

## CASE REPORT

# Benign symmetrical lipomatosis and pellagra associated with alcoholism\*

## Lipomatose simétrica benigna e pelagra, associadas ao alcoolismo

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**Abstract:** Paciente masculino, 42 anos, etilista crônico, apresentando quadro de tumorações em região cervical e ao redor dos ombros, lesões eritemato-violáceas, descamativas e algumas lesões bolhosas, nas áreas fotoexpostas dos membros superiores e inferiores. Baseado no quadro clínico e nos exames complementares, foi estabelecido o diagnóstico de pelagra associada à lipomatose simétrica benigna, sendo ambos os quadros justificados pelo etilismo crônico. Tratado com reposição de complexo B intravenoso e orientado quanto à importância da abstinência alcoólica, apresentou remissão completa do quadro cutâneo, porém sem alteração da lipomatose.

Palavras-chave: Alcoolismo; Lipomatose simétrica múltipla; Niacina; Pelagra

**Resumo:** A 42-year-old male patient, alcoholic, presented showing signs of tumors in the neck and around the shoulders, scaly, erythematous-violaceous lesions and some bullous lesions in sun-exposed areas of upper and lower limbs. Based on clinical features, laboratory tests and imaging studies we have established the diagnosis of pellagra associated with benign symmetrical lipomatosis, both justified by chronic alcoholism. Treated with intravenous B-complex and oriented about the importance of alcohol withdrawal, the patient showed complete remission of skin lesions, but with no change in the lipomatosis.

Keywords: Alcoholism; Lipomatosis, multiple symmetrical; Niacin; Pellagra

### INTRODUCTION

Pellagra is a disease derived from inadequate niacin and tryptophan dietary intake.<sup>1,2,3</sup> It mainly affects chronic alcoholics, gastrointestinal disease and severe psychiatric disorder patients.<sup>1,3</sup> Its clinical presentation is a classical triad: dermatitis, diarrhea and dementia.<sup>1,3</sup>

Benign symmetrical lipomatosis (BSL) is a rare illness, of which few cases have been reported. Its etiology is still unknown, but the presence of dysfunctional mitochondrial respiratory enzyme and association with alcohol-induced endocrinopathy have been described.<sup>4,5,6,7</sup> It is manifested by large fatty masses with symmetrical distribution involving the head, neck and shoulder areas.<sup>1,5,8,9</sup> Most of the affected patients are male, between 30 and 60 years of age and chronic alcoholics.<sup>4,5,9</sup>

Our patient presented the association of benign symmetrical lipomatosis type 1 and pellagra, diseases

that have in common the classical association with alcoholism as the triggering factor. Thus, although rare, the presence of both cutaneous manifestations in the same patient is justifiable.

### CASE REPORT

A 42-year-old male patient, construction worker, reported tumors in the neck and shoulder regions, asymptomatic for five months as well as pruriginous lesions on upper and lower limbs for three weeks. He also informed he had had unmeasured fever episodes. He denied diarrhea, weight gain and family history of similar disorders. An alcoholic for 29 years, he used to drink *cachaça*, a sugar cane brandy (1000 ml/day), having stopped 15 days before; he also had hypertension (regular use of captopril, 50 mg/day).

At the time of examination he presented slow

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thinking, blood pressure 150 x 80 mmHg, regular cardiac rate of 80 bpm and was afebrile. His liver was painless and could be palpated at a distance of 3 cm from the right back border. There was a palpable lymph node in the left retroauricular region. No macroglossia or relevant alterations were detected in the examination of abdomen, thorax and limbs. The dermatological examination showed scaly, erythematous-violaceous lesions with irregular limits on the forearms, legs, back of hands and feet and some bullous lesions on the legs, which spared areas protected from the sun. Multilobulated tumors were also observed, with an elastic and soft consistency, painless, affecting the cervical and shoulders area, as well as hyperplasia of the parotid glands (Figures 1 to 4).

The laboratory investigation revealed normal hemogram, glycemia, electrolytes, lipid profile, normal kidney and thyroid functions, and elevation of the uric acid level (7.9 mg/dl). Liver function presented elevation of gamma-glutamyl transferase (194mg/dl), with normal levels of transaminases, alkaline phosphatase, total bilirubin and fractions, total protein and fractions. Serologies were negative for HIV-1/HIV-2, Hepatitis B and C. Total abdominal ultrasound without alterations. Computerized tomography of the thorax did not reveal mediastinal involvement, while computerized cervical tomography showed multiple lipomas of homogeneous aspect up to the sternal notch (Figure 5).

