hair in the last two years, as well as facial skin-colored papules for about six months (Figure 3). The patient had recently noticed a progressive decrease of axillary hairs. At the initial examination, we observed thinning eyebrows and alopecia in the frontal region, with sparing of the implantation hairline. Frontal biopsy was compatible with FFA, corroborating our clinical diagnosis. Figure 3C shows the evolution of the clinical features, compatible with FFA.

As already reported by Pirmez *et al*., although the pseudo "fringe sign" can occur in patients with FFA, biopsies show the characteristic pattern of LPP, which may make diagnosis challenging.[5] In the reported cases, the presence of facial papules and thinning eyebrows contributed to the diagnosis of FFA, in detriment of LPP with alopecia plaques. In addition, the loss of vellus hair in the frontal region was not observed initially, but a loss after the frontal implantation line, affecting the terminal hairs of that region. Unlike TA, this fringe slowly becomes more rarefied, eventually leading to some vellus hair loss in the region in a later phase, with a scarring, shiny appearance and absence of follicular ostia to trichoscopy.

A study with a greater number of reported cases of this clinical presentation could help explain this type of manifestation, its etiopathogenic implications, and the immune response involved, which would help in therapeutic decisions. ❑

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Dapsone-induced agranulocytosis in patients with Hansen's disease*

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Dear Editor,

Agranulocytosis induced by sulphonamide or dapsone (44-diaminodiphenylsulphone – DDS) is characterized by a low concentration or absence of granulocytes due to sulfone cytotoxicity effects on bone marrow and mononuclear cells.[1]

DDS is a structural analogue of para-aminobenzoic acid (PABA) that acts as a competitive inhibitor of the enzyme dihydropteroate synthase in the folate pathway. It has anti-inflammatory, antibacterial, antiprotozoal, and antifungal activities. Used since 1943 to treat leprosy, it is also indicated for the treatment of malaria, rheumatoid arthritis, granuloma annulare, dermatitis herpetiformis, and other vesiculobullous diseases. DDS adverse effects include hemolytic anemia, methemoglobinemia, gastritis, headache, agranulocytosis, hepatitis, peripheral neuropathy, nephrotic syndrome, dapsone syndrome, among others.[1,2]

DDS is part of the multidrug therapy (MDT) used to treat leprosy. The regimen is a combination of rifampicin (supervised monthly dose of 600mg) and dapsone (supervised monthly dose of 100mg and 100mg/daily) for paucibacillary patients, with the addition of clofazimine (supervised monthly dose of 300mg and 50mg/daily) for multibacillar patients.[2]

We report a 61-year-old Caucasian female patient, resident in Juazeiro, state of Bahia, Brazil, complaining of a spot on the right elbow, which appeared 1 year before. Physical examination revealed a single hypochromic patch, approximately 1cm in diameter, with micropapular edges and absent thermal sensitivity. With a diagnosis of tuberculoid leprosy, we started a MDT regimen for paucibacillary leprosy. At day 14 after the first administration, the patient presented with adynamia, exertional dyspnea, normochromic normocyt-

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ic anemia with anisocytosis, and normal white blood cell (WBC) count. At day 34, she presented with fever, chills, adynamia, oropharyngeal pain, and cutaneous pallor associated with leukopenia with severe neutropenia. We suspended the MDT and, advised by a hematologist, introduced amoxicillin clavulanate, ciprofloxacin, and filgrastim (rHu G-CSF) 300 µg/daily for 5 days.

Serial blood test collection revealed a typical clinical presentation of agranulocytosis (Table 1).

After 8 days, the patient showed clinical and laboratorial improvement. Test levels remained normal during 1-month follow-up when we reintroduced the MDT substituting DDS by clofazimine. The patient completed 6 months of MDT.

Agranulocytosis is a rare but serious complication of sulfones caused by the myelotoxic effect of these drugs. An occurrence of 0.2-0.4% has been described in patients treated with dapsone. Although reversible, this infection can lead to sepsis and even death.[3]

Agranulocytosis is an adverse effect of dapsone manifested as bone marrow suppression, which is caused by the formation of antibodies against neutrophil progenitor cells, decreasing the granulocyte formation. Another possible mechanism is the sensitization to the drug that forms hydroxylamine, a toxic metabolite of dapsone responsible for methemoglobinemia and hemolysis.[3]

For the treatment of leprosy, the risk of developing DDS-induced agranulocytosis is about 25-33 times higher because of reduced immunity and high dosage of the drug, as compared, for example to the treatment of malaria with an incidence between 1:10,000 and 1: 20,000 is reported. [2,4]

