21-Year-Old Male with Ataxia Telangiectasia with Insulin Resistant Diabetes and Hypertriglyceridemia

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Introduction

Ataxia Telangiectasia (AT) is an autosomal recessive disorder characterized by cerebellar degeneration, telangiectasias, malnutrition, immunodeficiency, and premature aging[1]. As life expectancy has increased, some patients with AT develop severe insulin resistance and diabetes[2].The mechanism of AT related diabetes (ATRD) is not autoimmune, with severe insulin resistance and hypertriglyceridemia related to both IGF-1 & insulin receptor defects[2,3]. ATRD may require aggressive insulin therapy to achieve weight gain and glycemic control. We describe a case of ATRD and hypertriglyceridemia, treated effectively with a combination of Pioglitazone and an atypical insulin regimen.

Case Presentation

We describe a 21-year-old male with AT who was diagnosed with weight loss and new onset diabetes at age 15. He did not tolerate Metformin and required insulin at escalating doses. G-tube feedings, failure to thrive, diarrhea, and elevated liver enzymes limited typical diabetes management options. His complex insulin regimen evolved to AM Glargine, lunchtime regular insulin, and overnight NPH/regular insulin to maximize gastrostomy calories. Insulin pump therapy was unsuccessful due to lack of subcutaneous tissue. Despite improving glycemic control, he developed severe hypertriglyceridemia, which showed significant improvement after initiating Pioglitazone (a thiazolidinedione).

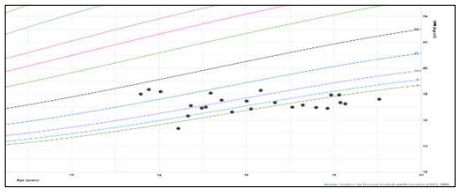

Figure 1: Graphical representation of patient's BMI: Like many patients with AT, this patient's BMI is < 1st %ile. Despite being low, it remains stable on current medication regimen.

Case Presentation

Mealtime	Medications
Breakfast	Glargine 14U Pioglitazone 15mg Fenofibrate 48mg
Lunch	Regular Insulin 14-16U
Dinner	Pioglitazone 15mg 44U NPH/Regular Insulin

Table 1: Most current Medication regimen (Weight 37.6kg)

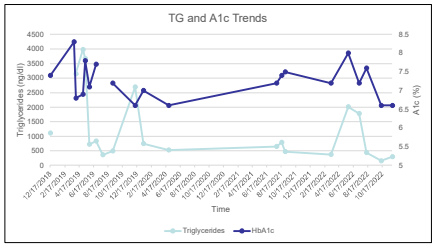

Figure 2: Graphical representation of Triglycerides and A1c over time

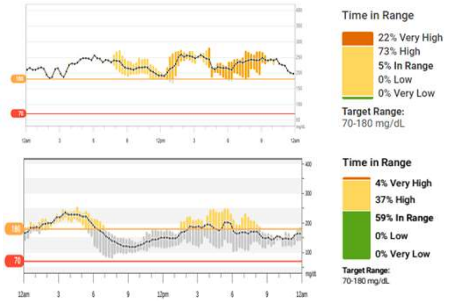

Figure 3: Blood glucose trends. Top graph represents blood glucose trends in May 2022. Bottom graph represents blood glucose trends on current medication regimen in November 2022

Summary of Results

Date	Triglycerides (mg/dl)	HbA1c (%)
12/17/2018	1113	7.4
3/26/2019		8.3
*5/3/2019	3982	6.9
5/13/2019	3674	7.8
5/30/2019	725	7.1
9/6/2019	492	7.2
**12/9/2019	2697	6.6
4/29/2020	531	6.6
8/19/2021	795	7.4
9/3/2021	476	7.5
3/14/2022	373	7.2
5/26/2022	2007	8
***7/11/2022	1784	7.2
8/11/2022	438	7.6
10/13/2022	153	6.6
11/28/2022	296	6.6

Table 1: Adjustments Required to Optimize Care:
* Initiation of Pioglitazone 15mg daily 5/3/19 and Fenofibrate 48 mg on 6/4/19
** Implementation of strict low-fat diet
*** Increase to Pioglitazone 15mg BID.

Insulin was first required for ATRD at age 15. Despite escalating insulin requirements, glycemic control remained sub-optimal and triglycerides (TG) rose to 3982 mg/dl. Within one month of initiating Pioglitazone, TG levels decreased substantially. His ATRD care required a careful balance to minimize weight loss by optimizing caloric needs while limiting dietary fat and improving glycemic control. Pioglitazone was increased further in July 2022 for increasing TG levels. This titration in Pioglitazone again led to significant improvements again in TG and glycemic control. Cardiology involvement and safety clearance with monitoring of heart failure risk were important aspects of his overall care.

Conclusions

As life expectancy for AT patients improves, developing strategies for managing this unique form of diabetes and dyslipidemia is necessary. ATRD presents unique challenges for glycemic and lipemic control, with atypical insulin regimens likely required. Adjunct Pioglitazone therapy can improve insulin resistance and related hypertriglyceridemia in these patients.

Further study of patients with ATRD and associated conditions may facilitate development of effective treatment modalities

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