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Pediatric necrobiosis lipoidica: case report and review of the literature

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Abstract

Necrobiosis lipoidica (NL) is a rare, granulomatous disease considered to be associated with diabetes. It is frequently seen in female and middle-aged patients and is rarely observed in children. We present a 14-year-old boy with poorly controlled type 1 diabetes who developed biopsy-proven NL. He had improvement, but not resolution of the plaque with improved glycemic control. Pediatric NL may be associated with diabetes and could be related to poor glycemic control. However, further investigation is warranted in this young population.

Keywords: diabetes mellitus, necrobiosis lipoidica

Introduction

Necrobiosis lipoidica (NL) is a rare, granulomatous disease, the exact etiology of which remains poorly understood [1]. It presents with yellow-brown to violaceous plaques, classically distributed bilaterally on the pretibial region [1–3]. Necrobiosis lipoidica has a strong propensity for female sex, with female patients representing upwards of 75% of patients in retrospective studies [3–5]. Necrobiosis lipoidica typically presents in middle age and diagnosis in children is uncommon [4,6,7]. Necrobiosis lipoidica is associated with diabetes mellitus (DM), typically type 1 DM, although both type 1 and type 2 DM have been associated with NL [5,7]. The strength of this association remains controversial as reported rates of NL patients who additionally have diabetes range from 11%-65% [1–3,5,7]. A diagnosis of NL in diabetic patients remains a rarity, estimated to affect only 0.3-1.4% of diabetic patients [3,8,9]. Of pediatric patients with type 1 diabetes, NL is even more uncommon, with an estimated prevalence of 0.06% in this population [10]. In addition to diabetes, NL has also been reported with thyroid disease, inflammatory bowel disease, rheumatoid arthritis, and sarcoidosis [1].

Case Synopsis

We present a 14-year-old obese male with type 1 diabetes who presented with a single indurated yellow-red plaque on his right shin for several months (**Figure 1**). He reported that it initially started

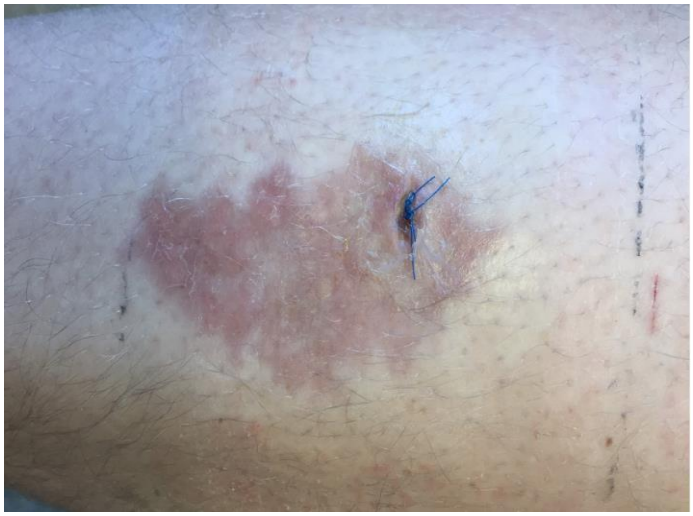

Figure 1. *Pre-tibial red-brown indurated plaque.*

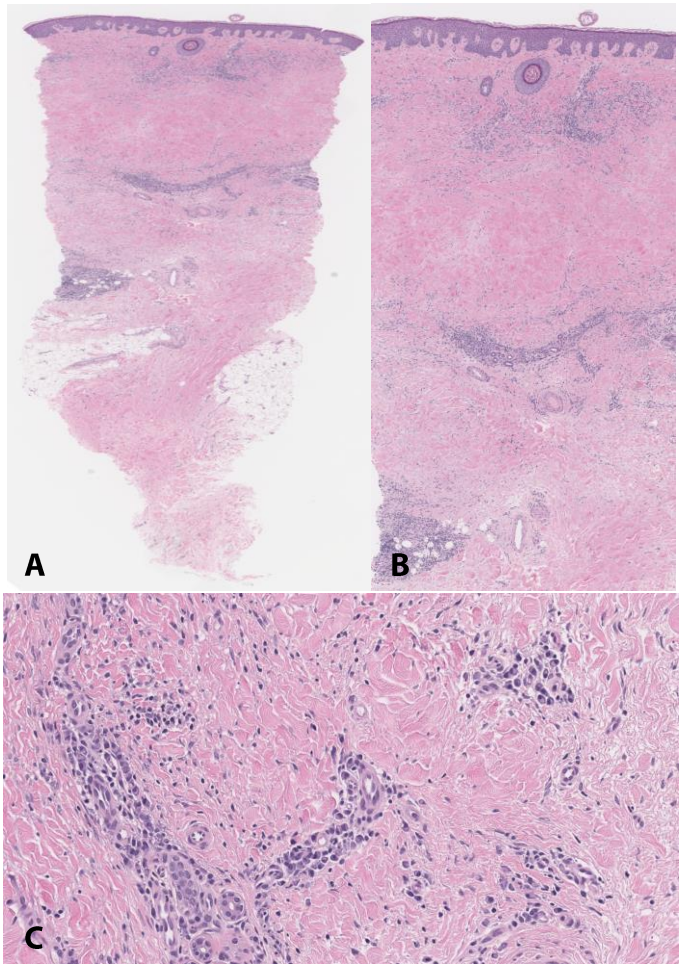

Figure 2. ***A, B)*** *Low power views show layers of altered collagen sandwiched between inflammatory cells.* ***C)*** *High power view shows an interstitial and perivascular infiltrate consisting of lymphocytes and plasma cells.*

as a smaller lesion, at a time when he had poor glucose control, and it had since grown.

