CASE REPORT

Eosinophilic Gastroenteritis, Gluten Enteropathy, and Dermatitis Herpetiformis

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Eosinophilic gastroenteritis is a disease of protean manifestations characterized by eosinophilic infiltrates in the gut wall. The association of dermatitis herpetiformis with the mucosal abnormalities of the celiac syndrome and in some cases with steatorrhea has been described (1). We report a case in which dermatitis herpetiformis and gluten enteropathy occurred in a patient with long-standing eosinophilic gastroenteritis.

CASE REPORT

A 39-year-old white male was admitted to Donald N. Sharp Memorial Community Hospital on October 12, 1965, with abdominal pain, distention, and vomiting. He had been admitted in 1958 with pain, distention, vomiting, diarrhea, weight loss, and marked peripheral eosinophilia. He was considered to have trichinosis and was treated with prednisone in small doses with improvement. Since that time he had been taking prednisone, self-adjusted as to dosage, for intestinal symptoms of varying severity. He discontinued the prednisone approximately two weeks prior to the 1965 admission. There was a long history of bronchial asthma. Amylase, SGOT, serum potassium, and serum calcium test results were all normal. There was peripheral eosinophilia (48% of 8,430 WBC/mm^3). An upper-gastrointestinal x-ray study revealed only slight rigidity of the duodenal loop. The patient was discharged and maintained on small doses of prednisone. In April 1968 he was admitted to the University Hospital of San Diego County for further evaluation. He had developed scattered, mildly pruritic skin lesions on the trunk and upper extremities, which began as papules, became pustules, drained, and then formed crusts prior to healing. Physical examination was unremarkable, except for the skin lesions. Eosinophila was again present (11% of 7500 WBC/mm^3). A biopsy of a skin lesion was interpreted as a nonspecific pyoderma and cultures grew coagulase positive staphylococci. A muscle biopsy was normal and the Trichinella skin test was negative. Prednisone was withdrawn.

Soon after the patient left the hospital he developed profuse, foul-smelling, greasy, painless diarrhea and began to lose weight rapidly. An x-ray examination of his stomach and small intestine revealed a rigid duodenal loop and a generalized malabsorption pattern (Figure 1).

The patient was readmitted to the hospital on May 15, 1968. He had lost 30 pounds in one month with continued diarrhea. Physical examination was normal, except for the previously mentioned skin lesions and evidence of weight loss. The white cell count was 9700/mm^3 with 11% eosinophiles. A 72-hour stool collection contained 49 g fat/24 hr. The prothrombin time was 21 seconds with a control of 12.5 seconds before parenteral vitamin K and 15 seconds with a control of 12.5 seconds after parenteral vitamin K. Serum albumin was 2.8 g/100 ml. Serum potassium was 3.5 mEq/liter. Serum calcium was 8.0 g/100 ml. Levels of immunoglobulins A, G, and M were normal. Serum amylase and lipase test results were normal. A peroral jejunal biopsy was performed with a Quinton biospy tube, revealing an intense mononuclear cell infiltrate of the mucosa.

The entire specimen, which had been improperly imbedded, was serially sectioned and showed an absence of recognizable villi and marked lengthening of crypts (Figure 2). A gluten-free diet was prescribed. Within three days the diarrhea stopped completely, the stools became grossly normal, and the patient began to gain weight.

He did well until June 3, 1968, when he ingested chocolate, a substance to which he had been found to be sensitive on skin testing ten years prior to this episode. Several hours later he noted colicky abdominal pain, distention, and vomiting. He was readmitted to the hospital with mild abdominal distention, tympany, and peristaltic rushes. Abdominal x-ray revealed signs of small-bowel mechanical obstruction. Leukocytosis was prominent with marked eosinophilia (15,600 WBC/mm^3 with 58% eosinophiles). The pain and distention subsided with conservative therapy. X-rays then revealed marked improvement in the previously noted malabsorption pattern, although there was persistent rigidity of the duodenum. At this time there was thickening of the terminal ileum, with irregular narrowing of the lumen and loss of normal mucosal pattern (Figure 3). The total white

