

Acute pancreatitis possibly due to arginine use: A case report

Muhtemelen Arginin'e bağılı gelişen akut pankreatit: Olgu sunumu

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Arginine has been used by millions of athletes over the past 20 years to enhance production of human growth hormone. The effects of arginine supplementation include increased fat burning and muscle building, enhanced immunity, and improvement in erectile function in men. Excessive doses of basic amino acids such as ethionine, methionine and lysine are known to damage the rat pancreas. Recent studies have demonstrated that excessive doses of arginine induce necrotizing pancreatitis in rats. In this article, we report a 16-year-old male patient hospitalized in our clinic because of severe pain in upper abdomen, nausea and vomiting who was suspected to have arginine-induced acute pancreatitis.

Arginin, son 20 yılda insan "growth" hormon üretimini arttırmak amacıyla milyonlarca atlet tarafından kullanılmaktadır. Arginin desteğinin etkileri; yağların yakılmasını arttırmak, vücut geliştirmek, immünitinin güçlendirilmesi ve erkeklerde erektil fonksiyonların artırılmasıdır. Etionin, metionin ve lizin gibi temel aminoasitlerin yüksek dozlarda rat pankreasında hasara yol açtığı bilinmektedir. Son çalışmalarda, arginin'in yüksek dozlarda ratlarda nekrotizan pankreatite yol açtığı gösterilmiştir. Bu makalede, üst abdomende ciddi ağrı, bulantı ve kusma nedeniyle kliniğimize yatırılan ve arginin'e bağılı akut pankreatit geliştiği düşünülen 16 yaşındaki bir erkek hasta sunulmuştur.

Keywords: L-arginine, pancreatitis, nitric oxide

Anahtar kelimeler: L-arginin, pankreatit, nitrik oksid

INTRODUCTION

L-arginine is a semi-essential amino acid found in our diet. The body converts L-arginine into nitric oxide (NO), which is a powerful vasodilator (relaxer of blood vessels) and increases blood flow. In the pancreas, L-arginine is used to release insulin. In the pituitary gland, it is a component of human growth hormone.

Recently, there have been numerous animal studies reported about L-arginine-induced acute pancreatitis (1-6). However, we could not find any such case report in the literature. In this article, we report a case of a young man who suffered from acute pancreatitis induced by L-arginine.

CASE REPORT

A 16-year-old male patient was admitted with severe pain in upper abdomen, nausea, vomiting and anorexia. Abdominal pain was at epigastric

location and radiated to the back. Patient's symptoms had begun two days previously, after dinner. His drug interrogation revealed the use of 500 mg/day L-arginine and 10 mg/day zinc over five months, for the purpose of body building. He was taking those drugs at his own will, without a doctor's prescription. His weight was 75 kg and height 193 cm. He had no alcohol intake, and no previous or recent trauma. Physical examination was normal except widespread tenderness of abdomen. The body temperature was 37.5°C. Other vital findings were stable.

The patient was hospitalized. Serum chemistry was as follows: leukocyte count 14,400/mm³ (normal, 4000-11000), erythrocyte sedimentation rate 7 mm/h, serum amylase 177 U/L (normal, 25-90), and urinary amylase 2288 U/L (normal, 0-480). There was no hyperlipidemia. Other laboratory findings were normal.

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Upright plain film of the abdomen, chest X-ray, upper abdominal ultrasonography and computerized tomography were normal (Figure 1). Endoscopy of upper gastrointestinal system disclosed gastritis. Occult microlithiasis and pancreatic divisum were not investigated because of the rapid response to therapy, there was no history of a previous attack and because of his refusal of invasive instrumentation. On the second day, serum amylase increased to 510 U/L and urinary amylase to 2813 U/L. With these findings, L-arginine-induced acute pancreatitis was diagnosed and all medications stopped. Oral nutrition was stopped as well. Ciprofloxacin and omeprazole were begun parenterally. The response to therapy was very quick. On the fourth day, an oral watery diet was started, which he tolerated. On the fifth day, serum amylase decreased to 199 U/L and urinary amylase to 1155 U/L. He was discharged at his own request on the same day.



