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Case Report

Newly diagnosed type II diabetes mellitus presenting with localized itch

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ABSTRACT

Type II diabetes is caused by insulin resistance resulting in high blood sugar levels. Although the typical symptoms of diabetes are described as polyuria, polydipsia and fatigue as many as 60% of newly diagnosed patients with type II diabetes are asymptomatic. Here authors present a case of a 39-year-old male patient who presented with localized pruritus affecting the medial aspects of his forearms and upper legs as the sole symptom of newly diagnosed type II diabetes mellitus. The itch symptom markedly improved on significantly reducing his dietary intake of sugars and with the use of metformin. Authors hope to alert clinicians to consider the possibility of underlying diabetes in such presentations to enable swift diagnosis and consequent treatment. It is unusual to find patients presenting with localized itch without any corresponding cutaneous manifestations as a presentation of type II diabetes.

Keywords: Itch, Localized, Pruritus, Type 2 diabetes

INTRODUCTION

Type II diabetes is caused by insulin resistance resulting in raised blood sugar levels. In the USA, more than 30 million people have diabetes (about 1 in 10) and 90 to 95% of whom have type II diabetes.[1] Although the typical symptoms of diabetes are described such as polyuria, polydipsia and fatigue as many as 60 % of newly diagnosed patients with type II diabetes are asymptomatic.[2] Skin disorders are commonly associated with diabetes, in one study of 750 diabetic patients just over 79% had some sort of skin disorder, however none had isolated pruritis.[3]

Itching, otherwise known as pruritus, is often believed to be a common manifestation of diabetes. It has also been reported to be secondary to diabetic neuropathy, metabolic derangements associated with renal failure, or autonomic dysfunction resulting in anhidrosis, xerosis, pruritus ani and pruritus vulvae.[4]

Pruritus itself can be the result of underlying dermatological conditions, systemic disease, an adverse effect of drug treatment or as part of a neuropathic or psychiatric disease. Generalized pruritus tends to be a symptom of underlying systemic disease, whereas localized pruritus is often a manifestation of local cutaneous disease.[5]

A detailed comprehensive literature review in November 2019 looking at original articles published in PubMed and Cochrane databases documented the presence of itching in diabetes to be between 18.4% and 27.5%.[6] Two factors were generally thought to be associated with the pathogenesis of itching, namely skin xerosis and diabetic polyneuropathy. A number of studies analyzed revealed an association between diabetes and generalized itching. A few other studies documented local itch in the anogenital area, thought to be secondary to candida or dermatophyte infection. There were two other studies in that review which observed an association between diabetes and localized itch. One was a large multicenter study in Japan which observed localized truncal itching in diabetes without any rash and the second study reported a correlation between scalp itch and elderly diabetic patients.[7,8] No other studies in that literature review

documented localized itching without any cutaneous involvement, out of the two studies that did, none described the localization of itching in the arms or legs as in this case.

Generalized pruritus has also been documented in 27.5% of 385 patients with type II diabetes, with higher postprandial glucose levels resulting in a higher probability of patients suffering from generalized pruritus.[9] There appears to be a positive correlation between glucose levels and pruritis in diabetic patients, at least as far as generalized itching is concerned. Such a relationship between diabetic patients and localized itching has not yet been demonstrated.

Diabetes is a commonly managed condition in Qatar, both in primary and secondary care. The latest government statistics indicate 17% of the adult population have the condition.[10]

In this paper authors present an unusual presentation of a newly diagnosed type II diabetic patient with the sole symptom of 3 months of localized itching affecting the medial aspects of the forearms and thighs without having any corresponding cutaneous pathology. This itch symptom markedly improved on significantly reducing the dietary intake of sugar and with concomitant use of metformin.

CASE REPORT

A 39 year old Indian man made a routine appointment and was subsequently seen shortly after at the Airport Health Center with a complaint of a three-month history of localized itch. This was localized around the medial aspects of his forearms, which did not affect his hands at all and which also affected the middle aspects of his thighs which spared the perineal area. He did not report any other symptoms, in particular no tiredness, polyuria or polydipsia.

Using a Numerical Rating Scale (NRS) for itch, this patient assessed his itch severity to be between 4-6 out of 10, with 0 representing 'no itch' and 10 representing 'the worst imaginable itch'.