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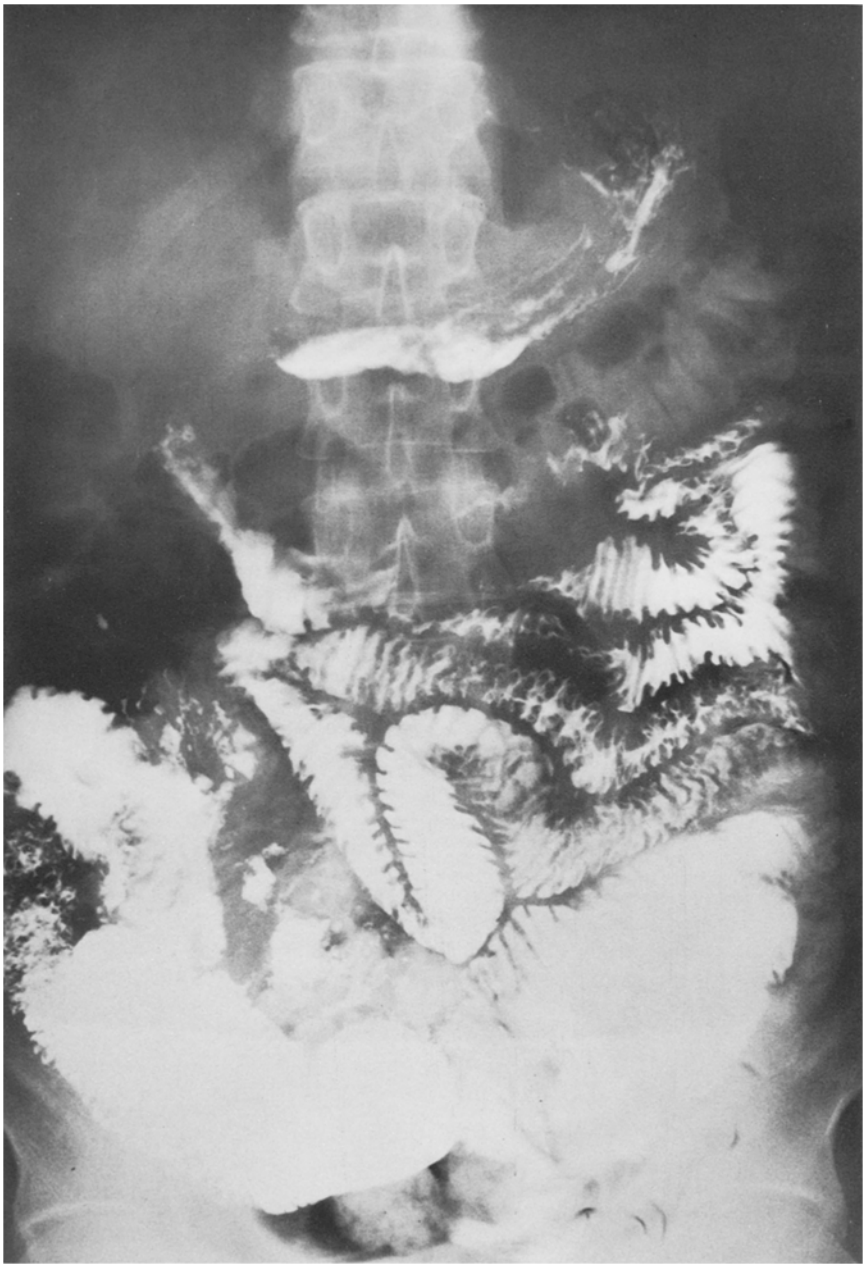

Fig 1. Small-bowel x-ray. Note the malabsorption pattern with thickened valvulae conniventes and dilated loops of bowel.

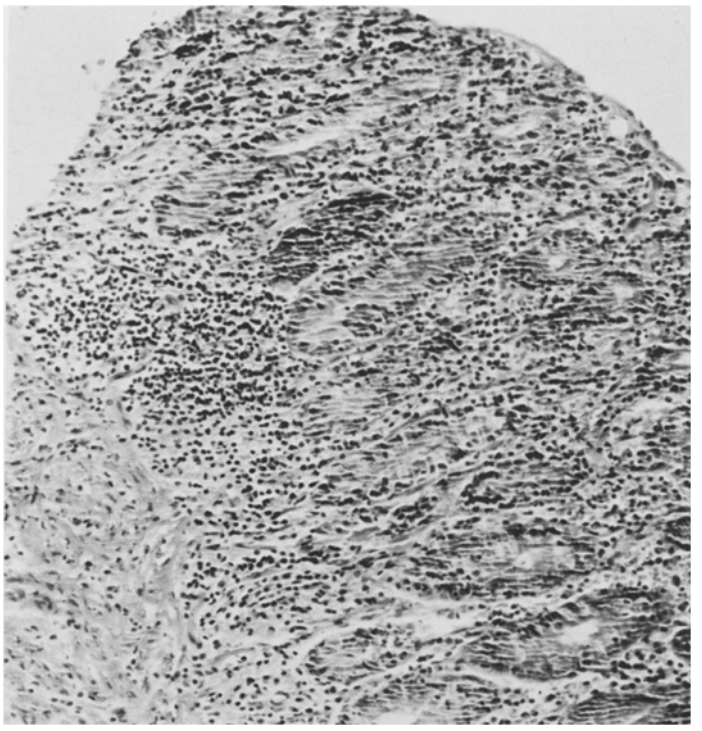

Fig 2. Small-bowel biopsy. Both marked inflammatory infiltrate and absence of villi are notable.