According to Silva *et al.* (2009),[1] Mishra and Chhetia (2006),[3] Bhat and Radhakrishnan (2003),[4] Carneiro *et al.* (2011),[5] and our case, the patients presented with abrupt symptoms associated with fever, oropharyngeal pain, chills, adynamia, hypotension, tachypnea, and chest pain. All of them, except Mishra and Chhetia (2006),[3] showed a significant reduction in WBC counts to values below 1,000 cells/mm^3, with neutropenia below 500 cells/mm^3.[4]

Although Silva *et al.* (2009),[1] Mishra and Chhetia (2006),[3] and Bhat and Radhakrishnan (2003)[4] reported cases in male patients; our report is in agreement with the literature in relation to the female predilection.[5] In relation to age, our report agrees Bhat and Radhakrishnan (2003),[4] showing a higher incidence around 60 years of age.

According to Mishra and Chhetia (2006),[3] Carneiro *et al.* (2011),[5] and our report, agranulocytosis occurs between 3 weeks and 3 months after the onset of the MDT.[5]

In the literature and in our case, patients started MDT to treat agranulocytosis, but DDS had to be discontinued due to side effects. The treatments continued with antibiotic therapy and filgrastim revealing leucometric and clinical improvement in a few days,[5] except for the patient followed by Bhat and Radhakrishnan (2003),[4] who died.

After clinical improvement, some patients had their MDT altered for ofloxacin, clofazimine, and minocycline, with each drug introduced at 30-day intervals, or for rifampicin and clofazimine, as in our report.

Table 1: Monitoring of a female patient with leprosy during paucibacillary multidrug therapy

DATE	06.30.2014	11.06.2014	11.26.2014	11.28.2014	11.30.2014 After 2 filgrastim injections	12.04.2014 After 5 prescribed injections	01.28.2015	Standards
Period of Treatment (MDT)	Before starting treatment with dapsone	Day 14	Day 34	Dapsone Interruption				
Hemoglobin (g/dL)	11.9	10.9	8.8	8.9	10	9.8	14.5	13-18 (men) 12-16 (women)
Hematocrit (%)	35.8	32.5	27	27.6	32.6	30.7	42.2	40-52 37-47
WBC count (mm^3)	4400	4000	1520	1000	1090	6300	4700	4000-11000
Bands (%)						13	1	1-5%
Segmented (%)	-	74	74	11	10	48	77	50-70%
Limphocytes (%)	21	22	25	8	84	24	20	20-45%
Eosinophils (%)	0	1	1	0	1	0	1	1-4%
Basophils (%)	0	1	0	2	0	2	0	0-1%
Monocytes (%)	2	2	0	1	5	0	1	2-12%
Platelets/ mm^3	211000	225000	212000	285000	324000	315000	206000	140-450 x 10^3

Table 2: Literature review of case reports about dapsone-induced agranulocytosis in patients with leprosy

	YEAR	LOCATION	AGE	GENDER	ETHNICITY	TIME UNTIL SYMPTOMS APPEARANCE	CLINICAL PRESENTATION	DIAGNOSIS	MANAGEMENT	CHANGES IN MDT	HOSPITALIZATION	OUTCOMES
Current paper	2015	Brazil	61	F	Non-Caucasian	After 34 days	Fever Chills Adynamia Odynophagia Paleness	-	Suspension of MDT ; Amoxicillin-Clavulanate; Ciprofloxacin; Filgastrim	Rifampicin and Clofazime Replaces Dapsone; Ofloxacin + Rifampicin + Minocycline	No	Patient improved after 8 days
Silva *et al.*	2011	Brazil	28	M	Non-Caucasian	before 30 days	Odynophagia Fever	Severe febrile neutropenia	Suspension of MDT; broad spectrum antibiotic; folic acid	*	*	Patient improved after 16 days
Carneiro *et al.*	2011	Brazil	56	F	Non-Caucasian	After 8 weeks	Odynophagia Fever Dry cough Progressive dyspnea Respiratory-dependent chest pain	Tonsillitis	Suspension of DDS; amoxicillin clavulanate; Ciprofloxacin; Cefepime; Oxacillin; Filgastrim	Ofloxacin + Clofazime + Minocycline	Yes	Patient improved after 14 days
Silva *et al.*	2009	Brazil	28	F	Non-Caucasian	After 35 days	Fever Chills Odynophagia	Tonsillitis	Suspension of DDS ;Figastrim; benzathine penicillin; broad spectrum antibiotic	Restarted Rifampicin (600mg/month) and Clofazimine (100 mg/day)	Yes	*
Ranawaka *et al.*	2008	Sri Lanka	21	M	Non-Caucasian	After 19 weeks	Fever Odynophagia	Hemolytic anemia and hepatitis	Suspension of MDT; broad spectrum antibiotic; Filgastrim. Linezolid; Amikacin; Filgastrim; Prednisolone; Vasopressors Cefotaxime; Prednisolone	*	Yes	Patient improved after 8 days
Mishra e Chhetia	2006	India	25	M	Non-Caucasian	*	High fever; Tachypnea; Hypotension; Pharyngeal congestion; Dyspnea; Cough; Lymphadenopathy	Pneumonia	Linezolid; Amikacin; Filgastrim; Prednisolone; Vasopressors	*	Yes	Patient improved after 7 days
Bhat e Radhakrishnan	2003	India	60	M	Non-Caucasian	After 21 days	Low fever; Cough; Dyspnea; Chest pain	Pneumonia	Cefotaxime; Prednisolone	*	Yes	Death

