

CASE REPORT

A Rare but Important Cause of Pancreatitis: A Case of a SPINK 1 Mutation in a Young Female

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ABSTRACT

The most frequent causes of pancreatitis classically have been known to be gallstones or alcohol. However, genetics can also play a key role in predisposing patients to both chronic and acute pancreatitis. The Serine Protease Inhibitor Kazal Type 1 (SPINK 1) gene is known to be strongly associated with pancreatitis. This gene can have a mutation in the serine protease inhibitor Kazal Type 1, which results in trypsinogen activation that leads to auto-digestion of the pancreatic tissue and eventually pancreatitis. Patients with these genetic polymorphisms struggle with multiple bouts of pancreatitis per year, and in some cases, they even suffer from high morbidity rates. Treatment for patients with genetic predispositions is similar to those without, and typically involves supportive care. Here we present a case of a young 17-year-old female with past medical history of recurrent pancreatitis, who initially presented with severe epigastric pain radiating to her back and abdomen. She has a history of the SPINK 1 mutation and has had two attacks per year since her first diagnosis. Her family history is significant for SPINK 1 mutation in both her father and brother. In the hospital, CT scan showed dilation of the pancreatic tail with no evidence of pseudocyst. She received supportive care with IV fluids, bowel rest and pain control, and her condition improved within two days. This case illustrates the variability in conditions which can contribute to pancreatitis and the importance of identifying patients who are at risk for recurrent acute pancreatitis and/or chronic pancreatitis due to genetic polymorphisms. Additionally, recurrent episodes of pancreatitis can also lead to pancreatic cancer. This is especially common in those who are found to have ductal abnormalities or pancreatic calcifications. In order to decrease the number of acute bouts of pancreatitis and to minimize the risk of potential pancreatic cancer development, we developed a specific outpatient monitoring regimen for our patient.

INTRODUCTION

Acute pancreatitis is typically known as an inflammatory condition which is frequently caused by gallstones or excessive alcohol use [1]. However, genetics can often predispose young and healthy patients to pancreatitis who do not have gallstone history and have minimal to no alcohol use [1]. In patients with genetic mutations, acute pancreatitis flare ups often lead to chronic pancreatitis. These chronic pancreatitis episodes can further lead to continuous pancreatic inflammation and irreversible insults to both the endocrine and exocrine pancreatic functions [2]. Chronic pancreatitis is a progressive condition which impairs patients' quality of life and compromises their functional ability due to continued pain, weight loss and even consistent steatorrhea [3].

While alcohol and gallstones have been recognized as the key contributors to pancreatitis, in the year 2000 another cause was found. The Serine Protease Inhibitor Kazal type 1 (SPINK1) was identified as a gene which had close ties to pancreatitis [4]. Pancreatic acinar cells secrete SPINK 1 as the first line in defense against premature trypsinogen, as SPINK 1 is an efficient inhibitor of trypsin-1 and trypsin-2 [5]. A mutated SPINK 1 gene can lead to unregulated activation of trypsinogen leading to auto-digestion of pancreatic tissue and subsequent pancreatitis [5]. This mechanism can propel continuous episodes of acute pancreatitis which can then lead to chronic pancreatitis.

Although pancreatitis has been recognized and treated for many years, genetic causes have only recently begun to be recognized as key players in its development. Furthermore, recent investigations have shed light on the link between genetic mutations and pancreatic cancer, making the role of genetics even more important. We present the case of a young patient who has the SPINK 1 mutation and highlight the treatment of acute pancreatitis as well as an outpatient regimen to prevent further pancreatitis episodes.