Based on the clinical presentation and supplementary tests, the diagnosis of Pellagra associated with Benign Symmetrical Lipomatosis was made, both justified by chronic alcoholism. The patient was treated with abstinence from alcohol and intravenous B complex replacement, with complete remission of the cutaneous symptoms, although without alteration of lipomatosis.



**FIGURE 1:** Cervical lipomatous masses and scaly, erythematous-violaceous lesions with irregular limits only on sun-exposed areas of forearms and back of hands.

## DISCUSSION

Pellagra is a disease caused by cellular deficiency of niacin (vitamin B3).<sup>1,2</sup> It results from inadequate niacin and tryptophan dietary intake.<sup>1,2,3</sup> The most affected populations are: chronic alcoholics, gastrointestinal disease and severe psychiatric disorder patients.<sup>1,3</sup> In the case here presented there was history of chronic alcoholism. Other possible causes are functioning carcinoid tumors, Hartnup disease and drugs such as isoniazid, 6-mercaptopurine, 5-fluoracil, pyrazinamide, ethionamide, hydantoin, phenobarbital and chloramphenicol.<sup>1,2,3</sup>

Its clinical presentation is a classical triad: dermatitis, diarrhea and dementia.<sup>1,3</sup>

Dermatitis is manifested by erythema and superficial, bilateral and symmetrical desquamation, similar to sunburn, sometimes with vesicles and blisters, pruritus and a burning sensation; it is localized in areas exposed to the sun, heat, friction or pressure.<sup>1,2,3</sup> They involute with brown-red hyperpigmentation and exacerbation may occur with further exposure to the sun.<sup>1</sup> It is frequently present on the face as a symmetrical eruption in the form of a butterfly's wings and on the anterior cervical region as a well-defined eruption known as "Casal's necklace".<sup>1</sup> Asymmetrical lesions may appear on sites of old lesions or stasis.<sup>1</sup> The case here reported presented pruriginous, scaly erythematous-violaceous lesions on sun-exposed areas of the limbs and bullous lesions on the legs. However, there was no involvement of the face nor of the cervical region.

Gastrointestinal symptoms are present in around 50% of the cases, usually pain, diarrhea and/or achlorhydria, a symptom complex that was not shown by our patient.<sup>1,2,3</sup>

The involvement of the central nervous system occurs in prolonged niacin deficiency.<sup>8</sup> In mild cases, it



**FIGURE 2:** Scaly, erythematous-violaceous lesions with irregular limits and some bullous lesions on the legs and dorsum of feet, sparing the area where the sandal protects from the sun



FIGURE 3: Multilobulated tumoral formations, with an elastic, soft and painless consistency involving the cervical region and shoulders area



FIGURE 4: Hyperplasia of parotid gland and lipomatous masses involving the cervical region and shoulders area

is manifested by unidentified mental disorders, mild depression or apathy.<sup>1</sup> In advanced cases frank disorientation, agitation or severe neurological symptoms may occur.<sup>1,2</sup> Peripheral neuritis and myelitis are occasionally found.<sup>1</sup> The patient had only slowed down thinking.

The histopathological examination is not specific and was therefore not done. There are no available laboratory tests for a definitive diagnosis, although diminished levels of N-methylnicotinamide and pyridone in the urine indicate niacin deficiency.<sup>1,2</sup>

Drug exposure, porphyria, photodermatitis, lupus erythematosus and actinic reticulosis play a role in differential diagnosis.<sup>1</sup>

The treatment of severe cases should be done with niacin replacement at the dose of 50-100mg, IV, 1-2 x/d.<sup>1</sup> In milder cases, oral niacin is utilized with a fractionated dose of 500mg/d.<sup>1</sup> Improvement is noticed within 1-2 days.<sup>1</sup> Prevention is based on food reeducation and avoidance of alcohol intake.<sup>2</sup> Our patient was treated with abstinence from alcohol and complex B intravenous replacement (since our hospital did not have niacin), which resulted in improvement of the skin symptom complex within two days.

The diagnosis is based on patient history and clinical presentation (classical triad)<sup>2</sup>. Our patient presented history of chronic alcoholism, excessive sun exposure due to his occupation, characteristic skin lesions and complete remission with treatment, confirming the pellagra diagnosis.

