

even though, myeloperoxidase (MPO)/p-ANCA perinuclear positivity is noted in patients with EGPA in 40–60% of patients.²

The pulmonary computed tomography findings consist of ground-glass opacities and diffuse alveolar hemorrhage (Supplementary Figure 1D). Moreover, computed tomography of the maxillary sinus area demonstrated minimal mucosal thickening. Our patient satisfied the American College of rheumatology 1990 criteria for the classification of EGPA from other vasculitides.⁵ We opted to use methotrexate 15 mg/week with oral prednisone 50 mg/day. The patient, in remission, continues with methotrexate 15 mg/week and prednisone 5 mg/day.

Just under half of all GPA patients (45%) will eventually develop cutaneous issues, however skin manifestations are only found in 9% to 14% of patients at initial presentation. The most frequent cutaneous manifestation is palpable purpura. Nonetheless, skin features can occur throughout the course of GPA most commonly involving the lower limbs, and encompass papules, nodules, vesiculo-bullae and pyoderma gangrenosum-like ulcers.² On the other hand, skin manifestations have been reported in 40–50% in EGPA and the most involved area is the extensor surface of limbs. Palpable purpuric lesions and nodules arising on a background of purpura are the most common features. It can also develop, to a lesser extent, with urticaria, erythematous maculo-papular rash and livedo.² In conclusion, the early recognition of these lesions by dermatologist is essential for the clinical suspicion, confirmation of diagnosis, adequate treatment and to contribute for the prevention of irreversible lesion in vital organs.

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Basal cell carcinomas are not only UV-related

An otherwise healthy 61-year-old man came to our attention for a skin nodular lesion of the scrotum. On clinical examination we observed a translucent, firm and painless nodule, freely mobile and not fixed to the underlying structures, localized in the right side of the scrotal bag and measuring about 2×1 cm (Figure 1A). The patient reported that this nodule appeared about 6 months before, and has gradually grown in size, without itch or pain. Both testes were normal, same the penis. There were no palpable masses in the scrotal bag, or in inguinal region; the abdomen was also negative. The patient underwent a surgical radical excision of the neoplasm. The histopathological examination confirmed the presence of a nodular BCC involving the reticular dermis. Inguinal lymph node sonography was executed and resulted negative. The patient was submitted to clinical and ecosonography follow-up every 6 months for five years. The patient has not reported any infection or disorder of the genital sphere including a recent or past HPV infection. In fact, PCR analysis was negative for HPV-DNA. In addition, his history was negative for exposure to ionizing radiation, familiarity for skin cancers, and he did not practice nud-

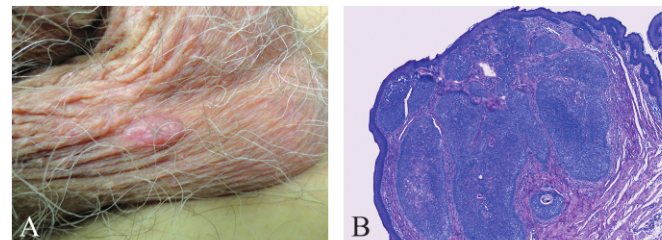


Figure 1. A) Nodular basal cell carcinoma of the scrotum; B) H&E (10×) histopathological aspects of scrotal nodular basal cell carcinoma.

ism or smoke. The only remarkable aspect in the patient's history was his work as a gas station for 25 years, where he was exposed to benzene and other toxic substances commonly present in this job. Radical surgical therapy and a follow-up every 6 months by dermatological inspection have been planned for this patient after the diagnosis of BCC confirmed by histological examination (Figure 1B).

Lindelöf *et al.*¹ published an interesting paper in which they compared the incidence of skin cancer between indoor and outdoor workers: their data showed a higher incidence of NMSC in some categories of indoor workers such as doctors, dentists or lawyers. Obviously, these categories of workers are not always exposed to the sun but the reason for this shift in the risk of BCC from outdoor to indoor occupations could be related to intermittent UV exposure during leisure-time, and not to the occupation. However, the Lindelöf's study is based on a cohort of Swedish patients and is an important bias to consider when interpreting the data; in fact, this is one of the few recent jobs in which solar damage predominates in indoor workers.¹

