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RESEARCH ARTICLE

NECROBIOSISLIPOIDICA IN TYPE 2 DIABETES:CLINICAL CASE AND REVIEW OF THE LITERATURE

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Abstract

Necrobiosis lipoidica is a rare chronic granulomatous disease, often associated with diabetes mellitus. It is due to collagen degeneration with risk of ulceration. Necrobiosis lipoidica affects 0.3 to 1.2% of diabetic patients, mainly in the leg. Its etiology is not yet well understood. The diagnosis is usually made clinically but a skin biopsy may be necessary in case of atypical lesions. The evolution is chronic with ulceration and degeneration into squamous cell carcinoma as the main complications, which remains exceptional. Several therapies have been proposed: topical corticosteroids in the first instance, but no treatment has proven to have a lasting effective response. Diabetes control does not seem to influence the evolution of the disease.

Introduction:-

Necrobiosislipoidicais a rare chronicgranulomatousdisease, oftenreported in cases of diabetesmellitus, especially type 1. It is due to a degeneration of collagenwith a risk of ulceration but itsetiology has not yet been elucidated.

Today, the broaderterm "necrobiosislipoidica" encompasses all patients with the sameclinicallesionsregardless of the presence or absence of diabetes.

In thisworkwe report a case of necrobiosislipoidica in a patient followed for insulin-requiring type 2 diabetes.

Based on the present case, we have tried to review the epidemiology, pathophysiology and varioustherapeuticmodalities of thispathology.

Observation:-

A 38-year-old female patient, known to be type 2 diabetic for 14 years, chronicallyunbalanced, with no otherassociatedpathologicalhistory, presentedwithasymptomatic skin lesions of the legs, the history of which dates back 3 yearswith the installation of popular lesionsprogressivelyincreasing in size.

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The generalexaminationrevealed a hemodynamically and respiratory stable patient, apyretic, with a weight of 70 kg and a height of 163 cm, with a body mass index of 26.34 kg/m2. The fastingblood glucose levelwas 1.45 g/l and the postprandial blood glucose levelwas 2.90 g/l, with a glycatedhemoglobin (HbA1C) of 14%.

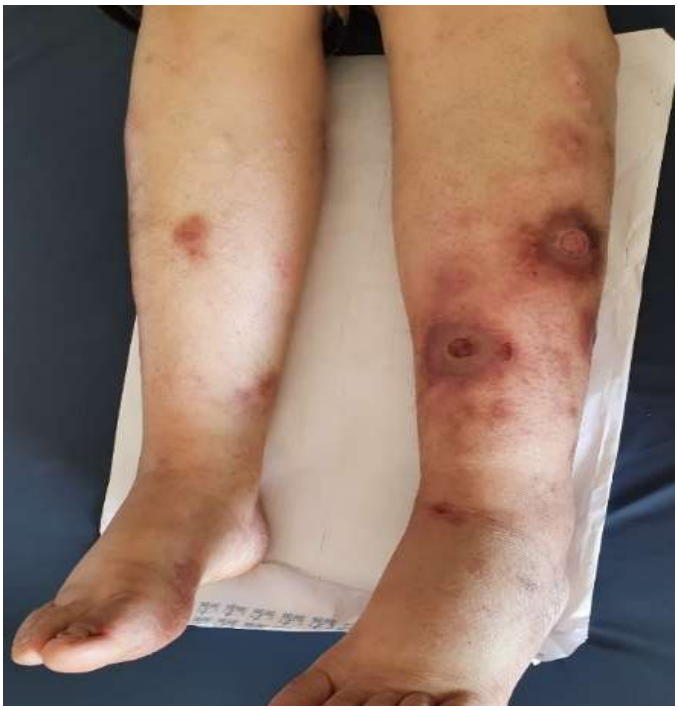
The dermatologicalexaminationrevealedgrey to blackishhyperkeratotic plaques on the axilla, suggestingacanthosisnigricans, associatedwithatrophic orange-red, smooth, telangiectatic, painless, locallyulcerated plaques of centimetric size, the largest of whichwas 6 cm long, located on healthy skin on the anterior aspect of the legs (Figs. 1 and 2).

