

disease that clinically resembles either scleroderma or eosinophilic fasciitis, and histologically resembles scleromyxedema [1-3].

In patients with NSF a rapid onset of swelling and tightening of the skin is recorded, usually involving the extremities. The condition may develop over a period of days to several weeks. In many cases, the skin thickening inhibits flexion and extension of the joints, resulting in contractures. Complaints of muscle weakness are common. Approximately 5% of patients have a rapidly progressive course leading to death.

The diagnosis is mainly histological [4]. The disease is characterized by thickening of collagen bundles, interstitial mucin deposits, and proliferation of fibroblasts, with increased elastic fibers. In the reticular dermis, spindle cells may extend to the septa and lobules of the subcutaneous fat. Such cells are distributed among the bundles of thickened collagen and are CD34 positive. The most important differential diagnoses are scleromyxedema, scleroderma and scleredema adultorum [1-3].

The mechanism for possible gadolinium-associated NSF is unknown [5]; probably NSF is caused by a toxic reaction from free gadolinium that might dissociate from the chelate and that cannot be adequately excreted due to impaired renal function. Once deposited in tissue, free gadolinium is phagocytated by macrophages and, perhaps, this intracellular deposit results in the release of profibrotic cytokines and/or growth factors that ultimately cause dermal or systemic fibrosis. Given these data, it would be most prudent to recommend that the use of gadolinium-containing contrast agents has to be excluded to the greatest extent possible in patients with renal disease; if this is not possible, after the MRI, patients must be immediately submitted to dialysis to excrete free Gadolinium as fast as possible.

Improving renal function seems to slow or arrest NSF. Treatments that have shown better results are photopheresis, prednisone, calcipotriol, IV immunoglobulin, photodynamic therapy, plasmapheresis, and renal transplantation. ■

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Allergic contact dermatitis from timolol complicating choroidal melanoma-related glaucoma

A non-atopic 40-year-old man presented with eyelid erythema and oedema of the right eye (*figure 1*), associated with an intense burning sensation and lacrimation of both eyes. The left eye showed only modest conjunctival hyperemia, without any relevant cutaneous lesions. These symptoms had appeared four months earlier and had gradually worsened. Three years before the patient had undergone proton beam radiotherapy to treat a malignant melanoma of the right choroid. Choroidal melanoma was diagnosed in concomitance to the detection of an increased intraocular pressure on both sides and a monolateral glaucoma developed as a complication of treatment with proton beam radiotherapy soon after this procedure. Since then the patient constantly used eyedrops containing timolol in both eyes.

The patient was patch tested with the SIDAPA (Italian Society of Allergological, Occupational and Environmental Dermatology) standard series, the eyelid series and the ophthalmic product used by the patient (Timololo Novartis®, Novartis Farma, Origio, Varese, Italy) as is, as well as its components, including timolol (Firma, Florence, Italy) at 1% aq. Patch tests were performed using Al-chambers™ (Euromedical, Calolziocorte, LC, Italy), and readings were made after 2 and 4 days (D2 and D4, respectively). Positive reactions (+++) were obtained at D2 and D4 to the commercial product as is, and to timolol 1% aq. Therefore, the patient was tested with an alternative commercial product containing levobunolol (Vistagan®, Allergan, Rome, Italy), as well as with levobunolol 1% aq. Skin prick tests with inhalant extracts were also performed, using saline solution and histamine (10 mg/mL) as negative and positive controls, respectively, and gave negative results.

Symptoms rapidly disappeared within ten days after Timololo Novartis® had been withdrawn and substituted with Vistagan® eyedrops, which has been well tolerated up to the last follow-up assessment at ten months of therapy. Timolol is a nonselective beta-blocker and is the drug most widely used against glaucoma. Topical beta-blocking agents can cause irritant or allergic contact reactions, although reports of contact sensitization appear to be relatively uncommon [1-3]. The actual prevalence of contact allergy is unknown and may be underestimated because of the occurrence of false negative reactions, attributable to either suboptimal test concentrations or insufficient patch test area, as well as other possible inappropriate test procedures [2-4]. Patients with allergic contact dermatitis to a beta-blocker can have positive patch test reactions to



Figure 1. A) Erythema and oedema of the right eye, site of previous choroidal melanoma; B) Positive patch test reaction to timolol 1% aq.

other beta-blocking molecules which have been regarded as cross-reactions by some authors and concomitant sensitization by others [5, 6], although a recent systematic evaluation in a large case series showed that cross-reactivity between beta-blockers appeared to be rare [2]. Our patient tolerated an ophthalmic product containing levobunolol well, which also gave a negative patch test reaction.