cell count during this period ranged from 13,000/mm³ to 20,000/mm³ and the eosinophiles from 38% to 70% of the total.

On June 10 a laparotomy was performed. The pyloric muscle was markedly enlarged and hard. The duodenum was rigid, with a consistency of cartilage, although the duodenal mucosa itself was grossly normal. The terminal 5 feet of ileum were thickened and firm. There were several large mesenteric lymph nodes present and a small amount of free peritoneal fluid. Biopsies were taken of the ileum, the pylorus, and a lymph node.

The postoperative course was uneventful. There was a marked drop in the leukocyte count and eosinophilia on the day of surgery, apparently coincident with the intraoperative administration of methyl prednisolone. The most striking abnormality in the biospy material was marked thickening of the muscularis propria of the ileum and the pyloric muscle, with sheets of eosinophiles splitting the muscle bundles. (Figures 4 and 5). There was prominent eosinophilia of the submucosa of the ileum as well, but the lamina propria and epithelium were normal. The lymph node showed only reactive hyperplasia and no malignant cells were seen in the peritoneal fluid. The patient was discharged on a gluten-free diet and small doses of prednisone.

He was readmitted to Sharp Hospital in April 1971. He reportedly had maintained a strict gluten-free diet and had had no recurrence of steatorrhea. Intermittent abdominal pain and distention had always responded to therapy with prednisone. He was found on this admission to have slight ascites and an intensely pruritic eruption of the skin of the back and upper extremities—but particularly in the interscapular areas—which was papular, vesicular, and pustular with areas of pigmented scarring. These lesions had been intermittently waxing and waning in severity. The skin biopsy at this time showed the typical findings of dermatitis herpetiformis (Figure 6). The ascites improved with prednisone administration and the skin disorder improved spontaneously soon after discharge.

DISCUSSION

This patient had a long history of abdominal complaints, eosinophilia, and asthma, characteristic of eosinophilic gastroenteritis. He devel-

