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Case Report

Eosinophilia and hyperglycemia: a friend or foe?

Surabhi V. S. Krishna[1]*, Atul Jha[2], Sunil K. Kota[3], Manish Bhartiya[4]

[1]Department of Endocrinology, [2]Department of Gastroenterology, [4]Department of Neurology, 151 Base Hospital, Guwahati, Assam, India
[3]Department of Endocrinology, Diabetes and Endocrine Clinic, Berhampur, Odisha, India

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***Correspondence:**
Dr. Surabhi V. S. Krishna,
E-mail: Krishna_svs@yahoo.com

ABSTRACT

Infectious disease can precipitate new onset diabetes, complicate diabetic ketoacidosis or derange hyperglycemia. There are well studied mechanisms like an increase in production of pro inflammatory cytokine (TNF A, IL-B, and IL-6) which causes spike in the blood glucose level. However, some observational and invitro studies have shown that eosinophil do have a role in glycemic stabilization through alternatively activated macrophages (AAM). A 40-year-old male, not a known diabetic, was referred to our hospital for evaluation of high eosinophil count and hyperglycemia. He found to have severe eosinophillia, serological test for filarial positive and responded to heterazan therapy. His repeated blood smear test for microfilaria was negative. He was initially started on insulin basal bolus regimen (10 units total per day) and attained quick glycemic control with omission of insulin and with single dose of metformin 500 mg. In vitro studies on animals have also shown that when mice were fed with a diet of helminth, they showed sustained metabolic response characterized by decreased fasting glucose, improved insulin sensitivity and glucose tolerance. We discuss the controversial concept of the association whether eosinophilia increases the risk profile or does it mitigate the risk of the deadly disease, diabetes.

Keywords: Eosinophilia, Hyperglycemia, Alternatively activated macrophages

INTRODUCTION

Infectious disease can precipitate new onset diabetes, complicate diabetic ketoacidosis or derange hyperglycemia in type 2 diabetes.[1] There are well studied mechanisms like an increase in production of pro inflammatory cytokine (TNF A, IL-B, and IL-6) which causes spike in the blood glucose level.[2] However some observational and invitro studies have shown that eosinophil do have a role in glycemic stabilization through alternatively activated macrophages (AAM).[3] We report a case of filariasis with high white blood cell count (eosinophils 63%) who had a new onset high blood glucose value with predisposing osmotic symptoms and had excellent glycemic control without any complications.

CASE REPORT

A 40-year-old male, not a known diabetic, was referred to our hospital for evaluation of high eosinophil count and hyperglycemia. A native of Bangladesh, he initially presented with gradual increase in swelling of left leg over a period of two weeks accompanied with a dragging sensation. He gave a history of mild fever and redness of left leg. He was treated with injectable antibiotics at peripheral hospital for 10 days where they had documented his left inguinal lymphadenopathy. There was no history of any management with steroids. On direct questioning, in view of hyperglycemia detected, he gave history of polyuria and weight loss of 4 kg over the last 3 months. No complaints of breathlessness, chest pain, cough, abdominal pain or joint swellings was elicited. There was no history

of similar complaints in the past or any history of diabetes in the family. He denied any history of known drug allergy.

On examination he was found to be afebrile, body mass index (BMI) 22 kg/m^2, pulse: 88/min regular, respiratory rate (RR) 16/min regular, blood pressure (BP) 130/80 mm of Hg. No pallor/cyanosis/LNE/pedal edema. Non pitting edema without any tenderness or raised temperature was noted in the left leg. There were no petechial spots, ecchymosis, joint or scrotal swelling seen. Abdominal examination: no organomegaly, respiration: bilateral air entry, no crepts or rhonchi heard. Other general and systemic examination normal.

On evaluation, hemoglobin (Hb) was reported to be 15 gm/dl, AEC: 13,250/cumm, blood sugar (R): 390 mg/dl, erythrocyte sedimentation rate (ESR): 40 mm fall in 1st hour, urine sugar detected and negative for ketones, microfilarial Ag test positive, CRP/HIV/HbsAg/anti HCV: negative, CDFI left lower limb: no evidence of DVT, chest X-ray PA view: normal study, fundoscopy: no evidence of diabetic retinopathy, electrocardiography (ECG): normal study; ultrasonography of abdomen (USG abd): grade I fatty liver, and simple parapelvic cyst right kidney (incidental detection) (Table 1).

His eosinophilic count remained high (Table 1). He had no features of any organ involvement like splenomegaly, cardiac involvement, lung, skin or neurological involvement. The peripheral blood smear did not show any blast cells, vacuolated eosinophils anaemia or thrombocytopenia to suggest any haematological disorders. Stool test had not shown any parasites/ova to suggest stronglyoides/helimenthic infections.

In view of unilateral non pitting edema of left leg (retrograde lymphedema) insidious onset and hailing from endemic area of microfilaria and presence of severe eosinophillia and serological test for filarial positive; a clinical diagnosis of filarial adenolymphangitis was made and he was started on heterazan therapy with albendazole. His repeated blood smear test for microfilaria was negative. He was initially started on insulin basal bolus regimen (10 units total per day) and was changed over to metformin single dose in view of rapid glycemic stabilization.

