Chronic Intestinal Pseudoobstruction Associated with Inflammatory Visceral Neuropathy

A Case Report

The pathogenesis of chronic intestinal pseudoobstruction (CIP) presents a broad spectrum of etiologies. Among them, visceral neuropathy and myopathy are two major pathologic conditions. We report here on a very rare case of CIP associated with inflammatory visceral neuropathy involving the terminal ileum, appendix and entire colon in a 64-year-old woman who did not have any detectable neoplasm or family history of this disease. Microscopically, the submucosal and myenteric plexuses showed a severe and diffuse lymphoplasmacytic infiltrate with degenerative changes of the ganglion cells and nerve fibers. The pathogenesis of the inflammatory reaction is unclear for our patient, but we think that this would be a rare example of idiopathic and sporadic visceral neuropathy resulting in chronic intestinal pseudoobstruction.

Key Words: Intestinal Pseudoobstruction-Neuropathy

Intestinal pseudoobstruction is characterized by the failure of the intestinal tract to propel its contents, leading to the signs and symptoms of bowel obstruction in the absence of any identifiable mechanical blockage. Those cases associated with systemic diseases, or the administration of drugs affecting bowel motility are considered as secondary intestinal pseudoobstruction, whereas those cases without any known underlying etiology are termed idiopathic intestinal pseudoobstruction. Idiopathic forms are further divided into the familial and sporadic types. The pathogenesis of idiopathic forms is poorly understood, but histopathological changes can be classified into three broad categories, the myopathic type, the neuropathic type, and a form without any specific histopathological changes. Secondary intestinal pseudoobstruction has been related to connective tissue diseases, herpes virus infection, and paraneoplastic syndrome associated with bronchial carcinoid, thymoma, ganglioneuroblastoma, and small cell lung carcinoma (SCLC). Some patients with paraneoplastic intestinal pseudoobstruction possessed antineuronal nuclear antibodies (ANNA-1 or Hu autoantibodies) in their sera. We searched for and found a few CIP cases in the Korean literature. They were associated with systemic lupus erythematosus, sporadic visceral myopathy and small cell lung carcinoma, respectively. We have recently experienced a case of CIP showing histological changes compatible with visceral neuropathy. The patient did not have neoplasm or any other detectable causes that may have led to secondary intestinal pseudoobstruction. In the English literature, we found two reports describing severe intestinal pseudoobstruction caused by inflammation of the myenteric plexus in patients who never showed a tumor on long-term follow-up. We think that our case belongs to this category, and this would be the first case of idiopathic and sporadic intestinal pseudoobstruction associated with inflammatory visceral neuropathy in Korea.

CASE REPORT

A 64-year-old woman was admitted to our hospital due to a
six-month history of nausea, vomiting, abdominal pain and constipation. She had no previous history of gastrointestinal illness, recent febrile illness, travel outside the Korea and medication. She developed diabetes mellitus ten years ago and her blood glucose level had been controlled well by regular injection of insulin; it was 96 mg/dL at the time of admission. Two months before admission, she visited another hospital for the same symptoms and had a cholecystectomy performed by exploratory laparotomy. The histological diagnosis for the gallbladder was acalculous chronic cholecystitis and cholesterolosis. She did not smoke cigarettes and did not drink alcohol. Clinical examination showed mild abdominal distension and markedly decreased bowel sounds. Plain abdomen X-ray showed moderate dilatation of small bowel loops with air-fluid levels being noted (Fig. 1). The colon still contained some contrast medium the patient had received two months earlier for a small bowel series and the barium enema she received in another hospital. Her chest X-ray was normal. Abdominal CT scan failed to find any bowel obstructive lesion. On the 10th hospital day, herpes zoster developed on her left thoracic 8th and 9th dermatome area. On the 39th hospital day, exploratory laparotomy was performed to exclude any possible mechanical obstruction of the digestive tract. The small bowel loops were located in the pelvic cavity, and their peristaltic movement was active. The colon proximal to the distal sigmoid was diffusely dilated and showed aperistalsis. Because clinical observation, radiologic studies and direct observation during surgery had all shown a complete lack of propulsive motility within the large bowel, a subtotal colectomy including terminal ileum, appendix, cecum, ascending, transverse, descending and sigmoid colon with ileorectal anastomosis was performed.