Benign symmetrical lipomatosis is usually a sporadic illness, probably derived from mitochondrial dysfunction.<sup>1,4</sup> However, some family cases have been observed, most of them with autosomal dominant inheritance.<sup>1,4</sup>

Also known as Multiple Symmetrical Lipomatosis, it is manifested by large fatty masses, not encapsulated and painless, with a symmetrical distribu-

tion involving the head, neck and shoulder areas.<sup>1,4,5,8,9</sup> When the mediastinum is involved, complications related to a mass effect may occur.<sup>1,4,8,9,10</sup> Our patient presented involvement of the cervical region up to the sternal notch, without involvement of the mediastinum.

Like our patient, the majority of affected patients are male, between 30 and 60 years of age, and 60 to 90% of them are chronic alcoholics, which may justify several associated disorders such as: severe autonomic and peripheral neuropathy, malignant tumors of the upper airways, macrocytic anemia, hyperuricemia, alcoholic hepatopathy.<sup>1,4-6,8-10</sup> In addition, it may be associated with: hypertriglyceridemia,



FIGURE 5: Cervical Region Computerized Tomography revealing the presence of multiple lipomas of homogeneous aspect in the cervical region (arrows), with no evidence of a compressive effect

increased HDL-cholesterol, glucose intolerance and renal tubular acidosis.<sup>1,4,10</sup>

The etiology is still unknown, although the presence of mitochondrial respiratory enzyme disorder, leading to a moderate dysfunction of fat metabolism has been described.<sup>4,5,7</sup> Gonzales-Garcia *et al* (cited by Hirose A, *et al.*, 2006) affirmed that a defect in stimulated adrenergic lipolysis would lead to adipocyte autonomy in BSL and that alcoholism seems to decrease adrenergic receptors, inducing disorder in the catalytic unit of mitochondrial DNA adenyl cyclase in adipocytes, which would justify the relevance of alcohol consumption for the onset of the disease.<sup>4,6,10</sup> The lipomatous tissue of these patients shows increased activity of lipase lipoprotein, a possible explanation for the increased HDL cholesterol levels of these patients.<sup>1</sup>

BSL may present two clinical phenotypes: type 1 and type 2. Type 1, also known as Madelung's Disease, affects men and presents an accumulation of adipose tissue around the neck, upper back, shoulders and upper part of arms, in a deformity known as "horse's collar".<sup>4,6,9</sup> Type 2, also called Launois-Bensaude Syndrome, affects men and women equally, with adipose tissue accumulation in a typically feminine pattern: upper back, deltoid muscle, upper limbs, hips and outer thighs, resulting in a "pseudo-athletic appearance".<sup>4,6,9</sup> According to this classification, our patient fits type 1.

The diagnosis is clinical and based on the typical distribution of adipose tissue on the trunk and proximal regions of extremities.<sup>4,6</sup> Imaging resources (Computerized Tomography or Magnetic Resonance) are indicated to characterize the nature and extension of the disease in cases where there is suspicion of malignancy, in the presence of cervical lipomatous

masses of large dimensions associated with a symptom complex suggestive of compression or at the pre-operative evaluation.<sup>4</sup>

Malignization is rare and should be suspected in the presence of lipomatous masses with heterogeneous aspect in the imaging examination.<sup>4,6</sup> In this case a biopsy is indicated to exclude the hypothesis of liposarcoma or malignant degeneration.<sup>4</sup>

Differently from lipomas, as the histopathological examination shows, the adipose tissue is not encapsulated, involves adjacent structures and is characterized by adipocytes of normal size or smaller than expected, with proliferation of fusiform cells, suggesting localized recruiting and differentiation of adipocytes.<sup>6,10</sup> The biopsy was not performed, as the typical clinical picture presented was sufficient for a conclusive diagnosis and the lipomatosis had a homogeneous aspect in the computerized tomography.

The treatment is difficult and based on alcohol abstinence for prevention of lesion progression.<sup>4,6,9</sup> Surgical excision or liposuction may be performed in some cases, but recurrence is common, as performing a complete excision is complicated.<sup>1,4,6,10</sup> Our patient continues maintaining alcohol abstinence, without progression of lesions. However, due to the unaesthetic appearance of lesions and his interest in correcting them, he was referred to the Plastic Surgery Department for surgical resection evaluation.

Benign symmetrical lipomatosis is a rare illness, with few described cases. Our patient presented the association of benign symmetrical lipomatosis type 1 and pellagra, diseases that have in common the classical association with alcoholism as the triggering factor. Therefore, although rare, the presence of both cutaneous manifestations in the same patient is justifiable. □

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