CASE PRESENTATION

We present the case of a young 17-year-old Hispanic female with the past medical history of SPINK 1 mutation

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Abbreviations SPINK1 Serine Protease Inhibitor Kazal type 1; EUS Endoscopic Ultrasound; NPO nil per os (nothing by mouth); CFTR Cystic fibrosis transmembrane conductance regulator

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and several recurrent episodes of pancreatitis. Family history is significant for a SPINK 1 mutation in both her father and brother. Social history was negative for any tobacco or alcohol use. As per her mother, her triggers for acute pancreatitis have been reported to be nasal congestion and upper respiratory infections. Prior to this presentation, she had just returned from a trip from New York where she had developed an upper respiratory infection as well as significant nasal congestion. This led to the classic epigastric pain which resulted from her acute pancreatitis attacks. In the emergency department, she presented with epigastric pain radiating to her back along with nausea and vomiting, but she denied any shortness of breath, fevers or diarrhoea. Upon presentation, her vitals were within normal limits. A CT scan of her abdomen and pelvis was performed and showed dilation of the pancreatic tail with no evidence of pseudocyst. The tail of the pancreas measured 6 mm and there was also a calcification in the body of the pancreas. All her vitals and labs including lipase, alkaline phosphatase, alanine aminotransferase, and aspartate aminotransferase were within normal limits. She was admitted and received IV fluid resuscitation as well as a pain regimen for her abdominal pain. She was also kept NPO to allow for complete bowel rest. Gastroenterology was consulted and recommended to continue supportive care with lactated ringer fluids, pain management and an outpatient EUS in two to three months to assess for pancreatic lesions and chronic pancreatitis changes. The patient's abdominal pain continued to improve, and her diet was advanced as tolerated. Her lipase and other liver enzymes continued to remain within normal limits. She improved clinically and was discharged within two days. Upon discharge she agreed to have a close follow up with gastroenterology for EUS every 3-6 months. As well as a regimen that included fluid rehydration and close monitoring of her symptoms.

DISCUSSION

This particular case highlights the importance of the SPINK1 mutation in the development of acute and chronic

pancreatitis, and potential pancreatic cancer. Several studies have been conducted and lend to comparative analysis keeping this data in mind, we developed a systematic outpatient regimen to help our patient with appropriate screening. It was decided that she would have imaging performed every 3-6 months depending on her symptoms. She had a EUS performed 3 months after her discharge, and fortunately no further pancreatic dilation or calcifications were appreciated at that time. Our patient was also taught about how to be vigilant of her symptoms and start prompt hydration with an oral rehydration solution she should start feeling symptomatic. Though our patient denied any tobacco or alcohol use history to begin with, we counseled her extensively on how alcohol can negatively impact her condition. She continues to follow up regularly with her gastroenterologist and has been thoroughly educated about not only her symptoms, but also what her genetic mutation can lead to in the future. SPINK1 mutations should remain as a top differential for those patients who present with recurrent pancreatitis episodes at a young age. A collaborative effort between patient and physician can help identify patients and improve outcomes (**Figure 1**).

One aspect of the SPINK1 mutation that is particularly concerning is its impact in the paediatric population. Per a cross sectional study done by Kumar et al, pancreatitis associated gene mutations like SPINK1 mutations were the most common risk factor for acute recurrent pancreatitis and chronic pancre

atitis in children under the age of 19. They had several emergency room visits each year due to pancreatitis related complications [6]. Many of them continued to struggle with debilitating effects of chronic pancreatitis for the rest of their lives including but not limited to, pancreatic insufficiency, vomiting, weight loss, steatorrhea, and continued epigastric pain [7]. These symptoms are very similar to those seen in our patient, who had had several emergency room visits before the age of 19. Her mother