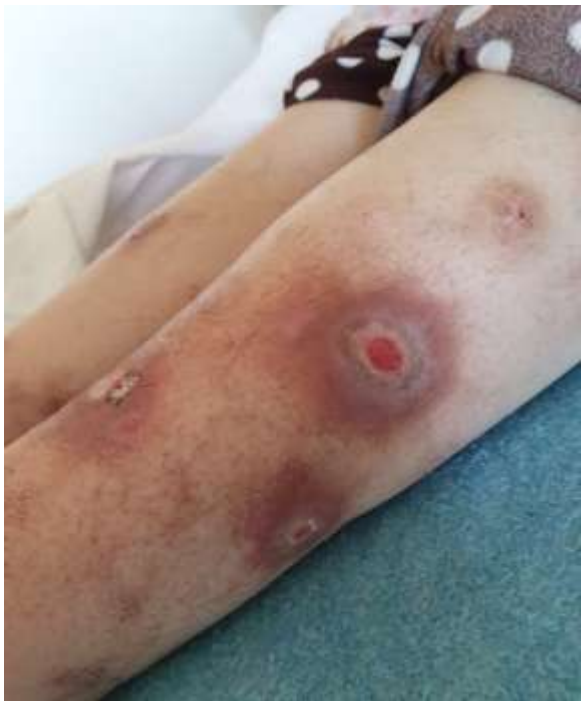
A skin biopsywasperformed but wasinconclusive, and the diagnosis of NL wasretained in view of the typicalappearance of the lesions.

The workup for degenerative complications revealed minimal bilateralnonproliferativediabeticretinopathy. Grade 1 diabeticnephropathywith a GFR of 118 ml/min wasidentified, but the urine microalbuminuria test wasnegative. The DN4 score wasrated at 3/10 revealing the absence of anyperipheralneuropathy. Liverfunction tests were normal.

The patient was put on insulintherapy (basal bolus regimen) withdermocorticoidsassociatedwith a healingcream and a fatty dressing for the ulceratedlesions.

The 6-month follow-up showed a betterglycemic control with HbA1C at 8% with a slightimprovement of the skin lesionsrequiringcontinued monitoring of the skin dressings. (Fig n°3)





Figures (1,2):- Atrophic, smooth, telangiectatic orange-red plaques, ulcerated in places suggestive of lipoidnecrobiosis.

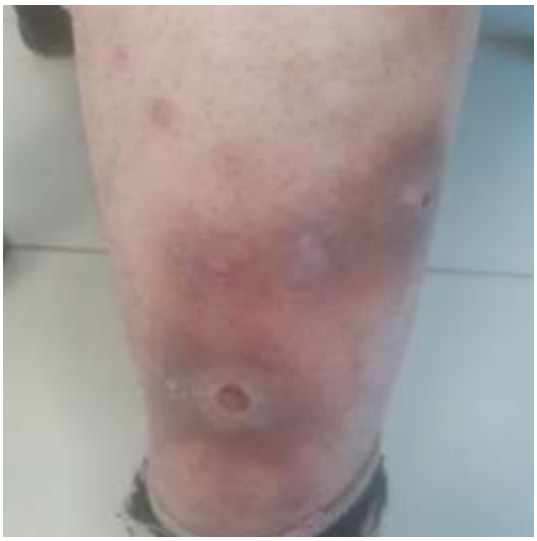


Figure 3:- Appearance of the lesionsafter 6 months of evolution (local corticoïdes, dressing).

Discussion:-

Necrobiosislipoidica, originallyknown by the eponym Oppenheim-Urbachdisease, is a rare inflammatorygranulomatousdermatosisdescribed as diabeticdermatitislipoidicaatrophicansin 1929, by Oppehheim. However, in 1932, Urbachrenamed the diseasenecrobiosislipoïdicadiabeticorum (NLD) [1].

Indeed, epidemiologysuggests an association withdiabetesin 10-40% of cases, or even more, althoughthis association has been questioned over time [4].

Currently, the broaderterm "LipoidNecrobiosis" (LN) encompasses all patients with the sameclinicallesionsregardless of the presence or absence of diabetes [1, 3].

The prevalence in the diabetic population isaround 0.3% to 1.2% [1, 5].

NL precedesdiabetes in about 14% of cases and appearssimultaneouslyin 24% of cases and occursafter the diagnosis of diabetesin 62% of cases. There is no provenrelationshipbetween the level of glycemic control and the likelihood of developing NL [1,4].

However, familial cases without association withdiabetes have been described [7]. Otherriskfactors for NL includegranulomaannulare, sarcoidosis, ulcerativecolitis and Crohn'sdisease [5], rheumatoidarthritis or thyroiddisease [2]. However, no linkwith infection or malignantpathology has been demonstrated [2].

The averageage of onsetisusuallybetween 30 and 40 yearswith a clearfemalepredominancein 77% of cases [2]. Our patient was 38 yearsold.