Table 1: Hematological and biochemical parameter of the patient during his course of hospitalization.

Day of admis-sion	Hb	TLC/ cumm	DLC %	Platelets	MP/ PBS	Urea/S. creatinine mg/dl	S. bilirubin mg/dl/ AST/ALT I.U/L	Microfil-aria	AEC/ cumm	Blood sugar (mg/dl)
1	15	26500	P24, E50, M04, L22	260000	Negati-ve	31/1.0	0.7/50/43	Negative	13250	[R] 390
3	14	24000	P20, E58, M04, L18		Negati-ve, no atypical cells					[F] 146/[PP] 246
6	14.8	19600	P13, E65, M06, L18	275000	Negati-ve	30/0.9	0.8/41/57	Negative	12500	92/127
14	14.2	16000	P16, E63, M3, L16						10000	
18										89/122

DISCUSSION

Immune system and metabolic regulations are in a state of harmony and any dysfunction can lead to type 2 diabetes and other chronic metabolic diseases like obesity and cardiovascular disease.[4] There are various factors like white blood cells (WBC) count, CRP, and cytokines which may play a role in the pathogenesis of type 2 diabetes mellitus.[5,6] Eosinophils have traditionally been known to be active in people with certain allergic diseases and infections. However, there is paucity of studies showing any association of eosinophils with diabetes mellitus. It is seen that patients with asthma are found to rarely develop diabetes mellitus. Papers in animal study have reported that helminth-induced adipose tissue eosinophilia enhance glucose tolerance. It was hypothesized that eosinophil might take an active part in the pathogenesis of type 2 diabetes mellitus (T2DM).[3] Yet in a study published by Neuirth et al, the authors have found that in type 1 diabetes, the expression of alpha–defensin mRNA is found in 30% of patients. Using quantitative RT-PCR, cell surface markers and confocal microscopy; they identified these cells to be eosinophils there by suggesting that eosinophils could be evolved in the development of diabetes.[7] Our patient had hyperglycemia with weight loss and polyuria which can be attributed to presence of T2DM, retrograde lymphedema, microfilaria and leucocytosis with eosinophilia [63%]. He had not been subjected to steroids for hypereosinophilia. He showed dramatic response to oral anti diabetic drugs after initial high blood sugar level of 390 mg/dl.

Meta analysis on WBC count and T2DM showed significant association between them.[8] Likewise the study by Vozarova et al found that WBC count was associated with a decline in insulin sensitivity.[3] In another, it was found that there is inverse association with T2DM and insulin resistance in Chinese adults. There was 37% decrease in insulin resistance for each SD-1 deviation of increase in eosinophil percentage.[9]

Eosinophil is typically associated with allergy and parasitic infections. It regulates the macrophage activation state alternatively activated macrophages (AAMs) in mammalian adipose tissue by producing IL-4 and IL-13 and may have an important role in metabolic homeostasis, by improving control of glucose metabolism. In adipose tissue, eosinophil that migrates from the blood into adipose tissue, can produce IL-4 and IL-13. They are associated with allergy causation and parasitic protection.[3]

The other mechanism that can be explained changes in glucose homeostasis by: peroxisome proliferator-activated receptor γ (PPAR γ), a downstream of IL-4 receptor (IL-4Ra) is known to inhibit the expression of genes that promote inflammation and protects against insulin resistance and these mutations in humans are also associated with insulin resistance; and predisposition to T2DM can occur if there are low levels of IL-4 and IL-3 because of absence of eosinophils in the adipose tissue, which fail to counter the effects of infiltration of T cells that produce Il-6 and TNF-a.[8,10,11]

Mice fed with a diet of helminth, showed sustained metabolic response characterized by decreased fasting glucose, improved insulin sensitivity and glucose tolerance. There is decreased perigonadal adipose tissue weight and increased perigonadal adipose tissue eosinophils.[3]

It is seen that where there is prevalence of intestinal parasitaemia, there is decrease in metabolic syndrome and eosinophilc count is high among people where metabolic syndrome is rare.[12] It is speculated that eosinophils have role in metabolic equilibrium during chronic parasite infection and in microbial infection there is insulin resistant state.[13]

CONCLUSION

With the rapid increase in the cases of diabetes mellitus worldwide and an ever-increasing factor leading to precipitation of metabolic syndrome in general and diabetes mellitus in particular; there is but one aspect which appears to be somewhat protective in nature. It seems that an elevated blood eosinophilia in presence of high total leucocyte count and hyperglycemia is a friend in disguise. There is need to study more on the mechanism which leads to persistence of AAM in normal human adipocytes and its interaction with other immune cells. To conclude, it may not be a far-fetched thought that a targeted therapy by modulating the number and function of eosinophils may be the new wonder treatment of diabetes mellitus.

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