Intestinal Emphysema (Pneumatosis cystoides intestinalis) in a Gnotobiotic Pig

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ABSTRACT

A gnotobiotic pig monocontaminated with an enteropathogenic Escherichia coli was subsequently hyperimmunized to produce a monotypic antiserum. At necropsy, multiple, air filled cysts were found in the wall of the large intestine. The etiology of this condition is still conjectural. However, select strains of E. coli may cause or contribute to intestinal emphysema in swine.

RÉSUMÉ

Cette expérience visait à infecter un porc axénique avec une souche entéropathogène d'Escherichia coli et à le rendre ensuite hyperimmun, afin de produire un antisérum monovalent. Lors de la nécropsie de cet animal, on découvrit plusieurs kystes emphysémateux, au sein de la paroi du côlon. L'étiologie de cette condition demeure toujours obscure. Certaines souches d'E. coli semblent cependant pouvoir causer ou favoriser l'emphysème intestinal, chez le porc.

INTRODUCTION

Intestinal emphysema (IE) has been described as an infrequent condition of swine characterized by the existence of gas filled bubbles or cysts within the intestinal wall and adjacent lymph nodes (9, 16). A similar condition commonly referred to as *Pneumatosis cystoides intestinalis* also occurs in man (1, 6, 10).

It is not known when the first case of IE was observed in swine, but Cloquet, as early as 1820, made comparisons to this condition in swine when describing a human case found at autopsy (4).

Although numerous explanations have been advanced as to the cause of this condition, the etiology remains unknown (1, 6). The most widely accepted theory in human medicine explains this condition largely on a mechanical basis associated with damage resulting from: a) respiratory disease with severe cough, b) trauma or injury resulting from sigmoidoscopic examinations, biopsy collections, etc. and c) gastrointestinal infections, gastric ulcers, malignancies and intestinal obstructions (1).

This report describes a case of intestinal emphysema in a gnotobiotic pig. The controlled and defined conditions under which this particular animal was maintained make these observations of interest and provides additional information which may help identify the factors associated with or contributing to this condition.

MATERIALS AND METHODS

The pig was one of a litter of nine germfree piglets. Methods of procurement and rearing were as previously described (14). At three weeks of age, the piglet was monocontaminated by oral inoculation and colonized with a culture of *E. coli* O8:K87, K88ac:H19. At six weeks of age, the pig was injected three times, subcutaneously, every other day with a sterile filtrate of the bacterial culture used above. A single booster injection was given 45 days after the last injection. Ten days following the booster injection, the pig was anesthetized with sodium thiopentol, exsanguinated and necropsied.

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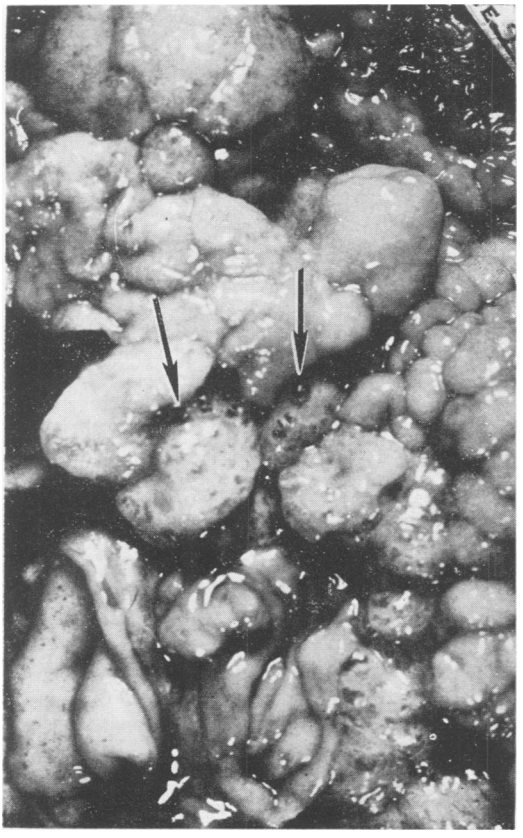

Fig. 1. Exposed colonic mucosa showing the irregular surface due to gaseous displacements in the submucosa. Gas filled vesicles (arrows) visible within the mucosa.

Tissues for histopathological examination consisted of brain, heart, lung, liver, spleen, kidney, mesenteric lymph nodes and segments from various levels of the G.I. tract. Tissues were fixed in neutral 10% formalin, trimmed, processed on an autotechnicon model 2A, embedded, sectioned at 5 μm and stained with hematoxylin and eosin, Harris method (9).

Heart blood, gastric, ilial and cecal contents were cultured aerobically on blood and MacConkey's agars at 36°C. Gram stained smears of this material were also prepared and examined.

RESULTS

Following the initial oral exposure to the *E. coli* culture the pig exhibited typical signs of enteric colibacillosis, characterized by diarrhea and dehydration. The pig recovered and appeared normal by the time the first series of injections were started. The *E. coli* readily colonized the gut of the animal, persisted in the intestine for the duration of the study and was the only microbial agent recovered or observed by Gram stain.

With the exception of the large intestine which contained diffuse vesicular lesions (Fig. 1), the internal organs appeared normal at the time of necropsy.

