Hypertrophic Keloid Formation in a Type 2 Diabetes Mellitus Patient (A Case Report)

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Abstract

Keloids are scars that extend beyond the original area of skin damage. They can develop after minor skin trauma in predisposed individuals. Many factors play a role in keloid scar formation, with certain systemic diseases being a risk factor for their development. Diabetes mellitus is a disease that affects a variety of organ systems including the skin. Multiple skin conditions have been implicated directly and indirectly with diabetes mellitus and their presence would often be a sign of insulin resistance or poor glycemic control. Here we present a case of hypertrophic keloid developing in a patient with Type 2 Diabetes Mellitus. The patient had no prior skin trauma, nor did she develop the lesions at the sites of insulin injection.

This raises the question of whether hypertrophic keloids might be associated with diabetes mellitus and whether recommendations for DM screening and guidance on use of insulin injections in those patients should be put in place.

Key words: Keloids, Hypertrophic, Diabetes, Insulin resistance

Abbreviations:
Diabetes Mellitus (DM),
Dipeptidyl peptidase 4 (DPP-4) inhibitors,
Angiotensin-converting enzyme (ACE) inhibitors

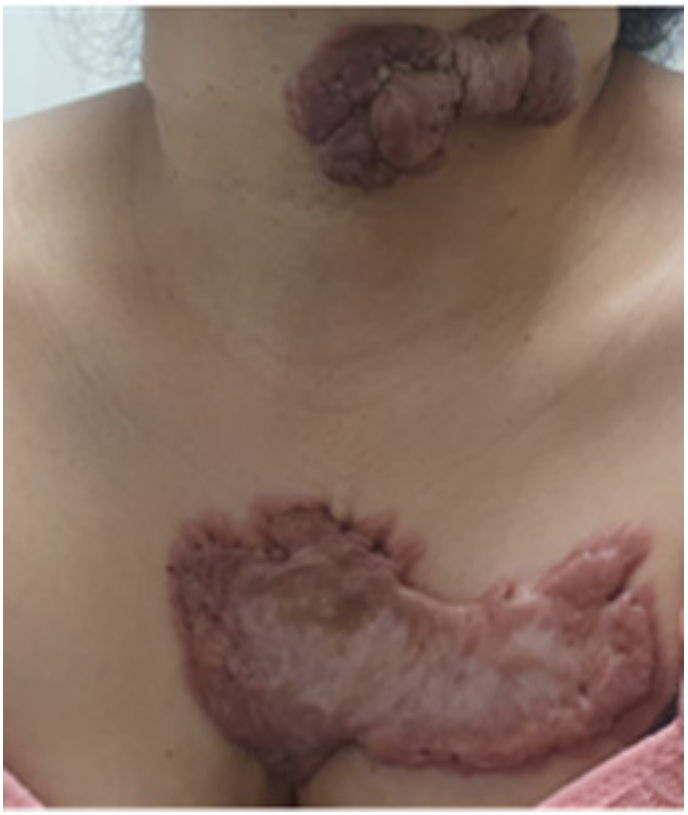
Introduction

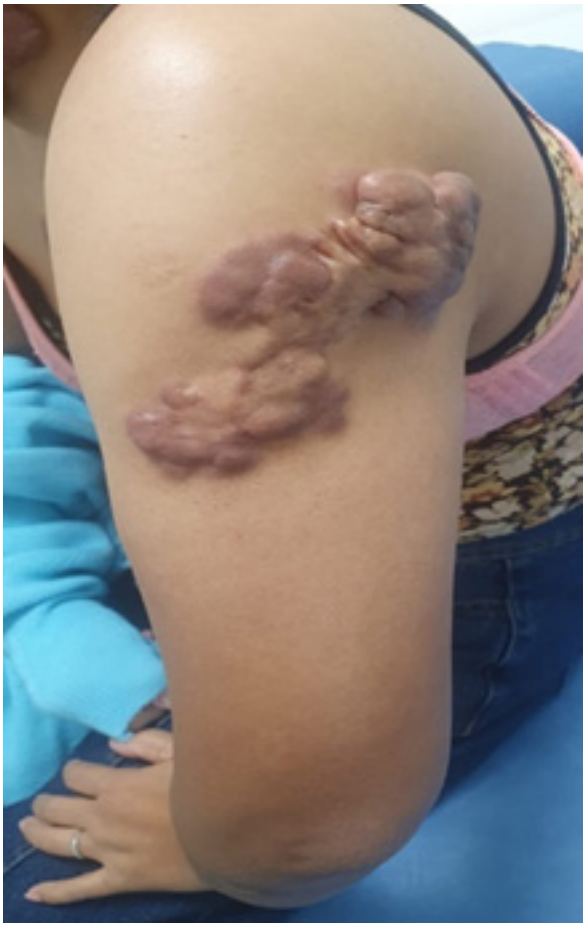
Diabetes Mellitus is a common endocrine disorder that can affect a variety of organs including the skin. Cutaneous manifestations can appear as the first sign of diabetes or may develop at any time in the course of the disease. They can have various health implications ranging from those that are cosmetically concerning to those that may be life-threatening. Thus recognizing these skin conditions may help in the diagnosis of diabetes, or may be followed as a marker of glycemic control (1).

