
症 例

An Experience of IVH Combined with FOY Administration in Upper Digestive Tract Fistula

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Introduction

Spontaneous closure of an upper digestive tract fistula is difficult because the digestive juice excreted from the fistula contains large amount of various proteolytic enzymes⁵⁾. Recently we have had a case of duodenal fistula which developed following operation for adhesive ileus in which closure was apparently stimulated by a systemic administration of FOY, a protease inhibitor, along with IVH (intravenous hyperalimentation). In this case the administration of IVH alone, while remarkably improving the nutritional state of the patient and decreasing the volume of enzyme excretion, gave no indication of bringing about spontaneous closure of the fistula even should the treatment be continued for more than a month. Therefore, after about two weeks FOY administration was begun. In this paper we present the findings in this case and discuss the significance of IVH and FOY administration.

Case report

The patient was a 48-year-old man who underwent gastric resection (Billroth II) because of gastric ulcer on 25th November '77. From the 12th day after the operation, fever and vomiting occurred.

Peritonitic signs such as muscular defense reaction over the center of the upper abdomen and Blumberg's sign, which were considered to be due to suture insufficiency were also observed. Thoracentesis produced about 100 ml of exudate from the right lower field. The symptoms of pleurisy and peritonitis were improved with antibiotics and supplemental infusion. The patient was then allowed to return home from the 27th December for several days. On January 1st, ileus symptoms such as vomiting, upper abdominal pain and

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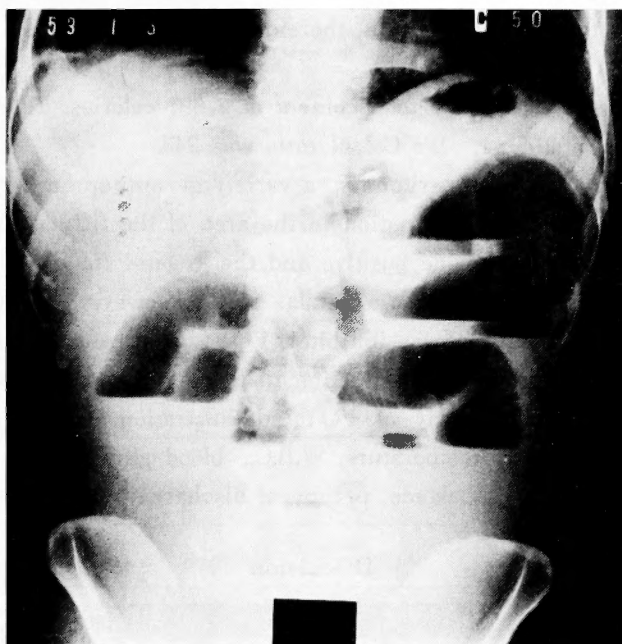


Photo. 1 A flat plate in the standing position before the second operation.

abdominal distension appeared. A flat plate of the abdomen in standing position revealed niveau formation in the small intestine. (Photo. 1) The patient was observed for a few days under conservative therapy. Since, however, nausea, vomiting and abdominal distension continued, laparotomy was performed on January 4th, '78.

Operative findings

An upper mid-line skin incision was performed. A small amount of serous exudate was found in the peritoneal cavity and the upper part of the small intestine was distended but not yet necrotic. The jejunum 20 cm below the site of the gastro-jejunal anastomosis had adhered to the liver bed causing ileus. At the same time, the transverse colon and the ileum about 30 cm above the terminus had formed a mass at a place which was considered to be the duodenal stump. The mass firmly adhered to the lower side of the liver and showed abscess formation. Postoperative peritonitis was presumed to be due to suture insufficiency of the duodenal stump. When the jejunum forming the funiculus was detached to relieve the ileus state and the adhesion of the duodenal stump to the transverse colon was ablated, the duodenum was found to be partially damaged and was repaired. Drains were placed at the duodenal stump and at the lower border of the spleen.

Postoperative progress

There was almost no discharge from the drain placed at the lower border of the spleen and the drain was removed on the 3rd postoperative day. From the area of the injured duodenum, however, a pale yellowish brown liquid containing bile was excreted and a

duodenal fistula was formed. The patient, therefore, was given nothing by mouth and IVH instituted.

The maintenance dosage had a total content of 2,697 calories. The ratio of glucose : amino acid : fat was 6 : 1.5 : 1. It's Cal/N ratio was 245.

For the treatment of the panperitonitis, a variety of appropriate antibiotics were used to produce localization of the inflammation in the area of the fistula. As soon as IVH was begun, the nitrogen balance became positive and the general state of the patient improved along with decreased discharge from the fistula. Since, however, the volume of discharge still exceeded 400 ml daily, a protease inhibitor, FOY, was given with a dosage of 300 mg daily. This resulted in a day-by-day reduction in the amount of peritoneal drainage with closure of the fistula on the 7th day of FOY administration. Fig. 1 shows the 4-weeks postoperative changes in body temperature, W.B.C., blood glucose level, calory intake, total protein concentration, nitrogen balance, peritoneal discharge and the dosage of FOY.