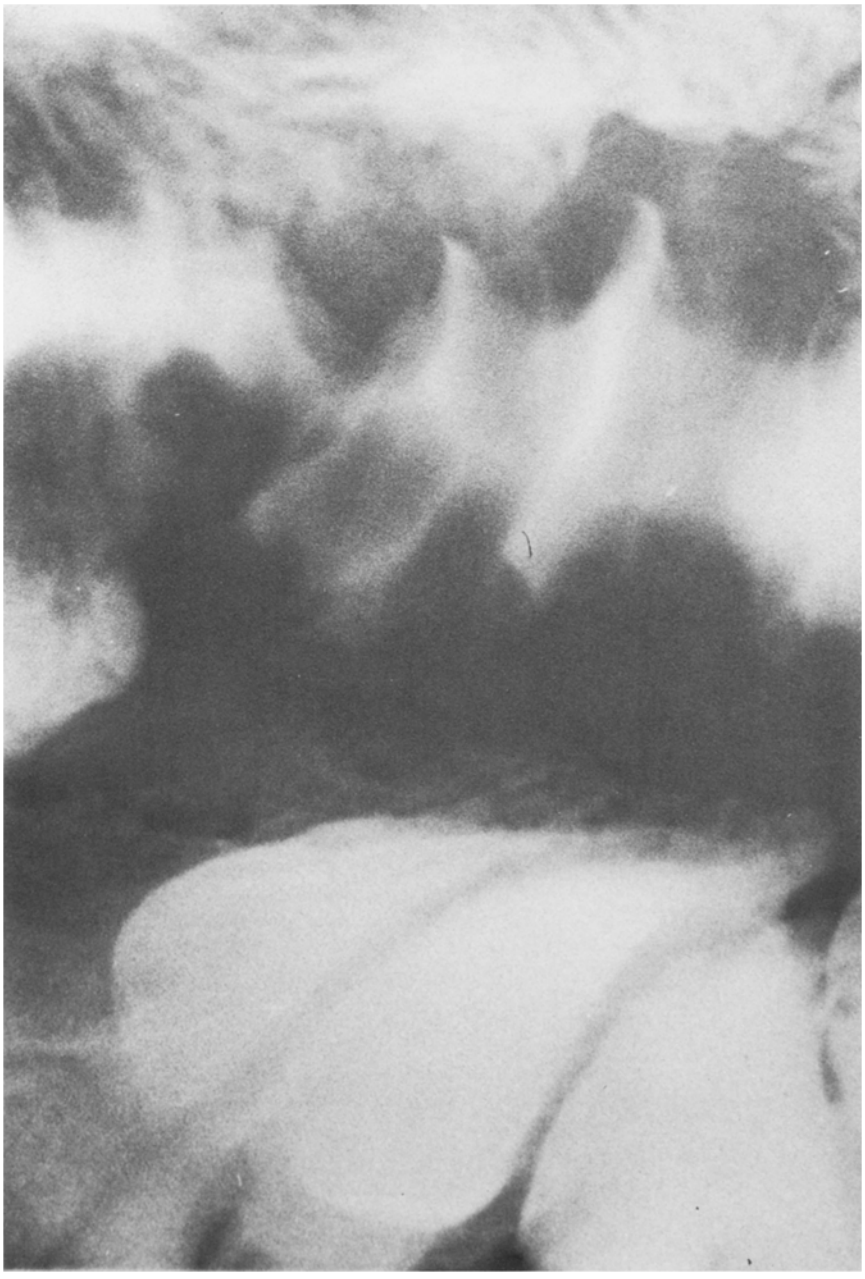

Fig 3. Spot film of terminal ileum. Thickening of the wall and abnormal mucosal pattern with edema are present.

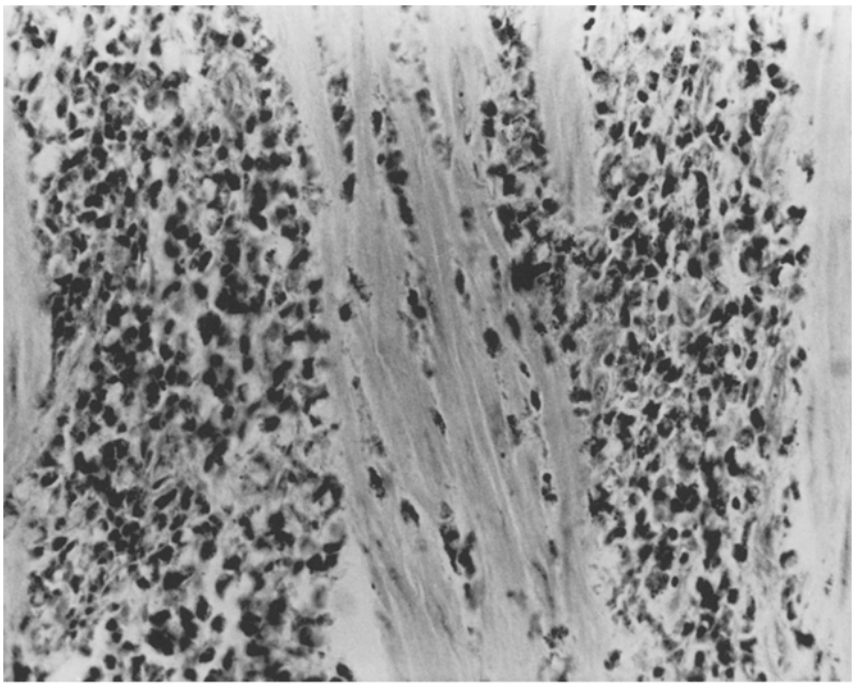

Fig 5. High-power view of pyloric muscle.