According to the literature, hospitalization is required in some cases, which did not happen in our case because of the early intervention (Table 2).[5]

Considering a reduced risk of agranulocytosis development and in accordance with Carneiro *et al.* (2011),[5] our aim was not to question DDS therapy for leprosy, but to stimulate clinical awareness of its risks by showing non-specific symptoms of agranulocytosis. We also highlight the need for laboratory test monitoring patients treated with DDS in order to favor the early treatment of this adverse effect, thus enhancing patient prognosis. ❑

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Pseudoxanthoma elasticum-like papillary dermal elastolysis*

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Dear editor,

Elastic fibers are important components of the extracellular matrix of the connective tissue. The elastic system comprises oxytalan and eulanin fibers. Various acquired and hereditary conditions are associated to changes of these fibers, among which we highlight pseudoxanthoma elasticum-like papillary dermal elastolysis (PXE-PDE).

PXE-PDE is an acquired condition, that is manifested by multiple asymptomatic, sometimes itchy, non-follicular yellow or normochromic papules, with a diameter of 2-3mm, symmetrically distributed, that can coalesce into "cobblestone" plaques with predilection for the neck area, but also supraclavicular, axillary, flexor aspect of forearms, inframammary and lower abdomen regions. The lesions develop slowly, in months to years, and are clinically similar to pseudoxanthoma elasticum. However, they are differentiated by histopathology and for the lack of systemic involvement.[1]

Histopathology features include loss or marked reduction in the papillary dermis elastic fibers.

Prevalence is believed to be underestimated for this rare condition, what reinforces the importance of better clinical and histological identification by dermatologists and pathologists, to avoid mistaking it for pseudoxanthoma elasticum. [2]

The patient was a 71-year-old woman who presented with

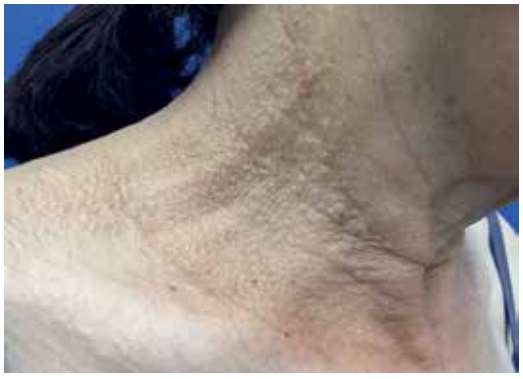

Figure 1: Normochromic non-follicular papules in the cervical region

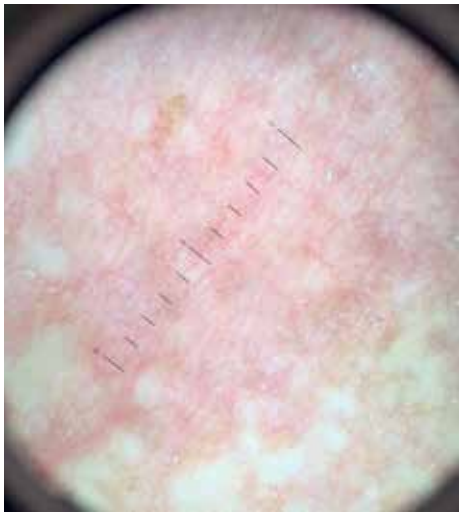

Figure 2: Linear vessels on dermoscopy