Discussion

Digestive tract fistula, especially that of the upper digestive tract, which develops as a complication following an operation on the digestive tract, often causes fluid and electrolyte abnormalities and a state of malnutrition due to the leakage of a amount of digestive juice⁴⁾. Furthermore, when panperitonitis and serious infections such as septicemia develop the prognosis of the fistula become worse¹⁾. Control of the general nutritional state has been dered-consi to be most important in the treatment of intestinal fistula²⁾. Since DUDRICK et al³⁾ reported a case whose traumatic duodenal fistula was spontaneously closed with IVH, IVH has been considered a favourable treatment of intestinal fistula. In fact, MACFADYEN et al⁸⁾. demonstrated the effectiveness of this therapy in 61 cases of intestinal fistula, in which 72.1% showed spontaneous closure and 90% of cases led to spontaneous and operative closure.

IVH when fasting is considered to be effective in intestinal fistula. The reasons are as follows : (1) No oral food intake gives a rest to the intestine, with accompanying diminished stimuli to the intestinal secretory glands. Consequently the amount of discharge from the fistula is reduced¹¹⁾. (2) Nutrition can be controlled parenterally regardless of the period of fasting. (3) IVH itself acts to inhibit the secretion of digestive juice, though its mechanism is unknown⁶⁾. (4) The nutritional state which is measured by body weight, albumine, N-balance etc. has a influence on wound healing¹⁰⁾ and the eventually closure of the fistula.

When an obstruction exists distal to the fistula or the fistular opening appears completely lip-like, spontaneous closure can hardly be expected with any kind of conservative therapy and hence surgical closure is necessary. Even in such intractable fistulas, pre-operative improvement of the nutritional state by IVH may enhance the rate of success on operation¹²⁾. The degree of peritonitis associated with the fistula is an important factor influencing the prognosis of intestinal fistula. In those patients with severe peritonitis, appropriate antibiotics should be given to localize the inflammation followed by as complete