Punch biopsy revealed palisading and interstitial granulomatous dermatitis with numerous perivascular plasma cells, and colloidal iron stain did not show increased mucin, consistent with necrobiosis lipoidica (**Figure 2**). The patient was then started on a daily regimen of topical fluocinonide under occlusion. At follow up after 6 weeks the patient demonstrated some clinical improvement, with flattening of the plaque, although he did not have complete resolution. He also had improved glucose control during this time and self-reported subjective improvement of the lesion with his glycemic control, even prior to initiating his topical corticosteroid treatment regimen. His hemoglobin A1C closest to the time of initial presentation was 9.3% and was later 8.1% near the time of his 6-week follow up.

Case Discussion

To the best of our knowledge there have only been 54 pediatric cases (age ≤18) of NL reported in the literature, largely through case reports as well as retrospective analyses that documented ages of individual patients. Characteristics of these reported cases are listed in **Table 1** [11-44]. This value may seem relatively inflated by the fact that NL is rare in children and diagnosis in pediatric patients often warrants publishing. Still, it can be compared to the cumulative many hundreds to thousands of adult cases recorded in the literature. Although some of the larger retrospective studies on NL have included pediatric patients in their cohorts, these studies additionally report a dominant prevalence of middle age patients, again highlighting the rarity of this diagnosis in children [4–6]. Interestingly, only four patients were age 10 or younger. Among the pediatric cases of NL reported, 48 (89%) were recorded as having a diagnosis of diabetes, much higher than any study of adults; 36 (67%) specifically had type 1 diabetes. Furthermore, 38 (70%) were female. Similar to these reported cases, our patient had type 1 DM and was a teenager, although his male sex makes him a relatively rarer case.

The precise pathogenesis of NL is unknown. An association with vascular insufficiency has been suggested. Study of microcirculation by Doppler flowmetry and oxygen partial pressure in NL lesions has demonstrated an altered microcirculation even in nondiabetics [45]. Glucose transporter 1 (*GLU1*) is expressed by the fibroblasts in areas of sclerotic collagen. This raises the possibility that a disturbance in glucose transport by fibroblasts may contribute to the histopathological features [46]. These features are variable, depending to some extent on the presence or absence of coexistent DM [47]. The palisading granuloma with necrobiosis is more typical of the diabetes-related variant, whereas a granulomatous sarcoidal type of reaction is more often a feature of nondiabetes-related necrobiosis.

Table 1. *Demographic information and diabetes of association of diabetes of reported pediatric patients with necrobiosis lipoidica.*

Variable	N (%)
Total Cases	54
Sex	
Female	38 (70%)
Male	15 (28%)
Unspecified	1 (2%)
Age	
Mean (range)*	14 (3-18)
Diabetes Association	
Any DM diagnosis	48 (89%)
DM1	36 (67%)
DM2	6 (11%)
MODY	1 (2%)
Unspecified DM	5 (9%)
No DM	6 (11%)

* Does not include 18 pediatric patients with unspecified ages.

Nevertheless, there is very considerable overlap and in the majority of cases one cannot predict on histologic grounds alone, which cases are, and which are not diabetes-related.

In a fully developed case, the characteristic features are present at the edge of the lesion. Histologically lesions show layers of altered collagen alternating with layers of inflammatory infiltrate, usually centered in the lower dermis, although the superficial dermis and subcutaneous fat may also be affected.

Glioma-associated oncogene 1 (GLI1), has been found to be expressed in a number of granulomatous skin disorders including NL. The explanation for this is not clear, but it suggests that inhibitors of GLI1 may be used in the treatment of the disease [48].

Standardized treatment of NL has not been established, and NL is difficult to treat [49]. In our case, we attempted treatment with topical corticosteroids, which was not fully successful. Aside from topical corticosteroids, other treatments commonly used for NL include intralesional corticosteroids, immunosuppressants, platelet inhibitors, phototherapy, occasionally surgery, and various biologic agents [49]. Although our patient's NL did not completely resolve with topical corticosteroid use, he did self-report improvement with better glycemic control, even prior to initiating treatment with topical corticosteroids. Although this improvement was only the subjective opinion of the patient and his parents, improved glycemic control has been observed to improve NL [50]. In our literature review, of the 48 pediatric patients with NL and DM, 13 were described as having "poor" glucose control at the time of NL presentation, with hemoglobin A1C values ranging from 9-14% [11,14,21,23,24,26-28,34,39,42,44]. Although the majority of cases did not report on glucose control at the time of NL presentation, this pattern suggests a link between glucose control and NL development. However, NL treatment by means of improved glycemic control remains controversial and warrants further study [50].

Conclusion

Based on our current understanding of NL in children, this diagnosis is rare and more often noted in female patients and in association with type 1 DM. Unfortunately, owing to this rarity, much of the pediatric NL data comes from individual case reports. Perhaps as a result, the available literature does not fully represent the NL pediatric population. For example, some of these above-mentioned articles focus only on cutaneous disease in diabetic children, thus perhaps underestimating the proportion of NL in non-diabetic children. Unlike in the adult population, large retrospective reviews of NL manifestations, associated diseases, and treatment viability have not been done in children. Additionally, in our pediatric patient, improved glucose management may have had some impact on NL resolution. However, in adults and children alike, there has not been sufficient research to validate any link between glycemic control and NL improvement.

Our report confirms that a diagnosis of NL should be considered in pediatric patients, particularly those with DM. We also emphasize the importance of further analysis of NL in the pediatric population and comparison with adults.

Potential conflicts of interest

The authors declare no conflicts of interests

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