Introduction

Pneumatosis cystoides intestinalis (PCI) is not too a frequent disease characterized by presence of multicellular cysts in the gastrointestinal wall. Idiopathic and secondary forms of the disease can be distinguished. There are presented several theories explaining pathogenesis in this article. The specific and non-specific symptoms are described. Attention is drawn to the pneumoperitoneum without signs of peritoneal irritation, what is a typical complication of this disease. The suspicion of pneumatosis cystoides intestinalis may be based on plain abdominal X-ray, and is usually confirmed by computer tomography or magnetic resonance imaging. The therapy can be conservative or surgical. In conclusion, although pneumatosis cystoides intestinalis is a rare disease, it may represent a problem in differential diagnosis of abdominal pain.

Etiology and pathogenesis

According to Kreiss et al. (33) PCI can be classified either the idiopathic with unknown etiology (15%) or the secondary one (85%), in which the mechanism of cysts origin has been explained. Several theories elucidating the pathogenesis of this disorder have been proposed.

Mechanical theory

The mechanical theory explains the pathogenesis of pneumatosis by physical factors. Two pathogenetic mechanisms have been proposed: air leakage from lung interstitium to mediastinum, retroperitoneum, mesenterium and intestinal wall, and leakage of intraluminal gas through gaps in intestinal mucosa. The first mechanism has been proposed in patients with chronic obstructive lung disease or with other illness of the respiratory system (48). A rise in intraalveolar pressure leads to alveolar rupture and leakage of air into lung interstitium. Air from lung interstitium is thought to dissipate via mediastinum, retroperitoneum and mesenterium into the gut wall (37). The second mechanism is represented by increase of intraluminal bowel pressure, which in connection with damage of the mucosa leads to intramural penetration of gas. This can explain the fact that PCI is often present in patients who have gastrointestinal disease - peptic ulcer disease, Crohn's disease (24,48) or necrotizing enterocolitis (11,27,32). Necrotizing enterocolitis with PCI has been induced experimentally by arterial and lymphatic ligation (46). Some others (41) explain PCI as a consequence of reparation after bowel ischemia.

Bacterial theory

Bacterial theory explains the pathogenesis of PCI by bacterial infection. This infection either damages the intestinal wall with subsequent intramural penetration of gas, or produces gas, which then penetrates into the gut wall. Gas can also enter the lymphatic vessels and cause their dilatation. This theory is supported by experiments in rats, where PCI was induced by Clostridium perfringens (52). The microorganisms playing role in origin of PCI are Clostridium difficile, cytomegalovirus (44) or Clostridium perfringens (7).

Immunopathological inflammatory reaction

Based on observation by Holl et al. (22) and their demonstration of histiocytes and foreign-body giant cells present in the afflicted part of the bowel, immunopathological inflammatory reaction has been proposed as a cause of PCI. The presence of monocytes and similar mononuclear cells has been confirmed by Gagliardi et al. (19).
Pneumatisosis cystoides intestinalis (PCI) is characterized by high level of hydrogen breath, patients with PCI excrete more hydrogen than others. Clinical features of PCI may be in consequence of abnormal hydrogen metabolism. In normal subjects hydrogen is consumed by methanogenic and sulfatereducing bacteria. The activity of these bacteria is missing in patients with PCI. This leads to the intraluminal gas accumulation, to an increase of intraluminal pressure and thus to intraluminal gas penetration (12,13). The mechanism just described can also explain cyst ruptures (5,13) of the hydrogen hyperproduction is only the initial reason for cysts origin. Their further persistence is caused by nitrogen and oxygen, which diffuse from blood (35).

Clinical presentation

Presence and character of symptoms

The character of symptoms is dependent on the localization of PCI and on presence or non-presence of basic disease. Symptoms, which can appear, are either non-specific or specific ones. Abdominal distension (29,34), diarrhea (10,19,29,39), abdominal pain (10,39), constipation (19,39), mesocolic distension (19,39), hypotension (38), mental bleeding (19,39), meteorism (14) and weight loss (10) belong to non-specific symptoms. Among the specific symptoms there belongs cysts, which can be sources of origin of invagination (1) or volvulus (5) and can cause interruption of motility and the mechanical obstruction (26). It is especially necessary to draw attention to cysts ruptures, which lead to pneumorrhachitis – pneumoperitoneum without alarming signs of peritoneal irritation (16,23,26,28,31). Pneumoretropitoneum develops by cyst rupture in retroperitoneal location (19,39). The character of symptoms is dependent on presence or non-presence of basic disease. PCI has been also described after bone marrow transplantation (6). The effect of long term steroid use, infection, immunosuppression, graft-versus-host disease are thought to cause disorder in these cases (36).