Keloids are scars with an abnormal fibroproliferative wound healing response. They extend beyond the original wound boundaries and usually develop after dermal injury such as trauma, surgery, vaccination, burns, skin piercing, folliculitis, acne, and herpes zoster infection (2). Keloid formation has been theorized to result from altered growth factor regulation, abnormal collagen turnover, genetics, immune dysfunction, sebum reaction, and altered mechanics (3). Some lines of evidence suggest that pathologic scars are due to endothelial dysfunction that leads to vascular hyperpermeability during the inflammatory phase of wound healing which allows the flow of inflammatory cells and factors into the dermis, causing excessive local inflammation and fibrotic activity(2). Some systemic diseases like Hypertension have been implicated with keloid formation due to the damaging effect on vascular endothelium(4). Diabetes mellitus is also a contributor to endothelial dysfunction(2), however, not many studies have discussed an association of keloids with DM. In this report, we present a diabetes mellitus type 2 patient on insulin, who developed keloids in areas without prior trauma and away from insulin injection sites. We are contemplating the possibility of keloids being a sign of DM and whether screening for DM in such patients would be recommended.

Case presentation

A 50-year-old female with multiple comorbidities presented to our health center for a Diabetes Mellitus follow-up visit. The patient had newly diagnosed type 2 diabetes, hypertension and dyslipidemia. During our initial encounter with the patient, she mentioned pain and tightness due to keloid lesions. She was feeling sad due to the impact this lesion has had on her, especially in terms of choosing clothes and going out with her friends and family. Her keloids developed in 2017 with a small pimple over the chest that increased in size with time. She now has keloids located over the chest, left upper arm, and anterior aspect of the neck. The patient denies any preceding injury or triggering mechanical factor. She received triamcinolone injections multiple times but later she was unable to tolerate the pain and noticed that the keloids were growing further. After several months, she mainly felt a painful tightness on her anterior chest, with itchiness. She does not have a family history of Keloids in her first-degree relatives and does not shave the hair at the site of lesions. Her current medication regimens include Amlodipine, Rosuvastatin, Metformin and insulin glargine, which was started 1 month prior to this visit. On physical examination she was vitally stable, keloid lesions were found on previously mentioned areas.





Labs: HBA1C, fasting sugar. No acanthosis nigricans was seen over the neck or axilla, no other lesions were detected by skin inspection including the site of insulin injections. A dermatology consultation was done over the phone, and the patient was prescribed Cobblestone cream for symptomatic relief with advice to avoid rubbing the lesions. Education on insulin injection was provided, where she was advised to avoid injecting the insulin dose on sites of keloid, rotate insulin injection sites every day, and closely monitor if any skin changes develop on the sites of injection. The patient has been following with our clinic since October 2022 and no lesions developed on insulin sites. She was referred to plastic surgery for further management.

Discussion

Keloids are fibroproliferative disorders that result from atypical wound healing in predisposed individuals following trauma, inflammation, surgery or burns. They are characterized by scars that invade beyond the original wound boundary(1). The pathogenesis of hypertrophic keloids, although partially understood, involves a dysregulation in one or more of the wound healing phases. Many cell types, cytokines and growth factors participate in pathologic scarring. There is some evidence suggesting that vascular endothelial dysfunction leads to vascular hyperpermeability during the inflammatory phase of wound healing. This leads to flow of inflammatory cells and factors into the dermis, resulting in dysfunctional fibroblast activity. Inhibiting this abnormal blood vessel regulation and vascular permeability could be a key therapeutic approach for keloids(2).

A retrospective analysis study was performed to see whether keloids were purely cutaneous or correlate with certain systemic conditions, so they compared prevalence of keloids in certain medical conditions against the general population (3). Results showed that participants with keloids had a higher prevalence of hypertension and obesity compared to the general population however there was no significant difference in the prevalence of diabetes compared to the general population. Although no such difference was reported, another paper showed an interesting familial association of keloids with diabetes mellitus in three successive generations (4).