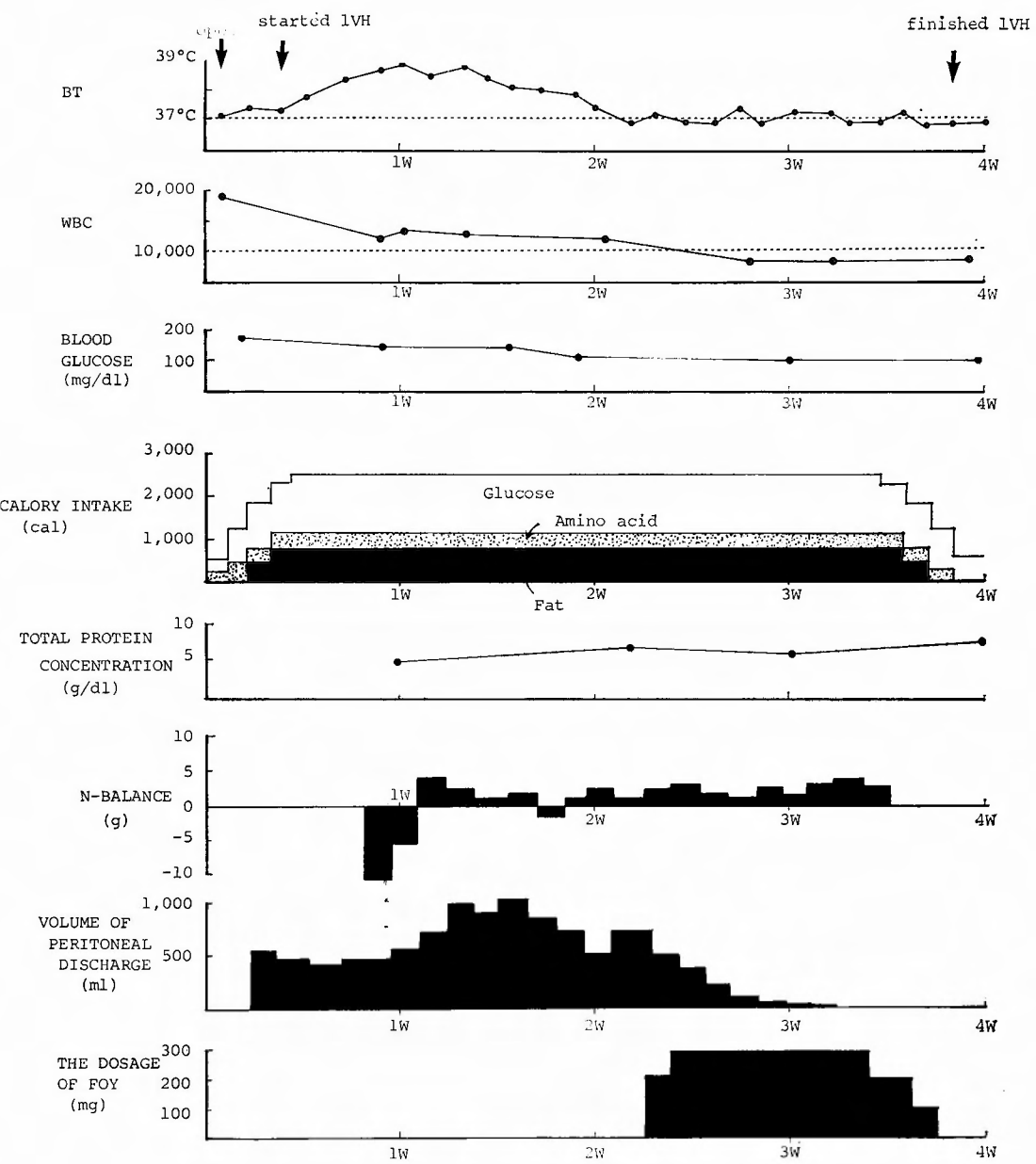


Fig. 1. 4-weeks postoperative changes in body temperature, WBC, blood glucose level, calory intake, total protein concentration, nitrogén balance, peritoneal discharge and the dosage of FOY.

drainage of pus as possible in order for the IVH to become effective.

Although the patient under discussion was suffering from panperitonitis, drainage was very efficacious and various antibiotics effectively localized the peritonitis in the area of the fistula. Immediate institution of IVH improved the general state of nutrition and decreased the discharge from the abdominal cavity. Since, however, this was a duodenal

fistula, it contained a lot of pancreatic juice. For this reason it was to be expected that spontaneous closure would require many days. As one of the local factors which prevent fistular closure, the proteolytic enzyme contained in the pancreatic juice is believed to cause erosion of the wall of the fistula, resulting in delayed healing. On this assumption, FOY which is a protease inhibitor was given systemically. FOY is chemically designated as Ethyl-p (6-guanidino hexamoyloxy) benzoate metanesulfonate and possesses similar action to that of Trasylol. Being a low molecular chemical compound, it is believed to develop little antibody and allergic reaction. Trasylol ointment has been reported to be effective in digestive skin erosion⁷⁾. However, the effect of systemic administration of protease inhibitors has not been studied.

The systemic administration of the protease inhibitor in the treatment of intestinal fistula is considered significant in the following points : (1) Particularly in case of upper digestive tract fistula, the digestive juice draining from the fistula contains a lot of proteolytic enzymes which causes erosion of the wall of the fistula thus making fistular closing difficult. (2) The presence of intestinal fistula results in some degree of peritonitis. If appropriate drainage and antibiotic therapy are not instituted, serious peritonitis or even endotoxin shock may develop. Endotoxin shock is closely related to the blood coagulation system, fibrinolytic system, Kallikrein and kinin system⁹⁾. FOY which is believed to inhibit these enzymes, should be effective in the prevention of such shock.

The treatment of intestinal fistula, particularly that of the upper digestive tract containing a large amount of pancreatic juice, should aim to first localize the peritonitis and then IVH therapy should be instituted. When the fistula becomes tubular and yet closure is delayed, systemic administration of FOY which is believed to cause the least side-effects among the protease inhibitors seems to be worthwhile.

Conclusion

A 48-year old man underwent surgery for adhesive ileus. Since a duodenal fistula was formed, IVH was instituted while in a fasting state. At the same time, a protease inhibitor, FOY, was given systemically. The patient showed remarkably good progress and the fistula completely closed. Apparently, the administration of both high calory infusion and FOY are very useful in the treatment of intestinal fistula.

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和文抄録

上部消化管瘻に対する高カロリー輸液， FOY 併用投与による 1 治験例

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上部消化管瘻は，瘻孔より排出する消化液の中に多量の蛋白分解酵素を含み，一般に自然閉鎖率は低いとされている。しかし高カロリー輸液療法が開発されて以来，腸瘻に対してもその病態生理上，自然閉鎖が期待され，又，自然閉鎖困難な難治性腸瘻に対しても，術前における栄養状態の改善という意味から，その良い適応であると考えられるようになった。最近，著者らは48才，男性で癒着性イレウスの術後，十二指腸瘻を形成し，これに対して高カロリー輸液を施行し，著明な栄養状態の改善と腹腔排液量の減少を見たが瘻孔閉鎖には到らず，自然閉鎖がなされるにも長期間の日数が必要であると思われた。そこで瘻孔閉鎖を障害す

る局所因子として，瘻液の中に含まれている蛋白分解酵素が瘻孔壁に糜爛を生じせしめ，それが治癒遷延因子になり得るとの推測のもとに protease inhibitor である FOY を 1 日量として 300mg を投与したところ，腹腔排液量は日ごとに半減し，投与後 7 日目には瘻孔は閉鎖した。

腸瘻，特に瘻液を多量に含む上部消化管瘻に対する治療は，できるだけ腹膜炎を局限させるとともに，積極的に高カロリー輸液を施行し，それにより瘻孔がいわゆる管状瘻になり得ても閉鎖困難と思われる場合には，protease inhibitor の投与も一考に値するものであると考える。