Diagnostics

When PCI is suspected the first examination is plain radiography of abdomen (26,51). There are seen the cysts in the bowel wall or free air under diaphragm in the case of their rupture and cyst rupture occurs (5,33). There is also described the incidence of PCI in other parts of alimentary tract - small intestine (35,42), stomach (4,6). Small intestine infection can be connected with malabsorption (39) or with coeliac disease (45), the gastric infection is unusual (15).

Age and sex

Beyond infancy the PCI rate is rare (44). In Bertram's et al. (7) opinion the period with the most frequent incidence of PCI is age between 30 and 50 years, a clear sexual predominance doesn’t exist.

Therapy

In asymptomatic patients with PCI no special therapy is recommended (9,18). If a basic disease is present, then it is necessary to treat it and secondary cysts regression is usually observed. PCI therapy could be conservative or surgical one.

Conservative therapy

Conservative therapy can be causal or symptomatic. The causal therapy includes ways suppressing supposed etiologic mechanisms. Inhibition principles of these mechanisms consist either in restriction of alimentary gas producing microflora - administration of antibiotics, especially metronidazol (7,29,31,47), or in inhibition of process leading to the hydrogen hyperproduction - hyperbaric oxygen therapy (19,27,31,42). In another way of treatment there is possible to include a diet low in flatulence-producing carbohydrates (14), parenteral nutrition (29,31), endoscopic sclerotherapy of alimentary loops (25), therapy with long-acting somatostatin analogue (30). Symptomatically therapy suppresses single symptoms (19) - as pain, constipation, diarrhoea.

Surgical therapy

Patients with pneumoperitoneum without signs of peritoneal irritation when diagnosis of PCI is known is not necessary to operate (23,44), it is sufficient enough to observe them (23) Surgery is indicated only in fulminant cases (3). The most frequent surgical goal is gut resection (7) or limbal colostomy (50).

Conclusion

To conclude: pneumatosis cystoides intestinalis is a rare entity with unrecognized complication by modern diagnostic methods. The practical importance of this paper is to inform about this problem and thus to enable to avoid the laparotomy in patients suffering from PCI with pneumoperitoneum without signs of peritoneal irritation.

References

9. Brenchley NEG, Dunn AG, Broomhead JG, Buttery DP, Hasleton PS. Pneumatosis cystoides intestinalis and high breath H2 excretion enables to detect higher breath level of hydrogen by patients with PCI (12).
Pneumoperitoneum can be caused by surgical intervention (8). The conservative therapy can be causal or symptomatic. The causal therapy includes ways suppressing supposed etiological mechanisms. Inhibition principles of these mechanisms consist either in restriction of intestinal gas-producing microflora – administration of antibiotics, especially metronidazole (7,29,31,47), or in inhibition of process leading to the hydrogen hyperproduction - hyperbaric oxygen inhalation (7,31,42). In another way of treatment there is possible to include a diet low in flatulence-producing carbohydrates (14), parenteral nutrition (29),31), endoscopic methods (13), and cysts sclerotherapy (25), therapy with long-acting somatostatin analogue (30). Symptomatic therapy suppresses single symptoms (19) - as pain, constipation, diarrhoea.

Surgical therapy

Patients with pneumoperitoneum without signs of peritonitis are diagnosed with PCI known is not necessary to operate (23,44), it is sufficient enough to observe them (23). Surgery is indicated only in fulminant cases (3). The most frequent surgical operation is gut resection (7) or limbectomy (50).

Conclusion

To conclude: pneumatosus cysts intestinals is a rare entity with uncomplicated recognition by modern diagnostic methods. The practical importance of this paper is to inform about this problem and thus enable to avoid the laparotomy in patients suffering from PCI with pneumoperitoneum without signs of peritonial irritation.