Figure 1. The normal appearance of the pancreas in abdominal computerized tomography

DISCUSSION

Arginine has gained recent attention in critical care nutrition and is considered a conditionally essential amino acid. Arginine is the specific precursor for nitric oxide production and a potent secretagogue for anabolic hormones such as insulin, prolactin, and growth hormone. Under normal circumstances, arginine is considered a nonessential amino acid because it is adequately synthesized endogenously via the urea cycle. However, research suggests that during times of metabolic stress, optimal amounts of arginine are not

synthesized to promote tissue regeneration or positive nitrogen balance (7). Research studies in animals and humans have shown positive outcomes from supplementation to include improved nitrogen balance, wound healing, and immune function, and increased anabolic hormones, insulin, and growth hormone (7).

Arginine is reported to damage pancreatic acinar cells. Arginine induced a dose-related necrotizing pancreatitis in rats, as shown by histological evaluation, and an increase in serum amylase. Severe pancreatitis induced by 4.5 g/kg arginine was accompanied by dramatic changes in the actin cytoskeleton. Arginine-induced acute pancreatitis alters the actin cytoskeleton and increases heat shock protein expression in pancreatic acinar cells (6).

Acute pancreatitis was induced in male Wistar rats by injecting 250 mg/100 g body weight of arginine intraperitoneally twice at an interval of 1 hour, as a 20% solution in 0.15 NaCl. In this study, Takacs et al. reported that endogenous nitric oxide is involved in the formation of pancreatic edema in arginine-induced acute pancreatitis by increasing the vascular permeability and protein extravasation (1).

Mizunuma et al. reported that a single intraperitoneal administration of arginine (500 mg/100 g body weight) results in selective pancreatic acinar cell damage in rats without any morphological change in the Langerhans islets (8).

Czako et al. reported that oxygen-derived free radicals and cytokines play a role in the pathogenesis of L-arginine-induced acute pancreatitis in rats (2). In studies about pathogenesis, it has been demonstrated that endogenous cholecystokinin does not seem to play an essential role (2, 5). Furthermore, prophylactic allopurinol treatment prevents the generation of reactive oxygen metabolites, reduces the serum amylase level, and partially attenuates the development of histopathological changes (2,3).

L-arginine sometimes reactivates latent herpes virus infections. Those with certain psychoses may experience worsened symptoms if they take L-arginine supplements. Persons who have not completed their bone growth (children and teenagers) and pregnant or lactating women should not use L-arginine. Diabetics and borderline diabetics should use growth hormone releasers with care. L-arginine might worsen a diabetic condition (9, 10).

Like our patient, world-class athletes and professional bodybuilders use L-arginine. The benefits of L-arginine supplementation are clearly dose-dependent. Beneficial dosages of L-arginine range from between 3 to 30 gr taken orally per day.

In our patient, no biochemical change was found except increased serum and urine amylase. It may be because of the low dose of L-arginine, i.e. 500 mg/day. The effect of arginine is enhanced when combined with zinc (Zn). Zinc contributes to the proper functioning of a number of hormones, including growth and sex hormones. Acute pancreatitis has been reported in humans and animals, following the ingestion of zinc as well (11, 12). The mechanism of toxicity is unknown, although the

pathophysiology may relate to the role of the pancreas in zinc excretion. Analysis of zinc in rats with acute pancreatitis showed the serum levels of Zn were significantly elevated. These observations indicate that Zn could play an important role in acute pancreatitis (13). But, we consider that L-arginine seems to be the likely cause of pancreatitis in this patient possibly via the mechanism mentioned above. Zn might have additionally contributed to this damage.

In conclusion, arginine may be a causative agent of acute pancreatitis; physicians must keep this in mind. We reported this case to note a possible consequence of arginine use for bodybuilding.

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