choosing to refrain from treatment.

Syringomas are uncommon neoplasms, described mainly in women before and during puberty, probably in relation to the presence of hormone receptors and the fact that dermatology consultation for cosmetic purposes is more common among women. They manifest as firm, rounded, pale pink or yellow-colored papules of 1-3 mm diameter. Syringomas have traditionally been classified according to site and form of onset on eyelids, the most common, and eruptive. In 1987, Friedman and Butler attempted to classify the multiple sites and described 4 clinical forms (Table): localized, familial, Down syndrome-associated, and generalized. Generalized syringomas included a multifocal form and another, more common, eruptive form. The eruptive form, described by Jaquet and Darier in 1887 as “eruptive hidradenoma,” is characterized by outbreaks of papular elements in the anterior and lateral region of the neck, trunk, axillae, abdomen, genital area, and limbs between 4 and 10 years of age. It has been related to heat stimuli.

Eruptive syringomas have been associated with Down syndrome, palpebral syringomas with Marfan and Ehlers-Danlos syndromes, and syringomas presenting with milia and atrophoderma vermiculata have been associated with Nicolau Balus syndrome. Cases of familial inheritance and others related to diabetes, alopecia, and tumors, such as carcinoids, have also been reported.

There are atypical presentations such as unilateral forms, urticaria pigmentosa, or milia.

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**Table.** Clinical Variants of Syringomas

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>Localized</strong></td>
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<tr>
<td>Solitary</td>
<td>Multiple-single foci</td>
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<tr>
<td></td>
<td>- Papular</td>
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<tr>
<td></td>
<td>- Genital</td>
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<td>- Acral</td>
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<td>- Unilateral</td>
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<td>- Frontal</td>
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<td></td>
<td>- Occult</td>
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<tr>
<td></td>
<td>- Scalp: alopecia</td>
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<td></td>
<td>- Simulating lichen planus</td>
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<td></td>
<td>- Simulating milia</td>
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<td></td>
<td>- Intraocular</td>
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<td></td>
<td>- Perianal</td>
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<td></td>
<td>In unilateral plaque</td>
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<tr>
<td><strong>Generalized</strong></td>
<td></td>
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<tr>
<td>Multifocal</td>
<td>Eruptive</td>
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<tr>
<td></td>
<td>- Simulating lichen planus</td>
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<td></td>
<td>- Simulating urticaria pigmentosa</td>
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<td></td>
<td>- Simulating milia</td>
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<tr>
<td>Down syndrome</td>
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<td>Familial</td>
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Adapted from Friedman and Butler.
Letters to the Editor

Psoriasis at the Site of Healed Herpes Zoster: Wolf’s Isotopic Response

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To the Editor:

A wide variety of dermatological processes can occur at the site of healed herpes zoster, mainly granulomatous processes, lymphomas, pseudolymphomas, and primary skin tumors or metastasis.1 These conditions occasionally appear in immunosuppressed patients with neoplasms or human immunodeficiency virus infection, but in other patients there may be no underlying disease. The interval between viral infection and second disease is extremely variable, from days to years.2 We describe a patient with paroxysmal nocturnal hemoglobinuria who developed guttate psoriasis lesions on the site of previous herpes zoster. A 41-year-old man who had undergone allogeneic transplantation of bone marrow for paroxysmal nocturnal hemoglobinuria and received

References


Acknowledgements

We would like to thank Dr JJ Rios-Martín of the Anatomical Pathology Department at Hospital Universitario Virgen Macarena de Sevilla in Seville, Spain.

Psoriasis was diagnosed on the site of a healed herpes zoster lesion. The patient denied any personal or family history of psoriasis. He was treated with topical corticosteroids, with complete whitening of the lesions within 2 months.

The isotopic response, defined by Wolf et al.\(^2\) as the onset of a new cutaneous disease at the site of another, already healed disease to which it is unrelated, would explain the appearance of psoriasis at the site of herpes zoster\(^1\) or varicella.\(^4\)

Herpes zoster is the disease most commonly presenting as the initial condition in an isotopic phenomenon.\(^2\) Although herpetic cytopathic alterations are not observed in a biopsy of the second disease, it has been suspected that virus particles persisting in the tissue could be responsible. Nevertheless, viral DNA has only been detected in post-zoster cutaneous lesions when they occurred in the first few weeks, and not found if the new process appeared months later, as occurred in our patient.\(^1\) However, it has been suggested that viral infection could alter local cutaneous immunity, and that such a change would favor hyperreactivity and, consequently, cause granulomas, pseudolymphomas, vasculitis, or eczematous reactions, or immunosuppression that would facilitate the onset of skin cancer and bacterial, mycotic, or viral infections.\(^5\) We suggest that tumor necrosis factor \(\alpha\) (TNF-\(\alpha\)) may have a role in the Wolf isotopic response.