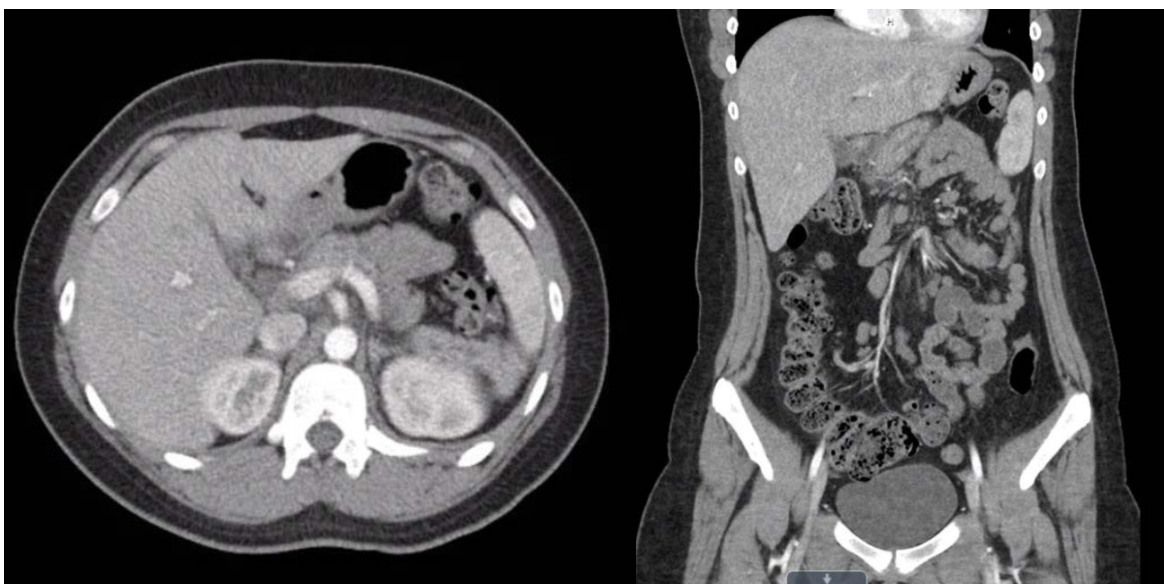


Figure 1. Axial and Coronal CT Scans of pancreatic dilations and calcifications.

reported that she also had bouts of steatorrhea, vomiting, and weight loss over the years.

In studies done by Gurhan et al, certain cases in India show a high prevalence of SPINK1 mutation in patients with development of acute and chronic pancreatitis. However Turkish patients showed less of a role in the mutation of SPINK 1 and pancreatitis. Therefore, demonstrating that, the SPINK1 mutation might be more prevalent in certain ethnic groups [8]. Studies conducted by Koziel et al. in Polish populations found that of those patients that had episodes of acute pancreatitis, those who had a more severe course were likely to have the SPINK1 mutation [9]. Our patient was a young Hispanic female, and more studies need to be performed on the role of SPINK 1 particularly in Hispanic populations. In 2018, James et al. performed a review which demonstrated that acute pancreatitis is a common condition with an annual cost of 2.6 billion dollars. The overall mortality rate associated with acute pancreatitis has remained unchanged over the years, but the incidence continues to increase [10]. Providing further evidence that pancreatitis deserves attention.

Per literature review, SPINK1 mutations have been found to be related to not only the development of more severe forms of pancreatitis but also to potential pancreatic cancer and colon cancer. In a study done by Ohmuraya et al., SPINK1 was found to be a signal peptide that was secreted from both pancreatic acinar cells and colon cancer cells [11]. It is therefore hypothesized that SPINK1 can have a role in autocrine and or/paracrine factors which are involved in both the primary tumor and metastatic spread of cancer [11]. Additionally, when Cazacu et al. performed a meta-analysis investigating the role of SPINK1 and the CFTR gene in pancreatic cancer, it was found that the SPINK1 gene may have a prominent role in cancer development [12]. Therefore, it is important for physicians to be alert in any patient case where there is early onset of pancreatitis and family history, as genetics could be the underlying cause and may propel further worse outcomes.

CONCLUSION

Keeping this data in mind, we developed a systematic outpatient regimen to help our patient with appropriate screening. It was decided that she would have imaging performed every 3-6 months depending on her symptoms. She had an EUS performed 3 months after her discharge, and fortunately no further pancreatic dilation or calcifications were appreciated at that time. Our patient was also taught about how to be vigilant of her symptoms and start prompt hydration with an oral rehydration solution she should start feeling symptomatic. Though our patient denied any tobacco or alcohol use history to begin with, we counselled

her extensively on how alcohol can negatively impact her condition. She continues to follow up regularly with her gastroenterologist and has been thoroughly educated about not only her symptoms, but also what her genetic mutation can lead to in the future. SPINK1 mutations should remain as a top differential for those patients who present with recurrent pancreatitis episodes at a young age. A collaborative effort between patient and physician can help identify patients and improve outcomes.

Conflicts of Interest

All named authors hereby declare that they have no conflicts of interest to disclose.

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