To better understand whether BCC and more generally keratinocyte skin cancers are to be considered occupational cancers, it is good to draw on data from a 2018 study by Zink *et al.* in which the authors carried out a cross-sectional study on farmers, gardeners and mountain guides. In this study, the overall NMSC prevalence in outdoor workers was higher compared to indoor workers. NMSC was further associated with outdoor professions ($rs=0.22$) with noticeable higher NMSC rates in all outdoor workers (mountain guides 33.3%, farmers 27.4%, gardeners 19.5%) compared to indoor workers (5.6%).² Other studies suggest an increased relation between sun exposure and the risk of developing skin cancer among athletes such as sailor. In fact, Zalaudek *et al.*³ carried out an epidemiologic study on sailors attending the biggest regatta in the world, named "Barcolana," showing that 14% of sailors of attending the event had a personal history of non-melanoma skin cancer (NMSC). During the dermatological examination performed, suspicious lesions for skin cancer (such as basal cell carcinoma, actinic keratosis, melanoma) were identified in 37% of the sailors. In addition to UV radiation, another risk factor for the development of BCC is represented by ionizing radiation such as radiotherapy. Karagas *et al.* reported that in 1690 patients previously treated with radiotherapy, the relative risk (RR) of total BCC tumors was 2.3 with a higher risk associated with young age and time since first treatment.⁴

It is well known that the main environmental and occupational causative agents in developing skin cancer are polycyclic aromatic hydrocarbons (PAH) and inorganic arsenic. PAH (*e.g.* in gasoline, asphalt, chimney soot), induces 4-times more cancer of the scrotum in workers using cutting oils or pitch than expected. The latent period varies from 20 years (exposure to coal tar) to 50 years or more (exposure to mineral oils). An increased risk of BCC is also associated with the consumption of water contaminated with arsenic, the use of drugs containing arsenic; while the effect of taking this semimetal with the diet, for example, rich in seafood, is not yet known.

Immunosuppression following an organ transplant is another important risk factor for the development of NMSC and is linked to the duration of therapy. In particular, the frequency of SCC increases 65 to 250 times compared to the general population, while the incidence of BCC has increased tenfold. Non-drug immuno-

suppression such as HIV is also associated with an increased risk of BCC.⁵

Chronic skin irritation, previous trauma and area of scars, exposure to ionizing radiation, immunosuppressive drugs may be responsible for the development of tumors at uncommon sites.⁵

From data available in literature, major causal determinants appear to be ionizing radiation, HPV infection, chronic venous stasis, poor hygiene and the exposure to toxic substances. Our patient's anamnesis was fully negative for these aspects, so we considered other risk factors such as a chronic toxic occupational exposure to PAH. It is remarkable that historically scrotal carcinoma was the first recognized occupational cancer as "chimney sweeper's cancer." The disease was related to exposure to soot and dust which contain the active agent as 3-4 benzopyrene.

Even if the management of occupational skin cancer is the same as the management of non-occupational skin cancer, according to the recent literature it seems that BCC of the scrotum metastasizes more easily than the other BCC.⁵ Tumor size more than 2 cm, muscle infiltration, meta-typical and morpheiform variants were more frequently involved in metastatic BCC. Also, it can metastasize after a long period of initial therapy. This is why, considering the aggressive nature of scrotal BCC, all these patients should be kept under surveillance for metastasis for 2 to 5 years after excision.

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Prurigo pigmentosa: a new Italian case

Prurigo pigmentosa (PP) is a rare inflammatory skin disorder characterized by a sudden onset of pruritic and erythematous macules, papules and plaques. Lesions resolve over time leaving post-inflammatory hyperpigmentation arranged in a reticulated pattern. It was first described by Nagashima in 1971 in Japan,¹ where hundreds of cases have been documented thus far. On the contrary, fewer cases have been described in Western countries; this might reflect underdiagnosis or misdiagnosis rather than a genetic predilection for Japanese.² We herein present a case of PP diagnosed in an Italian woman. To the best of our knowledge, only six cases diagnosed in Italian patients have been described so far.³