Hypertension may be associated with both the development of keloids and hypertrophic scars and their clinical severity. This is reflected through the damaging effect of hypertension on vascular endothelium and the state of hyperpermeability (5,6). Given that multiple medical conditions are associated with blood vessel disruptions, including diabetes mellitus, it would seem likely that they can be a predisposing factor for keloids and thus proper control of these diseases might be a step towards prevention of such abnormal scars.

There are genetic, patient, local, systemic, and lifestyle-related factors implicated in the development of keloid scars. They can occur sporadically or show familial tendency with development appearing to be higher in individuals of African or Asian ancestry (7,8). Hormonal factors associated with puberty may also play a role and there are several reports of worsening of keloids during pregnancy (9,10). Intradermal administration of vaccines can also rarely cause pathologic scarring due to dermal injury and subsequent inflammation (11). Mechanical stretching force is an important trigger in keloid generation as well. In one study they mentioned the chest region being involved with keloid due to the traction in that area (5). Although our patient developed keloid in the chest area, she also had keloids in other regions so the possibility of local traction in these areas cannot be definitely predicted.

Diabetes mellitus (DM) can affect a variety of organs including the skin. Between Thirty and seventy percent of patients with diabetes mellitus (both 1 and 2), present with a cutaneous complication of diabetes mellitus at some point during their lifetime. Such skin changes can offer insight into patients' glycemic control and may be the first sign of metabolic derangement in undiagnosed patients with diabetes. Some skin manifestations are a direct effect of DM, others appear in association with autoimmune types of DM, and others from effects of the DM medications. Some of these skin conditions include Acrochordons, Acanthosis Nigricans, Hidradenitis Suppurativa, Vitiligo, and skin infections (12). DM medication skin manifestations include those associated with subcutaneous insulin injection including lipoatrophy, lipohypertrophy, and post-inflammatory hyperpigmentation with localized Acanthosis Nigricans being an uncommonly reported cutaneous adverse local effect (13). There was a case reporting keloid scars appearing after insulin injections in a diabetic patient (14). However, our patient did not develop any lesions in the site of insulin injection. Moreover, a retrospective analysis showed that insulin therapy may be efficacious in preventing hypertrophic scars and in improving the scar quality (15).

Although each skin condition associated with diabetes mellitus may respond to a variety of specific treatments, many will improve with improved glycemic control. This raises the question of whether the same can be said about keloids and their possible connection to diabetes mellitus. Discussions on prevention of keloids in literature have mainly targeted the pathophysiology of the scar formation where the main strategies were minimizing local skin tension and reducing inflammation (16). In skin wound healing, which has definite, orderly phases, diabetes mellitus leads to improper function at all stages, and it is a known cause of microvascular complications (17,18). This disease mechanism might therefore guide us toward preventing keloid scar formation through again, proper glycemic control in diabetic patients. It is also noteworthy to mention that certain medications used in

diabetes mellitus have been reported in literature to play a role in managing keloid scars. One study revealed that dipeptidyl peptidase-4 inhibitors suppressed the onset of hypertrophic scars or keloids after surgery in humans (19). Two case reports have mentioned the role of Angiotensin Converting enzyme Inhibitor Enalapril in treatment of hypertrophic scar and Keloid, where the patients showed marked recovery after its use (20).

Our case therefore brings forth the possibility of hypertrophic scars or keloids as being a warning sign for diabetes mellitus. It raises the question of whether we should screen for diabetes mellitus in patients with keloid, and whether any preferred medications, like DPP4-Inhibitors and ACEI, should be considered from the beginning to reduce the size of the keloid. It also raises the issue of insulin and whether it should be avoided if the patient develops lesions at the site of injections. Also worthy of note is whether monitoring of keloids in diabetic patients should be done, and whether more frequent monitoring is needed in those requiring insulin. Thus, recommendations need to be put in place for proper guidance.

Conclusion

Many local and patient-related factors have been implicated in the formation of Keloid scars, including endothelial dysfunction. Diabetes mellitus is associated with multiple cutaneous presentations, and it is a known contributor to endothelial dysfunction. Thus, larger observational cohort studies are needed to decide whether screening for DM is necessary in patients with keloids. In addition, we want to emphasize the role of certain medications like DPP-4 inhibitors and ACE inhibitors and whether they should be used as first line in diabetic patients who develop keloids. Finally, our case highlights the importance of establishing recommendations for insulin use in patients with keloids, especially in regards to frequency of monitoring injection sites, and also clearly defining whether there is a risk imposed with insulin.

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Statement of Ethics
Consent was obtained from the patient.
Declaration of interest
The authors report no conflicts of interest.
Authors contribution:
All authors contributed equally to writing the manuscript.

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