Case Report

Recurrent seasonal severe hypertriglyceridemia-induced acute pancreatitis; a case report

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ABSTRACT

Introduction: Acute pancreatitis (AP) is a serious inflammatory condition of the pancreas. Hypertriglyceridemia (HTG) is considered an uncommon cause of AP. The current study aims to present a unique case of recurrent seasonal severe HTG-induced AP (HTG-AP); treated with insulin and heparin.

Case report: A 36-year-old male presented with recurrent attacks of severe upper abdominal pain that was radiating to the back and associated with repeated vomiting. The condition has being occurring every autumn-winter for the last three years. He had thalassemia minor and had a history of HTG-AP. His TG levels were relatively normal from February to August; however, from September to February, his TG levels highly elevated which has resulted in HTG-AP every year for the past three years. The condition was confirmed via a contrast-enhanced computerized tomography scan of the abdomen. To prevent the next HTG-AP, his TG level was monitored monthly. When TG levels spiked again, the patient was put on an insulin infusion with heparin, glucose, and potassium to rapidly reduce TG level. After two days, serum TG was dramatically reduced (<500 mg/dL).

Discussion: Despite multiple theories being proposed, the pathogenesis of HTG-AP is yet to be understood. Usually, HTG-AP is a single episodic, and recurrent HTG-AP is considered uncommon finding. Previous reports are contradictory regarding TG level and seasonal variation. There is currently no standard management approach to treat HTG-AP cases.

Conclusion: HTG-AP rarely reoccurs on an annual basis, and seasonal variation seems to play a major role in its onset. The condition can be managed with insulin, heparin, and glucose infusions.

1. Introduction

Acute pancreatitis (AP) is a serious inflammatory condition of the pancreas associated with severe morbidity and mortality [1]. It is a highly prevalent gastrointestinal condition and one of the leading causes of hospitalization, with an incidence of 4/10,000 in western countries and rising [2,3]. Excessive alcohol use and gallstones are the most frequent etiologies for AP, constituting 80–90% of the cases [4]. Hypertriglyceridemia (HTG), which is denoted for high levels of triglycerides (TG) in the blood, is considered an established but still rare cause of AP, accounting for only 1–4% of the cases. However, the association between the two conditions is yet to be completely understood [5,6]. Amongst the mentioned etiologies, HTG-induced AP (HTG-AP) is reported to result in the most severe form of AP, increased risk of complications, and a higher mortality rate. Hence, the management of HTG-AP can be more challenging when compared to AP due to other etiologies [3]. There is currently no standard management approach for the treatment of these cases, and the existing literature is scarce and
conflicting regarding this aspect [7]. Previous studies have suggested that an elevated level of serum TG above 1000 mg/dL significantly increases the risk of HTG-AP, and for every 100 mg/dL increase in TG level, the risk of HTG-AP rises by 4% [8]. Most cases of HTG-AP are single episodic (75.9%), and the incidence of recurrent HTG-AP is even more uncommon (24.1%) [9]. Even though seasonal variation has been proved in the levels of some blood lipids, reports regarding minimum and peak values of serum TG according to the seasons have yielded contradicting results [10].

The current study aims to present a unique case of recurrent seasonal severe HTG-AP; treated with insulin and heparin, with a brief review of the literature. The CARE guidelines have been taken into account in the writing of this paper [11].

2. Case presentation

Patient information: A 36-year-old male presented with recurrent attacks of severe upper abdominal pain that radiated to the back with repeated vomiting. The condition has been occurring every autumn-winter for the last three years. He was a non-smoker and non-alcoholic. He had thalassemia minor and had a history of HTG-AP, but no other clinical conditions. The patient was on Fenofibrate tab 200 mg, Atorvastatin tab 40 mg, and Ezetimibe tab 10 mg as medications to manage his blood lipid levels. His mother was diabetic and hypertensive, and his brother died due to renal failure. His family history was negative for dyslipidemia.