In the case herein described, clinical manifestations of contact allergy were much more evident in the right eye, although the culprit ophthalmic drug was applied to the same extent in both eyes. It is possible that proton beam therapy previously used to treat choroidal melanoma had induced local changes responsible for congestion and an enhanced inflammatory response, which can justify the different degrees of clinical manifestation between the two eyes. ■

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Unilateral angiokeratoma of the breast

Angiokeratomas are several unrelated conditions that represent acquired telangiectasies in combination with hyperkeratosis, characterized histologically as one or more dilated blood vessel(s) lying in the upper part of epidermis, and in most cases and showing an epidermal proliferative reaction [1, 2]. We present a case of angiokeratoma localized unilaterally on the breast, associated with enlargement of the underlying breast.

Case report

A 50-year-old woman attended our outpatient clinic with multiple 0.5-1 cm sized dark purple papules on her left breast. Some of the papules were slightly hyperkeratotic and some of them were coalescing and arranged in a reticulate pattern (figure 1A). The patient's left breast was bigger than her right breast. The lesions had first appeared

30 years before when she was breastfeeding her third child and had increased in number and size during the intervening years. The patient had 5 children and she only used her left breast for breastfeeding. She did not know when the enlargement of the left breast occurred. The patient had no significant medical history except diabetes mellitus. No family member had similar complaints. Complete blood count and routine biochemical tests were within normal levels except elevated blood glucose. Vision and neurological examinations were normal. The histopathological examination of the lesions revealed acanthotic epidermis, dilated vascular structures in the papillary dermis and erythrocytes in the thin-walled vascular structures (figure 1B). Based on clinical and histopathological features a diagnosis of angiokeratoma was made. Doppler ultrasonography of the breasts revealed enlarged venous vascular structures in the left breast. No solid mass was observed in either breast. No further examination could be performed as the patient refused detailed examination and no treatment was given as the patient was asymptomatic.

Discussion

Angiokeratomas are red-blue variably hyperkeratotic papules, occurring in isolation or in groups, mostly on

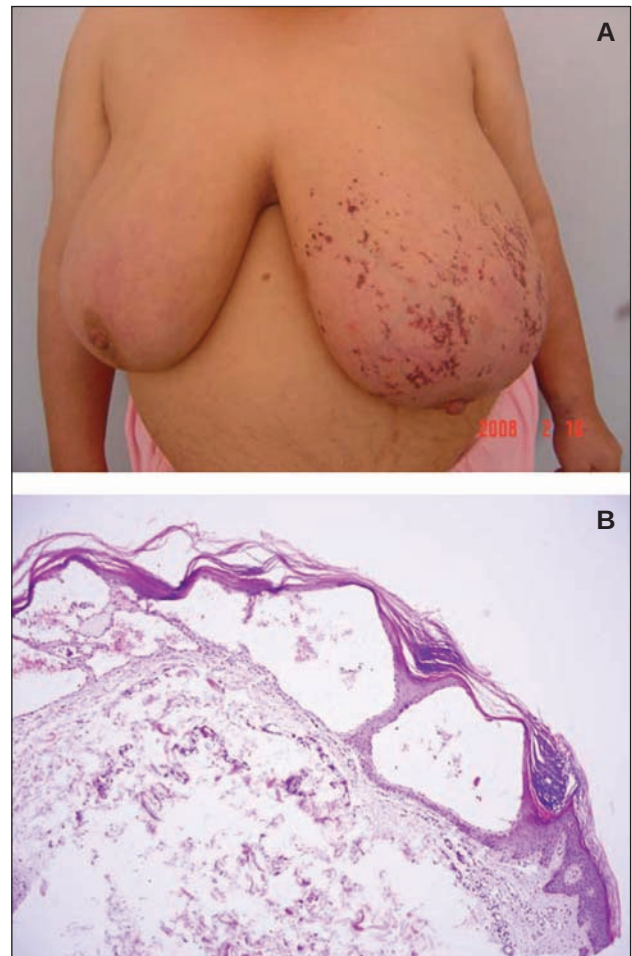


Figure 1. A) 0.5-1 cm sized dark purple papules on the left breast. Left breast is bigger than the right breast. **B)** Dilated vascular structures in papillary dermis (H&E × 100).