The major histologic abnormalities were numerous large endothelial-lined cystic structures surrounded by elastic fibers within the mucosa, submucosa, muscularis and the periserosal areas of the large intestine (Fig. 2). The majority of the cysts were within the submucosa and muscularis resulting in a marked displacement of the muscularis. The walls between cysts in many cases contained a mixture of neutrophils, eosinophils, lymphocytes, monocytes, fibroblasts and an occasional multinucleated giant cell. In the submucosa of the colon, cysts displaced portions of the lymph follicles. Cysts were not observed within the mesenteric lymph nodes although some eosinophilic infiltrates were present. In

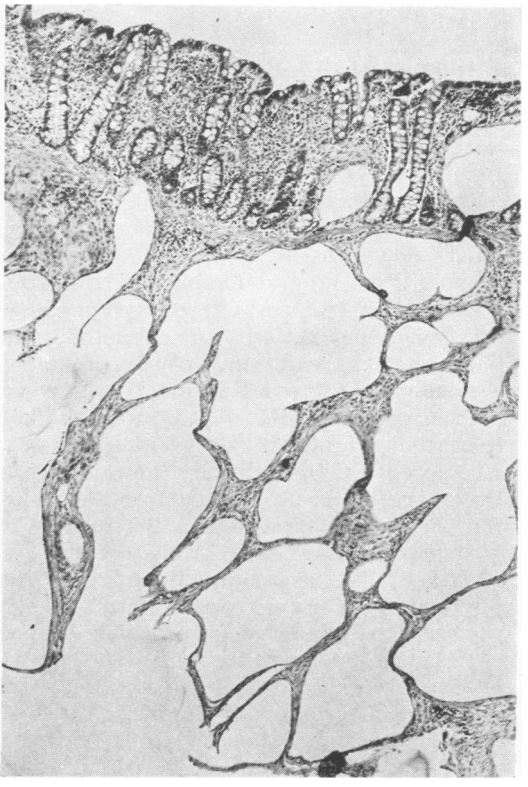

Fig. 2. Section of colon showing distribution of vesicles in submucosa and mucosa. H & E.

the lungs there was a very mild focal interstitial pneumonitis with an occasional small area of emphysema, changes conparable to those seen in both normal conventional swine and those coming to necropsy for other than pulmonary diseases.

DISCUSSION

The incidence of this condition in the swine population has been decreasing since the early 1940's and today, with some possible exceptions (7), is extremely low. The reason for this decline is unknown but conceivably is related to improvements in swine management and nutrition (16).

The condition does not affect the acceptability of the carcass (11) and it is doubtful the disease (if it may be called a disease) has ever been of economic significance.

Although it might be expected that animals with extensive involvement would suffer from some degree of malabsorption, afflicted pigs clinically appear normal and the condition is first recognized at slaughter (7, 9, 16).

In man *Pneumatosis cystoides intestinalis* is also known as cystic lymphopneumatosis, peritoneal lymphomatosis, intestinal pneumatosis and bullous emphysema of the intestine (6). There are no pathognomonic symptoms.

In infants, diarrhea is usually present. Although adults are usually asymptomatic, others may present an irritable colon syndrome with vague abdominal distress, constipation, meteorism (6) or symptoms of intestinal obstruction (10). Whether similar situations exist in swine is unknown.

Considering the wide variety of factors associated with IE, it appears unlikely there is a single cause or simple etiology (1, 6). It would appear, however, that there are at least two factors necessary for the development of IE, the production of gas and its access to tissue spaces.

Although a bacterial etiology has been discounted in recent years (6) there is growing experimental evidence in support of this theory, particularly in the reports of Stone *et al* (18) and the recent work of Yale and Balish with germfree rats (19, 20). Of the bacterial species thus far implicated (Coliforms and Clostridia) it is interesting to note that all are potent gas producers.

The occurrence of this disease in a monocontaminated gnotobiotic pig maintained under control conditions was fortuitious and lends support to a bacterial etiology. However, nutritional (8) and host factors should not be discounted. In this study the pig was raised solely on a sterile, fortified milk diet and in years past this condition was frequently observed in swine fed dairy wastes (13), a practice now relatively uncommon. Host factors such as carbohydrate and milk intolerance may also have a significant role either alone (2, 3) or in combination with bacterial enteric pathogens (5).

The gross and histopathological lesions observed in the gnotobiotic pig were somewhat atypical for swine (9, 16) and resembled more closely the mild benign type described in the human adult (10, 17). The lesions were most prominent in the wall of the large intestine rather than the serosa of the small intestine. The mesentery was not involved.

The absence of both gross respiratory disease, one of the suspected causes of this condition, and lesions in the mesentery and serosa tend to speak against air reaching the intestines peritoneally as a consequence of alveolar rupture (1). Likewise, the absence of endoscopic examination rules out mechanical damage to the colon from this source.

Although neither gastric ulcers nor intestinal obstructions were seen at necropsy, the particular strain of *E. coli* is known to induce marked gastric dilation, congestion and erosions in germfree pigs (12). It is hypothesized that the intestinal emphysema observed here may have been the consequence of the enteric disease resulting from the *E. coli* infection induced several weeks prior to the inoculations. The marked involvement of the mucosa and submucosa (Fig. 2) support the idea that the gases are absorbed directly from the intestine.

The low incidence of this disease with its negligible economic impact, tends to preclude much research into its cause. Consequently, it is anticipated this disease will remain largely a curiosity of academic interest.

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