TNF-\(\alpha\) is an essential cytokine in defense mechanisms, with broad effects in both the innate and adaptive immunity and with well-established antiviral activity.\(^6,7\) TNF-related cytokines are critical effector molecules in the immune response against viral pathogens. TNF receptor binding activates apoptotic and nonapoptotic mechanisms that have antiviral effects. This cytokine is elevated in the primary immune response against VZV infection, in re-exposure to this virus, and during herpes zoster episodes.\(^8,9\) Furthermore, TNF alteration has been implicated in a wide variety of inflammatory diseases, including psoriasis,\(^10\) and its role in inducing and maintaining granulomas at multiple levels is also known.\(^11\)

Because granulomatous processes, such as granuloma annulare, sarcoid granuloma, tuberculosis granuloma, vasculitis, and granulomatous folliculitis, are the conditions most commonly reported after herpes zoster,\(^1,2,5\) we suggest that a TNF alteration or overexpression, induced locally by VZV infection, could play a crucial role in the pathogenesis of these complications. Such local TNF production would also explain psoriasis cases described following VZV infections in genetically predisposed individuals.

### References

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To the Editor:
We describe an 88-year-old woman with various lesions in the right submammary region that had remained stable for more than 40 years. She reported rapid growth and ulceration of one of the lesions in the past year. The examination showed a firm tumor of diameter 7 cm below the right breast. The surface of the tumor was keratotic at the periphery and ulcerated in the middle with foul-smelling serous exudate. Adjacent to the lesion, there were various smaller erythematous brownish tumors with a velvety surface, and with a linear distribution (Figure 1). No enlarged local or regional lymph nodes were palpated. Laboratory workup, chest x-ray, electrocardiogram, bilateral mammography, and right axillary ultrasound were all normal. An incisional biopsy of the larger tumor and another biopsy of one of the adjacent lesions were taken. In the first case, the hematoxylin-eosin stain showed irregular, anastomosed islets composed of intraepidermal tumor cells, some of them pigmented, with a clearer cytoplasm than the surrounding keratinocytes. Abundant atypical cells with large, irregular, hyperchromatic nuclei were observed inside the tumor masses. In some sections, cystic spaces within these nests of basaloid cells could be seen. The epidermis presented hyperkeratosis, foci of parakeratosis, and irregular acanthosis (Figure 2 A and B). A biopsy of the smaller lesion showed well-defined nests of uniform cuboidal cells with rounded, basophilic nuclei showing no atypia, and with cystic structures in the interior (Figure 2 B).
3). The tumor cell cytoplasm contained positive p-aminosalicylic acid (PAS) granules in both cases. Immunohistochemical staining showed tumor islets stained with monoclonal anti-cytokeratin antibodies AE1/AE3 and 34betaE12, and antibodies against epithelial membrane antigen (EMA), but no immunoreactivity for cytokeratins 7 or 20, or with the CAM5.2 anti-cytokeratin antibody; there was also no immunoreactivity for carcinoembryonic antigen (CEA), or gross cystic disease fluid protein-15. Malignant hidroacanthoma simplex (MHS) from hidroacanthoma simplex (HS) of linear distribution was diagnosed; the ulcerated malignant tumor was removed surgically. A year and a half after diagnosis, the patient remained asymptomatic with no evidence of distant metastasis in the follow-ups, which included physical examination every 3 months as well as blood tests, chest x-ray, and abdominal ultrasound every 6 months.

In 1956 Smith and Coburn were the first to refer to HS, using the term to designate a benign intraepidermal tumor of sweat gland origin and described its malignant counterpart, MHS, proposing the name “intraepidermal eccrine poroma.” Since that time, several cases of HS and MHS have been published, and HS continues to be considered an intraepidermal variant of eccrine poroma, whereas MHS has been given several names, including in situ porocarcinoma, eccrine porocarcinoma, and hidroacanthoma simplex with invasive growth. The clinical presentation of HS is not characteristic, but is usually located on the lower limbs of elderly patients, with a slight predominance among women. A literature review revealed 2 descriptions of nonintraepidermal eccrine tumors with a linear distribution—1 eccrine porocarcinoma located on the buttock and an eccrine poroma along 1 leg. Thus, our case appears to be the first description of MHS on a linear HS.