He had used over the counter moisturizing creams on occasion which produced small, short lived improvements in itch intensity at the time. He reported playing cricket once a week but denied ever using any protective pads over his arms or legs. He also did not report any diurnal variation of his itch. Probing further into the history, he reported varying intensity of the itch at different times seemingly without any pattern. In general, the itch symptom was reported as much the same during the previous last 3 month. Curiously during exacerbations of itch intensity, the patient noticed that all the affected areas would flare up in unison, the affected areas of the arms being the same intensity as in the thighs.

There was nothing within his work or social life could easily explain his symptoms.

The patient did smoke for 3-4 years, but this was more than 20 years ago. He denied ever drinking alcohol or using illicit drugs.

On enquiry into his family history, the patient mentioned that his mother has type II diabetes, but no other family members were affected.

There was nothing abnormal to find on examination of his skin; there was no rash or excoriation marks and his skin did not appear dry. The areas identified by the patient as itchy did not appear to lie within any recognized dermatomal distribution. The patient did appear overweight, his measured weight at presentation was 90kg. His height was measured at 1.73 meters, resulting in his calculated BMI at just over 30.

Looking through the patient's medical record it was noted that he was seen almost exactly a year ago to the day of his recent presentation, requesting screening bloods to be performed. These demonstrated a raised fasting sugar, HbA1c and alanine aminotransferase (ALT). The fasting glucose was reported as 6.8 mmol/L (122.5 mg/dL) and HbA1c 7.5% (58.5 mmol/mol). At that stage, the patient had no documented symptoms and was otherwise fit and well. The fasting glucose was repeated a week later and was raised again, reported as 8.0 mmol/L (144.1 mg/dL). Within the liver function tests, the ALT was noted to be raised at 77 U/L, the rest of the liver enzymes reported within the normal range. Apart from reduced vitamin D levels (reported as 12 ng/mL) the other screening blood test results were within the normal reference range. The patient did not return for follow up at that stage for further management and was thus unaware of all the abnormal results and indeed had completely forgotten all about the blood tests performed with the passage of time

Considering the patient's raised glucose in the past, family history and ethnic background, it was arranged for the patient to have fasting blood tests with particular emphasis on repeating the fasting glucose, HbA1c, liver function tests and Vitamin D levels, together with other screening blood tests.

The latest blood results demonstrated raised fasting glucose and HbA1c as expected, the fasting glucose was reported as 7.7 mmol/L (138.6 mg/dL) and HbA1c as 7.9% (62.8 mmol/mol). The ALT was reported as 66.2 U/L, the rest of the liver enzymes being in the normal reference range. The vitamin D was reported as 11 ng/mL.

The fasting glucose was repeated together with further bloods to rule out obvious causes of the raised ALT. The repeated fasting glucose was reported as 7.2 mmol/L (129.7 mg/dL), still in the diabetic range and the hepatitis screen (B and C) was negative. The iron profile

(including transferrin) and ceruloplasmin were all reported well within the normal range as was the kidney function and thyroid function, CBC and ESR.

The urine was tested for microalbumin and this was also reported within the normal range with an albumin to creatinine ratio (ACR) reported as less than 0.2 mg/mmol.

On further examination, there was no hepatomegaly, jaundice, ascites or any other signs of liver disease. There was no evidence of peripheral neuropathy detected using a 10g monofilament and the patient's blood pressure was measured at 143/79.

Based on the results of the blood test, a diagnosis of type II diabetes mellitus was made and shared with the patient together with the raised ALT, reduced vitamin D and suboptimal blood pressure. The patient was already engaging in regular light exercise but disclosed that his diet was very rich in high sugar foods on a daily basis. There was a considerable amount of sweets, chocolates and sugary biscuits consumed throughout the day as well as having tea with a high concentration of sugar on most days. He was quite motivated to amend his diet and enthusiastic to engage with all the medical interventions that were required.

Metformin was prescribed at the time of diagnosis in accordance with the American Diabetes Association's guidelines, starting with 500mg of the modified release tablet and increasing after a week to 1000mg once a day.[11]

Additionally, the patient was referred to the local dietician to provide help and support in engaging with an appropriate diabetic diet and he was also referred to the local eye clinic for retinopathy screening.

Further referrals were made for a liver ultrasound scan to further explore the reasons behind the persistent raised ALT.