The pathophysiology of NL remainsunknown but severaletiopathogenichypotheses have been proposed over the years[3,5,6] :
- therewas a high association betweendiabetes and necrobiosislipoidica, soseveralstudiespointed to diabeticmicroangiopathy as the main etiologic factor especiallysince the ocular and renalvasculature changes in diabetics are comparable to the vascularalterations in NL.
- Somesuggestthatantibody-mediatedvasculitiswithdeposition of immunoglobulins, C3 and fibrinogen in vesselwallsmayinitiatebloodvascular changes and laternecrobiosis [5].
- Othertheorycentered on collagenabnormalitieswithdefectivecollagenfibrilscouldexplain the thickening of the basal membrane in NL.
- There maybealteredneutrophil migration leading to increasednumbers of macrophages, possiblyexplaining the formation of granulomas in NL.
- Tumornecrosis factor (TNF)-alpha has been noted to have a potentially crucial role in diseasessuch as NL and disseminatedgranuloma. It isfoundelevated in serum and skin of patients withthese conditions [1].

The clinicalpresentation of NL is distinct but there are stillmanyatypical manifestations. Granulomaannulareis the most important differentialdiagnosis. Sarcoidosis, xanthoma, morphea, pyodermagangrenosum, tertiary syphilis, radiodermatitis, atypicalmycobacteriosis, and actinicgranulomamayalsobeconsidered [5].

The diagnosis of NL isusually made clinically, but skin biopsymaybenecessary in case of atypicallesions [1,6].

Histologicalexaminationreveals a granulomatousinfiltratethroughout the dermis. This infiltrateisarranged in a palisadearound the reworked connective foci and includes lymphocytes, dendrocytes, histiocytes, plasma cells as well as epithelioidcells and multinucleatedgiantcells [7].

Granulomas are organized in layers and are mixed with plaques of degenerativecollagen [1]. Vascularlesionscanbeobservedwithswelling of endothelialcells and thickening of bloodvesselwallsfrom the mid to deepdermis [1,9].

Direct immunofluorescence microscopy shows IgM, IgA, fibrinogen and C3 in the bloodvesselscausingvasculartthickening [1,9].

Regardingtherapeutic management, no treatment has been proven to be effective in NL.

In the absence of ulceration or symptoms, itisreasonable not to treat NL as up to 17% of lesionsmayresolvespontaneously. Compression therapycontrolsedema and promoteshealing in patients withassociatedvenousdisease or lymphedema [1, 10, 11].

If ulcerationoccurs, the principles of wound care for all diabeticulcersapply.

First-line treatment relies on potenttopicalcorticosteroids for earlylesions (clobetasolpropionate), and intra-lesionalinjectedcorticosteroids in active lesionboundaries. For inactive atrophiclesions, topicalsteroidsshouldbeavoided as theymayexacerbate the atrophy and increase the risk of new ulcerations [1]. Our patient was put on local steroids but withoutmuchefficacy.

Topicaltacrolimus (topicalimmunosuppressant) allowedregression of the inflammatory aspect and subsidence of the papular border with good clinicaltolerancewithout, however, achievingregression of the lesions [12],

Someisolated reports propose the use of topicalretinoids and psoralenscombinedwith ultraviolet therapy (Puvatherapy) [13]. Recently, photodynamictherapy has been described as another option in the management of NL [6,11].

Calcineurininhibitors, ciclosporin (2.5mg/kg/d) have also been usedsuccessfully in some cases especiallyulceratedlesions. The mechanism of action isto prevent T cell activation [12, 13].

Aspirin and dipyridamole have shown variable results. Different types of laser treatment have been described (pulseddyelaser, CO2 fractional laser) [18].

Unfortunately, none of the proposedtreatments has resulted in an effective and durable response. Surgical excision down to the fascia and variable thickness skin graftingremain the last therapeutic option for recalcitrant NL ulcers [6,12, 14].

The evolutionismostoftenchronic. The main and mostserious complication isulceration, whichoccurs in 1/3 of cases. Degenerationintosquamouscellcarcinomaisexceptional [17].

However, diabetic control does not influence disease progression. A studyconducted by Bhavik D et al in 2017 highlighting the paucity of qualityevidence on the relationshipbetweenglycemic control and NL development in diabetic patients [16]. Indeed, the data obtained in thisstudysuggestthatimprovingglycemic control can lead to resolution of NL in patients withdiabetesmellitus, particularly type 1 diabetics. There iscurrentlyinsufficientevidence to support or refutethis claim [16].

Our case shows a type 2 diabetic patient whodevelopedtypical NL lesions. The therapeutic management remainsdifficult and not consensual. In all patients, our focus shouldbe on ulcerprevention and if possible improvement of the aestheticappearance.

Conclusion:-

NL is a rare skin complication of diabetesmellitus, and itsdiagnosis and management are extremelydifficult. Skin lesions are best managedwith a multidisciplinary team (dermatology, endocrinology, infectiousdiseases, and wound care nurse).

Although the etiopathogenicmechanisms of NL remainpoorlyelucidated, significantknowledge has been gained about itspathophysiology and treatment. It wouldbebeneficial to have more randomizedcontrolled trials on the treatment of this condition.

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