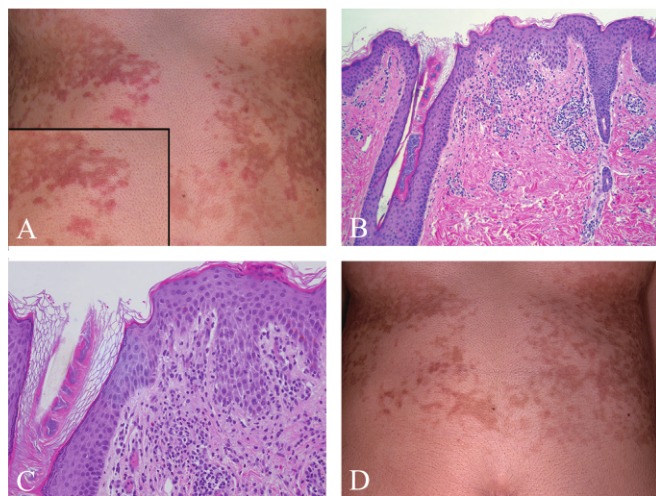


Figure 1. A) Clinical picture at the first examination: papules and hyperpigmented patches arranged in a reticulated pattern; papules were coalescent and erythematous (inset); B) histopathological picture featuring a "mixed" pattern with focal spongiosis and a mild vacuolar interface dermatitis; C) the superficial "insect bite-like" inflammatory pattern with bacterial colonies within a hair follicle; and D) clinical picture after minocycline therapy: only a reticulated pigmentation is apparent.

A 21-year-old Italian woman was seen for a 2-month history of pruritic and erythematous papules on her trunk. She did not take any medications and denied any allergies and/or a familial history of skin diseases; additionally, she denied being on a diet. The skin eruption involved the trunk and was made by symmetrically distributed erythematous papules admixed with hyperpigmented areas; both papules and hyperpigmented areas were arranged in a reticulated pattern (Figure 1A). The patient had been treated with topical corticosteroids without any benefit. The skin biopsy showed a "mixed" pattern with focal spongiosis, a mild vacuolar interface dermatitis (Figure 1B) with a few dermal melanophages, and a superficial "insect bite-like" pattern (perivascular lymphocytes with interstitial eosinophils; Figure 1C); few mast cells were present in both perivascular and interstitial areas. Coccobacillary colonies within the hair follicles with no concurrent folliculitis or perifolliculitis were a noticeable feature (Figure 1B, C). Mild signs secondary to chronic rubbing (parakeratosis and hypergranulosis) were also present. Periodic acid Schiff stain was negative. The clinicopathological features of the case were considered to be consistent with PP. Treatment with minocycline 100 mg bid for one week and then once a day per 2 weeks was followed by a fast improvement of the clinical picture (Figure 1D).

Prurigo pigmentosa is a rare cutaneous disorder that is still not fully recognized in patients from Western countries. The male to female ratio is approximately 4-6:1 with an average age at diagnosis of 25 years.²

The etiology and pathogenesis are not fully understood but cases in association with ketoacidotic states (diabetes mellitus, fasting, dieting, anorexia nervosa) are reported. Possible worsening factors include sweating, sunlight exposure, physical trauma, friction, and contact allergens.² PP is characterized by frequent recurrences followed by remission periods lasting from weeks to years.²

Multiple infectious agents such as *Borrelia spirochetes* and *Helicobacter Pylori* have been investigated as possibly associated with PP. Kaffle *et al.* found that two-thirds of patients with PP had pathological involvement of pilosebaceous units, with bacterial colonies within the hair follicles w/o folliculitis or perifolliculitis; thus, these authors suggested that PP is a reactive inflammation associated with/subsequent to bacterial folliculitis.⁴

Clinically and histologically, PP changes according to the stage of the disease.² At the beginning, the skin lesions appear as symmetrically distributed pruritic and erythematous macules and papules coalescing into plaques, with a predilection for the trunk, neck and chest. The abdomen and shoulders are less involved; alterations of the hair, nails, and mucous are not observed. Excoriation, scaling or crusting can be seen. Subsequently, the lesions quickly resolve with a post-inflammatory hyperpigmentation arranged in a reticulated pattern. No underlying systemic symptoms are associated.

The histopathological features of PP have been described in detail by Boer *et al.*⁵ The early stage of the disease shows a superficial perivascular and interstitial infiltrate of neutrophils edema of the papillary derma, epidermal spongiosis and neutrophilic exocytosis. The next stage is characterized by a predominantly lymphocytes infiltrate in a lichenoid pattern. Eosinophils and neutrophils are variable; the epidermis is spongiotic, with vacuolar basilar changes and numerous necrotic keratinocytes. In the late stage, melanophages are seen in the upper derma with a scattered lymphocytes infiltrate. The epidermis becomes hyperplastic with focal parakeratosis and few scattered necrotic keratinocytes; melanophages accumulate within the superficial derma.