The terminal ileum measured 20 cm in length and 5 cm in luminal circumference, and the colon from the cecum to the sigmoid measured 110 cm in length and 10 cm in average luminal circumference. The colon showed diffuse and mild dilatation (Fig. 2). The mucosa of terminal ileum and colon looked normal. Histologically, the myenteric and submucosal plexuses of the colon, terminal ileum and appendix were infiltrated by mature small lymphocytes and abundant plasma cells (Fig. 3A). Ganglion cells were reduced in number and some of them presented with degenerative changes, including retraction and dark cytoplasm (Fig. 3B). The lymphoplasmacytic infiltrate was more abundant in the myenteric plexuses that were rich in ganglion cells. The plexuses with a complete lack of ganglion cells showed resolved inflammation or the absence of inflammation (Fig. 3C), and they were sparse and distributed haphazardly. The inflammatory change was diffuse and it involved the resected ends of terminal ileum and sigmoid colon. No intrinsic abnormalities of the mucosa, submucosa or muscularis propria were noted. On immunohistochemical stains, the lymphoid infiltrate predominantly consisted of T cells (Fig. 4). We could not find viral inclusions or
vacuolization of the ganglion cells in the inflamed plexus. PCRs for HSV type 1 and 2 (HSV one tube nested PCR kit; Neodin, Korea), CMV (US14 region-nested primer set; Bioneer, Korea), EBV (EBNA primer; Bioneer, Korea) and VZV (VZV PCR kit; Biocore, Korea) were all negative on the patient’s colon. We reviewed the histologic slides of the gallbladder that had been removed in another hospital two months before admission. Some of the perimuscular autonomic nerve plexuses having ganglion cells showed a lymphoplasmacytic infiltrate similar to submucosal and myenteric plexuses of the intestine.

After the subtotal colectomy, she had been taking prednisolone (10 mg/day), but her condition deteriorated with severe abdominal pain and distention. An L-tube and rectal tube were applied to decompress her abdomen. On the 74th hospital day her chest X-ray revealed pneumonic infiltration. She failed to recover from the pneumonia and died of septic shock. No autopsy was performed.

**DISCUSSION**

The presence of inflammatory cells in the myenteric plexus usually serves as a marker of plexus injury. An inflammatory
process within the myenteric plexus is generally associated with intestinal motor dysfunction, and this condition has been reported in Chagas’ disease, cytomegalovirus infection and paraneoplastic visceral neuropathy. In Chagas’ disease, as well as in paraneoplastic visceral neuropathy, it was suggested that trypanosomal or tumor antigens induce a cellular immune response that cross-reacts with neural tissue of the myenteric plexus.\textsuperscript{13,17} Viral inclusions for VZV, EBV and CMV were described in the myenteric plexus of the patients with CIP.\textsuperscript{3-5} Debinski \textit{et al.}\textsuperscript{6} have detected EBV and CMV by PCR in the small intestine of patients with inflammatory visceral neuropathy, and they suggested that DNA viruses might be the etiological agents for some sporadic CIP. There was no cytopathic change for neurotropic viral infection in our patient’s intestine, but we searched for the viral DNA in the intestinal tissue using nested PCR because she had herpes zoster during hospitalization. We excluded the possibility of viral infection of the patient’s intestine by the negative results for PCRs and the absence of cytopathic change for viral infection. SCLC was the most common malignancy associated with paraneoplastic visceral neuropathy. Approximately 80\% of SCLC patients had ANNA-1, and the obstructive symptoms started from a few months to 1.5 years before the detection of the tumors, and even more than a few years after removal of the tumors.\textsuperscript{10-12} Paraneoplastic CIP was accompanied with other neurologic symptoms including peripheral neuritis, cerebellar degeneration and autonomic dysfunction in some patients.\textsuperscript{10} Our patient was a non-smoker and had neither pulmonary or other organ neoplasm nor neurologic symptoms. Her chest X-ray and abdominal CT scan failed to find out any neoplasm, yet we could not completely rule out the possibility of paraneoplastic CIP because an autopsy was not performed in this case and CIP may precede the occurrence of tumor. Diabetes mellitus is one of the most common endocrine disorders related to gastrointestinal motility disorders, but no specific lesion has been found in the constipated colon of diabetic patients by ordinary histologic examination.\textsuperscript{18} Our patient had an insulin-dependent form of diabetes; still, it was well controlled by regular injections of insulin and was not accompanied with diabetic complications. We thought that the intestinal pseudoobstruction in our patient seemed to be more related to the inflammatory destruction of the enteric plexus with neuronal degeneration rather than with diabetes-associated motor dysfunction. Other reports have described severe intestinal pseudoobstruction caused by inflammation of the myenteric plexus in patients who never showed a tumor on long-term follow-up.\textsuperscript{19,20} We thought that our case would belong to this category. But their main differences from ours were that the submucosal plexus remained intact in their cases, and the patients had ANNA-1 in their sera. Evaluation for the presence of ANNA-1 and other autoantibodies in our patient might have given us a clue to the pathogenesis of the disease.

Although the underlying mechanism for the intestinal pathology is unclear in our patient, we suspect the cause to be idiopathic and sporadic intestinal pseudoobstruction associated with inflammatory visceral neuropathy. However, we cannot completely exclude the possibility of an autoimmune pathogenesis of the paraneoplastic visceral neuropathy. First, we did not check the ANNA-1 and we did not perform autopsy. Second, intestinal symptoms may precede the occurrence of tumor. Treatment of choice is not well established for this type of case. As in paraneoplastic visceral neuropathy of an autoimmune pathogenesis, steroids or immunosuppressive drugs can be attempted, yet the irreversible loss of ganglion cells in the myenteric plexus is responsible for the failure of treatment.\textsuperscript{7}

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REFERENCES