Histologically, the HS is characterized by islets of small, uniform, basophilic or poorly stained cells that are clustered within an acanthotic epidermis and that contain PAS-positive cytoplasmic granules. Ductal differentiation (recognizable ducts, intracytoplasmic lumens, or cystic structures) is observed; the ducts can be seen with PAS stain and show positivity for EMA or CEA, although there are several cases published in the literature in which CEA was negative. An MHS lesion is composed of the cells described above, but shows cytological pleomorphism, frequent mitoses, and an invasive structure.

Several cases of malignant transformation of HS have been published, and its potential for degeneration has been discussed extensively. In our case, the HS lesions adjacent to the MHS had been present for more than 40 years and, therefore, we believe there is evidence of malignant degeneration.

The prognosis of MHS is not accurately known due to the limited number of case reports that describe the patient’s progress and the lack of long-term follow-up. The suggested treatments are extensive local excision or Mohs microscopic surgery in the case of HS, due to its potential risk for degeneration. Other alternatives are electrosurgery or radiation.

In conclusion, although several tumors of eccrine origin with a linear distribution have been described, we did not find any case of linear HS with degeneration to MHS.

References

Hypersensitivity to the Antioxidant Ethoxyquin

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To the Editor:
Further to case reports published on occupational illnesses due to contact dermatitis caused by the antioxidant ethoxyquin,1,2 we report a patient with delayed hypersensitivity to this product who experienced a flare-up after patch testing. Ethoxyquin is used to prevent the oxidation of feed and essential oils, and in some countries to preserve the color of spices and fruit.3

The patient was a 38-year-old man with episodes of eczematous lesions, angioedema, and bronchospasm after workplace exposure to the antioxidant ethoxyquin (Capsoquin Liquid), which has the chemical formula 1,1-dihydro-6-ethoxy-2,2,4-trimethylquinoline. He worked as the chief mechanic at a company that manufactured chicken-based dog food, and had associated the onset of symptoms with product inhalation and once to contact. The symptoms manifested about 12 hours after exposure. The patient was able to tolerate consumption of chicken meat.

The blood tests, which included complete blood count, biochemistry, erythrocyte sedimentation rate, total proteins, immunoglobulins, serum complement levels, and tryptase were completely normal, except for moderate eosinophilia. Hypersensitivity to common aeroallergens and to foods was ruled out by a standard battery of skin prick tests. No specific immunoglobulin E was found against chicken serum proteins, droppings, or feathers. Skin prick tests with feed components treated with ethoxyquin (soy flour, chicken meat, and chicken feathers) were negative when read immediately and positive after 24 hours.

Patch tests with a European battery of contactants (Laboratorios Bial-Aristegui, Bilbao, Spain) were negative. Patches were prepared in 2% and 4% petroleum jelly with each separate feed component, and reading was delayed until 48 and 72 hours, as recommended by the Grupo Español de Investigación en Dermatitis de Contacto (Spanish Contact Dermatitis Research Group).4,5 The test was positive for 2% and 4% ethoxyquin (+++), soy flour with 2% and 4% ethoxyquin (+++), and soy flour with 2% sodium hydroxide and ethoxyquin (++). The reading was negative to sodium hydroxide, ethoxyquin-free soy flour, and soy flour with 4% sodium hydroxide/ethoxyquin. Flare-up was observed, with onset of eczematous lesions at some distance from the area where the patches were placed, in areas initially affected by previous adverse reactions. In 2 healthy controls with 2% and 4% ethoxyquin, the reading was negative.

The quinolines, the group to which ethoxyquin belongs, are of little relevance in Spain,6 although of sufficient prevalence to be included in the European battery of contactants.7 In our case, no reaction was observed to these compounds and, therefore, it did not appear that ethoxyquin had any cross reactivity with other quinolines that could have acted as primary sensitizers.

We are unaware of the clinical impact that eating meat from animals fed with feeds containing this antioxidant could have among hypersensitive patients, although it could be related to the appearance of disseminated eczemas classified as idiopathic.

References