A family physician with a specialist interest in dermatology reviewed this patient shortly after the diagnosis was made to ensure no other tests or referrals were necessary with regards to the ongoing itch. A local dermatologist was also involved where the case was discussed at length. The absence of rash or any other cutaneous manifestations in the area of this patient's itch made it very unlikely that some kind of dermatitis or fungal infection was causing the itch. Equally, without the presence of any obvious local factors that solely affected the itchy areas, it was deemed very unlikely that the cause was due to some kind of irritation or local reaction due to occlusion, sweat or fabric. The dermatologist noted that the rash area did not conform to any recognized dermatomes (either in the arms or thighs) and so this finding made rare neurological pathology very unlikely indeed.

It was agreed that the likely etiology of this itch was due to diabetes, which was expected to improve once the sugars were controlled by the lifestyle changes and the commencement of metformin.

With the consent of the patient, it was agreed to delay treating the low vitamin D until further review 3-4 weeks after the commencement of the low sugar diet and metformin. This patient had a similar low vitamin D a year previously and was clearly not displaying any symptoms of the deficiency. The patient felt it was important for him to know if his itching responded to sugar lowering measures and so treating the low vitamin D concomitantly would confound the issue.

Four weeks on from initial presentation, the patient had been seen by the local eye clinic who confirmed the absence of any retinopathy and the ultrasound scan confirmed the presence of fatty liver. Subsequently, the patient was referred to a gastroenterologist with an interest in hepatology for further management of the fatty liver. This would include the enhanced liver fibrosis test, to gauge the degree of liver fibrosis rather than relying on his liver function tests as per the latest National Institute for Health and Care Excellence (NICE) guidelines.

The patient was successful at reducing his dietary sugar intake to negligible levels and reported tolerating the metformin dose well, taking 1000mg of the modified release tablet once a day at that stage.

The patient was also very happy to report the severity of the itch had much improved as compared to the previous 3 months, the NRS being assessed as 1 out of 10 with also a number of non-itch days reported. The previous distressing itch was now reduced to a trivial annoyance. The patient reported that the itch improved 3-4 days after the commencement of a substantially reduced dietary sugar intake and starting metformin. Consequently, the patient was now happy to commence vitamin D to address the low levels previously detected.

As a result of the lifestyle modifications that had been implemented, the patient's weight had reduced by 2kg to 88kg. On review two months after his initial presentation, the patient reported no itching at all. Curiously he did notice that the localized itch symptom reappeared the following day if he consumed high sugar foods. The itch subsided within a day if he kept to a low sugar diet. Although the patient's blood pressure remained suboptimal, he was not keen on any medications to control this as he wanted to rely on the effect of his lifestyle modifications in the first instance. He was keen to continue his diet and was determined to gradually increase his exercise intensity.

This patient was advised to stay on metformin and have regular blood tests including the HbA1c with regular follow up at the Airport Health Centre for his newly diagnosed diabetes, along established clinical pathways.

DISCUSSION

The American Diabetes Association (ADA) documents localized skin itching as a common association with diabetes and puts this down to either yeast infection, dry skin or poor circulation. When itching is attributed to poor circulation, the ADA states this will affect the lower parts of the legs.[12]

Localized pruritus has been documented in diabetic women in the perianal/genital area, due to Candida albicans or dermatophyte infection. The predisposing underlying mechanism has not been entirely understood. Whether metabolic abnormalities due to renal failure, autonomic dysfunction with anhidrosis or diabetic neuropathy are responsible is unclear.[13]

Perhaps the earliest hint of an association between underlying diabetes mellitus and localized itch without any obvious cutaneous manifestation was noted in a letter to the editor published in 1977, in the journal of the American Medical Association (JAMA).[14] Scribner was relying on the observation of his own medical practice in a series of patients spanning over 10 years. He noted many patients presenting with severe itch of the scalp with no cutaneous manifestations indicating underlying disease, apart from scalp excoriation marks. The itch in these patients began in a sporadic fashion but gradually became continuous and unrelenting, frequently severe enough to interfere with sleep. Each patient experienced complete resolution of the itch when control of the underlying diabetes was achieved. It was surmised that itching of the scalp without any apparent reason should alert the clinician to the possibility of underlying diabetes mellitus.

There are other features of this patient that have documented associations with various dermatological conditions; the patient was obese at presentation, had low vitamin D levels and also had fatty liver (confirmed on ultrasound scan) with a raised ALT.

Obesity has been associated with acanthosis nigricans, skin tags, striae distensae (stretch marks), plantar hyperkeratosis, candida intertrigo, perineal dermatitis, lymphedema and pressure ulcers.[15]

Obesity presenting solely with pruritus has not been documented in PubMed using relevant searches.