Clinical findings: There was no significant finding. His vital signs showed a blood pressure of 110/70 mmHg, a heart rate of 80 b/m, a breathing rate of 18 b/m, an SPO2 of 97%, and a temperature of 36.5 °C.

Diagnostic approach: According to the patient’s previous year’s routine laboratory testing, from February to August his TG levels were relatively normal; however, from September to February, the TG levels were highly elevated which has resulted in HTG-AP every year for the past 3 years. The last HTG-AP was confirmed at the time via contrast-enhanced computerized tomography (CECT), which showed enlarged pancreas with homogenous uniform enhancement, no definite cyst or solid lesion, peripancreatic fat stranding picture of AP, and no main pancreatic duct dilation. In addition, the level of cholesterol was also increased in those months. After he visited our health care center in January, his TG level was carefully monitored from the beginning of 2021, and the same pattern was found, as later in autumn, the patient had elevated TG levels measuring 1000–4000 mg/dL. Investigation of all the systems (cardiovascular, respiratory, abdomen, and neurology) revealed no abnormal findings.

Therapeutic intervention: Although the patient was still asymptomatic, he was hospitalized because of the concern of developing a 4th HTG-AP. To prevent HTG-AP from occurring due to another spike in TG level, the patient was put on an insulin infusion with heparin, glucose, and potassium as a temporary measure to rapidly reduce the lipid levels. After two days of using these medications, a dramatic reduction was found in serum TG level (<500 mg/dL). The patient was then sent to a nutritionist for dietary modification.

Follow-up and outcome: After one month of strict dietary regimen and continuation of his previous medications, the lipid levels reached the normal range. Hence, the fourth HTG-AP attack was prevented.

3. Discussion

Although uncommon, HTG is an established cause of AP, constituting 1–4% of all cases [7]. Meanwhile, gallstone and alcohol consumption account for the majority of AP (80–90%) [4]. Other less common etiologies of AP include hypercalcemia, pancreatic trauma, medications, and autoimmune conditions, with a small percentage being idiopathic [3]. It has been suggested that an increased level of TG is directly linked to an increased risk of HTG-AP; however, this risk is irrelevant in the case of moderate hypertriglyceridemia of less than 500 mg/dL [4]. Meanwhile, a TG level of 1000 mg/dL contributes to an increased incidence of HTG-AP by 5%, and levels above 2000 mg/dL increase the risk to 20% [12]. Both genetics and other secondary causes can also provoke the development of HTG-AP, such as disorders of lipid metabolism, diabetes mellitus, certain medications, and pregnancy [13]. The current case lacked the previous conditions but had thalassemia minor. Although the pathogenesis mechanism of HTG-AP is yet to be fully understood, multiple theories have been proposed. One theory postulates that the accumulation of free fatty acids in the pancreatic capillaries due to the breakdown of excess triglycerides by pancreatic lipases (PL) will result in blockage, ischemia, lipotoxicity, and cause damage to the pancreatic ducts leading to acute pancreatic inflammation [14,15]. Another theory suggests that a high concentration of chylomicrons due to elevated TG levels results in hyper blood viscosity and impaired pancreatic circulation; this will expose the chylomicrons to PLs and causes damage to the pancreatic acini [6].

The presentations of AP are often mild and self-limiting, which includes abdominal pain in the left upper quadrant that may radiate to the back, vomiting, nausea, and low-grade fever. Similar presentations were observed in this case. AP patients usually recover within only a few days, but in a portion of severe cases, it may lead to organ failure or even death [13,16]. HTG-AP presentations are reported the same as AP due to other etiologies, and it is associated with a mean age of 42 years and male predominance (65%). This is higher than the average age of AP of other causes [3,17]. The literature is conflicting regarding the severity of HTG-AP when compared to other etiologies. However, many studies point out that HTG-AP causes the most severe form of AP with an increased risk of complications and mortality [2,14].

