A rare cause of pediatric acute pancreatitis: Perindopril intoxication

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Abstract:
Acute pancreatitis is a reversible inflammatory condition of the pancreas. It usually develops on the basis of trauma, structural abnormalities, and chronic systemic diseases. A definitive causal correlation between a drug and acute pancreatitis is quite difficult for clinicians. Drugs play a vital role in the etiology in approximately 10% of children with pancreatitis. More than 50 drugs including angiotensin-converting enzyme inhibitors have been reported to cause pancreatic damage. There was no pediatric case report developed pancreatitis following perindopril use. A pediatric case of pancreatitis following perindopril intake was presented in this article to emphasize pancreatitis, which is one of the complications that may occur after drug intake.

Keywords:
Acute pancreatitis, children, perindopril

Introduction
Acute pancreatitis is a rare cause of abdominal pain in children and is less common than in adults. The most common cause in children is systemic diseases; it may also develop autoimmune diseases, infections, neoplasia, structural abnormalities, toxins, trauma, and drug exposure.[1,2] Drug intoxication, while it is generally a result of accidental intakes in childhood, is suicide intended in adolescence. In cases of poisoning, various complications may occur depending on the route of administration, amount, and mechanism of action of the substance. A definitive causal correlation between a drug and acute pancreatitis is quite difficult for clinicians; most of the data on drug-induced pancreatitis consist of case reports.[3] More than 50 drugs including angiotensin-converting enzyme (ACE) inhibitors have been reported to cause pancreatic damage.[4] We discussed our acute pancreatitis case following the intake of perindopril in the light of literature.

Case Report
A 15-year-old female patient with no known illness presented to the emergency department within 30 min of taking 10 tablets of 5 mg perindopril (1 mg/kg/dose) as an attempt to commit suicide. Gastric lavage was performed after admission to the emergency department, and parts of the pills were seen in the lavage fluid. The patient was hypotensive (85/50 mmHg) at the time of her first admission. 10 ml/kg serum physiologic was administered intravenously in 15 min, and blood pressure remained normal after the fluid bolus. There was no feature in the family history of the patient. There was no history of alcohol or use of illegal substance. Her physical examination was normal. There were no pathological results observed in hemogram...
The causes of pancreatitis are different in childhood than in adults. While traumas in young children constitute an important cause of acute pancreatitis, there was no reason detected to cause pancreatitis in around 22% of the cases. Biliary system diseases, systemic diseases, infections, pharmacological agents, structural causes such as pancreatic divisum, and familial causes are found when the other etiologic causes are inspected.\cite{1,3}

Drug-induced pancreatitis is actually an exclusion diagnosis. After the diagnosis of acute pancreatitis is confirmed, all etiologies except drug etiology should be excluded. The use of drugs that may cause drug-induced pancreatitis should be discontinued. Possible mechanisms that cause the disease are drug effect and the construction of biliary tract, cytotoxic and metabolic effects of drugs, accumulation of toxic metabolites of drugs, and hypersensitivity reactions. ACE inhibitors reduce the destruction of bradykinin and cause local angioedema in the pancreatic duct. In addition, angiotensin II receptors are important for the secretion and microcirculation of the pancreas. ACE inhibitors contribute to the development of acute pancreatitis with this mechanism.\cite{3,4,7} Some cases of acute pancreatitis have been reported in patients taking perindopril\cite{7} or other ACE inhibitors such as captopril,\cite{8} lisinopril,\cite{8} and enalapril.\cite{10,11}

Drugs play a role in the etiology in approximately 10% of children with pancreatitis. The history of drug use in patients must be questioned carefully. Generally, drug-induced pancreatitis has a mild course, has a self-limiting clinic, and has a good prognosis.\cite{12} Medicines play a role in the formation of idiosyncratic, direct toxic effect, or angioedema-causing pancreatitis. In our case, it was thought that pancreatitis developed due to the use of perindopril as a result of absence of alcohol intake, absence of gallstones on abdominal ultrasonography, history of acute viral infection, normal triglyceride and calcium levels, and absence of any other medical or herbal drug intake. ACE inhibitors such as perindopril cause pancreatitis with localized angioedema. ACE inhibitors increase the vascular permeability of the pancreas by decreasing bradykinin destruction, cause localized angioedema around the pancreas duct, and cause organ damage and development of pancreatitis due to the pancreatic enzyme and other toxic substances remaining in the pancreas.\cite{13} The patient had no fever, rash, or eosinophilia at any time during the course of disease, which eliminates the possibility of an allergic or immune-mediated mechanism. Our patient was symptomatic for toxic pancreatitis; furthermore, clinic and biochemical complete recovery could be seen in 3 days. As in our patient, a metabolic idiosyncratic reaction seems to be the most likely explanation of perindopril-associated toxic pancreatitis. We considered the idiosyncrasies.

Perindopril is a form of ACE inhibitor used in the treatment of hypertension and heart failure in adults.
While the first case report\textsuperscript{[7]} of pancreatitis following perindopril use was made in a 70-year-old patient in 1997, the second case\textsuperscript{[14]} was reported in a 72-year-old patient in 2005. There was no pediatric case report developed pancreatitis following perindopril use in our study based on the PubMed data.

Treatment of acute pancreatitis is supportive. It consists of cessation of pain, hydration, resting of the pancreas, and close monitoring of complications.\textsuperscript{[2]} After the oral food intake of our patient was stopped and hydration was applied, the treatment process was completed without the need for painkillers and without complications and was discharged with no problem during the follow-up.

**Conclusion**

It should be kept in mind that acute pancreatitis may develop due to drugs, one of which may be perindopril which is an ACE inhibitor. Epigastric pain, nausea, and vomiting should not be attributed only to gastrointestinal side effects after drug use; it should be noted that complications such as pancreatitis may develop.

**Author contributions statement**

We verify and confirm that each author contributed to every stage of this manuscript equally.

**Conflicts of interest**

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**References**