With regards to vitamin D deficiency, no cutaneous consequences are described in Holick's extensive review of the health implications of vitamin D deficiency and inadequacy, in 2008.[16]

A small case control study involving 60 patients published in 2017 did demonstrate an inverse relationship between the severity of atopic dermatitis and serum vitamin D levels in children. However, the authors concluded that Vitamin D supplementation has not been included in the routine treatment of atopic dermatitis because of conflicting results in other studies.[17]

This, together with the well-known role of topical vitamin D analogues in the treatment of psoriasis point to a likely influence of vitamin D on the skin. By extension, the deficiency may possibly produce or at least exacerbate existing cutaneous pathology, an area that clearly requires further research. It is sufficient for the purposes of this case report to state that it would be very unlikely for vitamin D deficiency to present solely with pruritus, with respect to current published evidence.

This patient also had a raised ALT level with fatty liver detected during ultrasound scanning. He denied ever drinking alcohol and was not taking any regular medications prior to presentation. Given this patient's presentation, particularly with respect to being obese and having type II diabetes and the results of his blood tests, it was reasonable to diagnose non-alcoholic fatty liver disease (NAFLD).

It is well understood that patients with early NAFLD do not present with any symptoms initially. With more advanced stages patients may present with pain in the right upper quadrant, extreme tiredness, unexplained weight loss and/or weakness. Itching of the skin is described only when the extent of NAFLD reaches the very advanced stage of cirrhosis.[18]

A recent multi-center study based in Japan conducted on 1631 patients with ten distinct chronic liver diseases in 2017 documented the prevalence of pruritus in NAFLD as 44.7%.[19] Interestingly, the researchers noted that the presence of diabetes was an independent risk factor associated with pruritus and that aspartate aminotransferase (AST) levels were significantly higher in pruritus patients than those without. However, the ALT level was one of the twelve factors excluded when statistically analyzing the data using a multivariable regression model. The most common cited location for pruritus in the study was the back, reported by 63.1% of all those patients experiencing itch. Other localized itchy areas were reported in the study but the collected data in the study did not differentiate between the ten different types of liver disease the patients suffered from and the various locations of the itch the patients reported.

Along with NAFLD, the patient in this case study certainly has an independent associated risk factor for pruritus, namely being diabetic. However, the absence of diurnal variation in the itch makes the presence of pruritus in more advanced stages of NAFLD unlikely. This is because the vast majority of patients affected with cholestatic pruritus report a diurnal variation of itch intensity, with worsening symptoms in the late evening and early night time.[20]

Additionally, an expert consensus review published in 2017, aiming to formulate the best clinical practice in the

diagnosis and management of chronic pruritus stated that any liver disease with cholestasis can give rise to the development of pruritus which tends to be generalized and without any rash.[21]

Reviewing the published evidence, it can be safely concluded that the presence of obesity, vitamin D deficiency and fatty liver with raised ALT were all very unlikely to produce localized itching as a sole symptom. Moreover, the eventual substantial and swift amelioration of this patient's symptoms shortly after substantially reducing his dietary sugar intake would suggest the etiology to be due to the presence of hyperglycemia associated with type II diabetes mellitus in this particular case.

The recurrence of this patient's itch after consuming high sugar and subsequent amelioration on abstinence has not been documented before. The time lag associated between the high sugar food consumed and the itch may give some idea of the possible underlying pathophysiology at play.

The decision to test this patient for diabetes at presentation was not a difficult one as this patient had already fulfilled a number of the ADA's conditions for screening for diabetes; being obese, having a first degree relative with diabetes, having previous abnormal blood glucose tests and his ethnic background.[22] Furthermore, if the patient had returned for follow up as instructed, he could have been diagnosed with diabetes a year previously despite being asymptomatic as both the HbA1c and the fasting glucose were in the diabetic range on two separate occasions.[23]

Authors hope to highlight the association of localized itch and underlying diabetes to alert clinicians to consider diabetes as a differential diagnosis in patients where diabetes, or screening for diabetes may not be so obvious.

CONCLUSION

In conclusion, cutaneous manifestations and associations with diabetes mellitus are well known and described. What is not well documented is the association between diabetes and localized pruritus without any corresponding cutaneous manifestations. It is clear that preventative measures are very important in the long-term management of the escalating diabetes epidemic, but in the presence of established and undetected diabetes, any strategies that would help identify as early as possible, those not already diagnosed are to be welcomed.

Authors hope this case study goes some way in helping the collaborative efforts to that end.

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