Usually, HTG-AP is single episodic, and recurrent HTG-AP is considered uncommon [18]. In a study by Yan et al. a total of 206 HTG-AP patients were studied. Their data showed that 75.9% of them were single episode, and only about 24.1% of the cases were associated with two or more episodes [9]. Variation in the level of some lipids, such as cholesterol, has been detected based on seasonal variation. Some studies have tried to detect minimum and peak values of serum TG levels according to seasonal variation; however, these studies have yielded contradicting results [10]. Most cases of recurrent HTG-AP found in the literature are not annual and have occurred randomly throughout the years, and no association between the reoccurrence and the seasons has been pointed out [5,9,18,19]. The case in the current study is associated with recurrent HTG-AP that occurred annually for the last three years in winter-autumn.

Regarding the diagnosis of AP, the fulfillment of two of the following three criteria are indicative for AP; increased levels of amylase and lipase, abdominal pain radiating to the back, and observing AP features on CT, ultrasonography, or magnetic resonance imaging [20]. However, amylase levels can be normal upon AP presentation; hence caution is required in its interpretation [15]. HTG-AP is diagnosed based on the elevated level of TG (>1000 mg/dL) when other AP etiologies are absent. Serum TG evaluation is best conducted within 24 hours of the condition’s onset since fasting and other intravenous medications can decrease TG level back to normal [14]. The current case fulfilled the above diagnostic criteria.

Even though multiple management modalities have been proposed for HTG-AP, such as plasmapheresis, oral antihyperlipidemic medications, heparin, and insulin infusion, there is still no standard approach to treat these cases, and there are conflicting reports regarding this aspect [7]. The initial treatment for HTG-AP is conservative and the same as AP of other causes. After this, it is required to rapidly lower serum TG level to less than 500 mg/dL [14]. Plasmapheresis allows for rapid reduction of serum TGs by removing circulating fatty acids and toxic agents from the blood [3]. However, plasmapheresis is not available in all hospitals as this approach is highly expensive, and it is associated with a high risk of bleeding, anaphylaxis, and infection [14]. Insulin infusion stimulates lipoprotein lipase activity which will, in turn, increase the breakdown of chylomicrons, hence lowering serum TG level.
Heparin infusion is also used to reduce serum TG levels by promoting the release of lipoprotein lipase enzyme, which breaks down TGs. However, extended use of heparin can lead to the depletion of lipase and, in turn, inhibit TG degradation, which will increase the risk of recurrent HTG [7]. After the reduction of TG level below 500 mg/dL, it is important to implement long-term management of HTG-AP through dietary modifications and using lipid-controlling medications [13]. In the current study, insulin with heparin, glucose, and potassium infusions was used to rapidly lower the TG level.

In conclusion, recurrent HTG-AP is uncommon, especially when occurring on an annual basis. Seasonal variation seems to play a major role in the onset of recurrent HTG-AP, more specifically in autumn-winter. When recurrent HTG-AP is predicted, it can be effectively prevented and treated with insulin, heparin, and glucose infusions.

**Ethical approval**

The manuscript approved by ethical committee of the University of Sulaimani.

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**Author contribution**

Abdulwahid M. Salih: major contribution of the idea, final review and approval of the manuscript. Shaho F. Ahmed, Pshtiwan H. Qadir: physicians managing the case, final approval of the manuscript. Hawbash R. Mohammed, Fahmi H. Kakamad: literature reviews, writing the manuscript, final approval of the manuscript. Sasan M. Ahmed, Karzan M. Salih, Berwn A. Abdulla: literature review, final approval of the manuscript.

**Guarantor**

Fahmi Hussein Kakamad is Guarantor of this submission.

**Consent**

Consent has been taken from the patients and the family of the patients.

**Provenance and peer review**

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**Declaration of competing interest**

There is no conflict to be declared.

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**Appendix A. Supplementary data**

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jamsu.2022.103406.

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