References

Introduction

The potential for the exposure to highly toxic organophosphorus compounds (OPs), called nerve agents, exists on the battlefield (e.g. Iran-Iraq war) as well as in a civilian sector as a threat to a terrorist group (e.g. Tokyo subway - 12) or as an accident as a part of current demilitarization efforts. OPs elicit their toxic effects by irreversible inhibiting acetylcholinesterase (AChE, EC 3.1.1.7) in the central as well as peripheral nervous system allowing accumulation of acetylcholine (ACh), excessive stimulation of postsynaptic cholinergic receptors and consequent signs of neurotoxicity. Signs of acute toxicity with extensive AChE inhibition include autonomic dysfunction (e.g. excessive salivation, lacrimation, urination and defecation), involuntary movements (e.g. tremor, fasciculation), respiratory dysfunction and other signs and symptoms (9, 19).

OP-induced cholinergic effects are usually manifested immediately following high-level exposure (9, 19), nevertheless, there are numerous studies in both humans and animals showing that survivors of high-level OP exposure can experience subtle but significant long-term neurological and neuropsychological outcomes that are detectable months or even years following the recovery from acute poisoning (2). The rapid onset of signs and symptoms of poisoning following OP exposure can be explained in terms of ACh accumulation following AChE inhibition but no mechanism has been identified for the induction of long-term effects.

Material and methods

Male albino Wistar rats weighing 180-200 g were purchased from VUFK Konarovic (Czech Republic). They were kept in an air-conditioned room and allowed access to standard food and tap water ad libitum. The rats were divided into groups of ten. Handling of the experimental animals was done under supervision of the Ethics Committee of the Medical Faculty of Charles University and the Purkyně Military Medical Academy in Hradec Králové (Czech Republic).

The rats were exposed to various low concentrations of sarin (obtained from Military Technical Institute, Zemianske Kostolany, Slovak Republic) for 60 minutes in the inhalation chamber. Three low concentrations of sarin were chosen: 1. To study the influence of low-level sarin exposure on cognitive functions, male albino Wistar rats were exposed to three various low concentrations of sarin (LEVEL 1–3) for 60 minutes in the inhalation chamber. Testing of cognitive functions was carried out using the T-maze evaluating learning and spatial memory. The behavior of sarin-exposed rats in the T-maze was tested several times within five weeks following sarin inhalation exposure to look for any cognitive impairments. The alteration of cognition was evaluated by using a method studying memory elicitation in response to appetitive motivation in a multiple T-maze. 2. Statistically significant, short-term deficiency in the T-maze performance was observed in rats exposed to symptomatic (LEVEL 3) as well as clinically asymptomatic concentration (LEVEL 2) of sarin. The repeated exposure of rats to clinically asymptomatic dose of sarin (LEVEL 2R) did not change the effect of low-level sarin exposure on spatial memory compared to the single exposure to the same dose of sarin. 3. Thus, sarin is able to influence the cognitive functions (e.g. spatial memory) even at low doses that do not cause clinically manifested intoxication following the inhalation exposure. Nevertheless, the alteration of spatial memory lasts for a short time only, in contrast with the severe sarin poisoning.

Key words: Sarin; Low-level inhalation exposure; Spatial memory; T-maze; Rat

Original Article

LONG TERM EFFECTS OF LOW-LEVEL SARIN INHALATION EXPOSURE ON THE SPATIAL MEMORY OF RATS IN A T-MAZE

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Summary: 1. To study the influence of low-level sarin exposure on cognitive functions, male albino Wistar rats were exposed to three various low concentrations of sarin (LEVEL 1–3) for 60 minutes in the inhalation chamber. Testing of cognitive functions was carried out using the T-maze evaluating learning and spatial memory. The behavior of sarin-exposed rats in the T-maze was tested several times within five weeks following sarin inhalation exposure to look for any cognitive impairments. The alteration of cognition was evaluated by using a method studying memory elicitation in response to appetitive motivation in a multiple T-maze. 2. Statistically significant, short-term deficiency in the T-maze performance was observed in rats exposed to symptomatic (LEVEL 3) as well as clinically asymptomatic concentration (LEVEL 2) of sarin. The repeated exposure of rats to clinically asymptomatic dose of sarin (LEVEL 2R) did not change the effect of low-level sarin exposure on spatial memory compared to the single exposure to the same dose of sarin. 3. Thus, sarin is able to influence the cognitive functions (e.g. spatial memory) even at low doses that do not cause clinically manifested intoxication following the inhalation exposure. Nevertheless, the alteration of spatial memory lasts for a short time only, in contrast with the severe sarin poisoning.

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