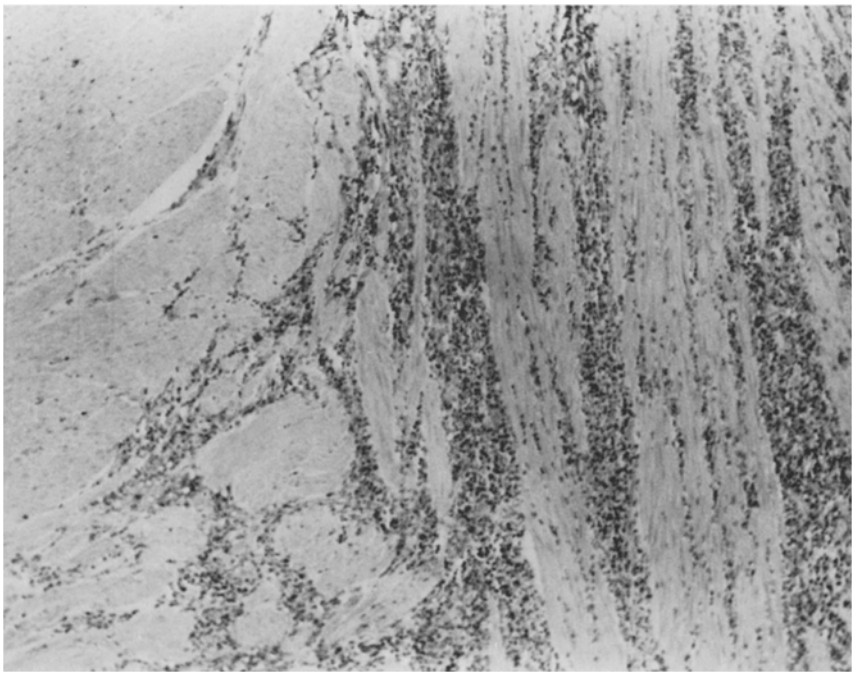

Fig 4. Pyloric muscle, with sheets of eosinophiles separating muscle bundles.

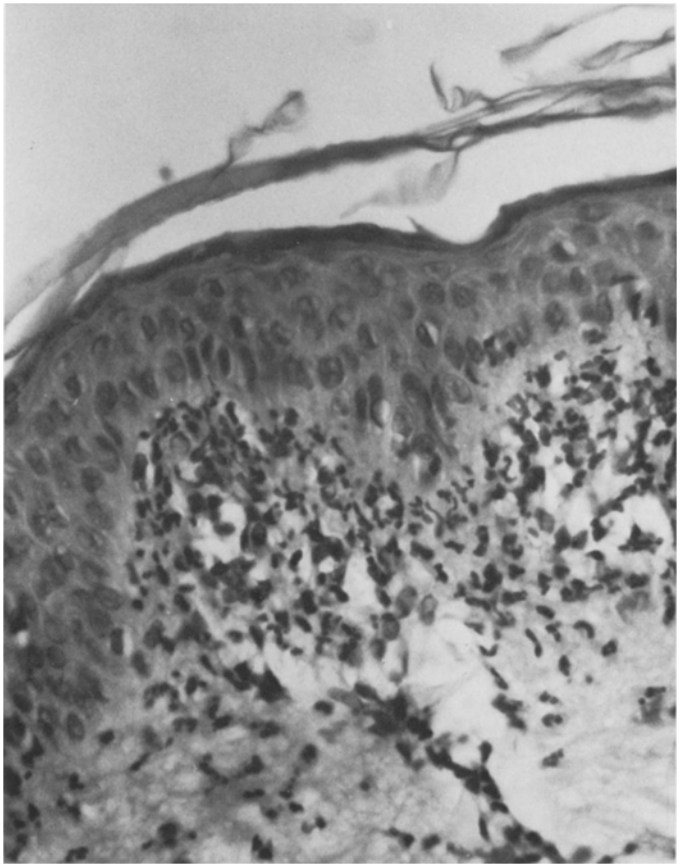

Fig 6. Skin biopsy showing dermatitis herpetiformis.

oped a malabsorption syndrome with the mucosal changes of celiac sprue, had a dramatic clinical response to gluten restriction, and developed dermatitis herpetiformis. Marks and Shuster described the mucosal changes in the small bowel associated with dermatitis herpetiformis, later confirmed by others (1–3). Malabsorption is generally nonexistent or mild. Steatorrhea and mucosal abnormalities improve on gluten restriction. Until the recent paper by Fry, which describes clearance of the skin lesions with prolonged gluten withdrawal, the skin disease was not known to respond to this therapy. On the assumption he adhered to his gluten-free diet, our patient has had progression of the skin disease during this time (4, 5).

Eosinophilic gastroenteritis, when reviewed by Ureles in 1961 was considered to be a disease of the peripheral coats of the intestinal and gastric wall, sparing the mucosa, and a malabsorption syndrome was not considered part of the picture (6). Since that review, protein-losing enteropathy and steatorrhea have been reported (7, 8). Klein reclassified the disorder into three categories: predominant mucosal involvement with malabsorption, iron deficiency, or enteric protein loss; predominant muscular involvement characterized by obstructive symptoms; and predominant serosal involvement characterized by ascites (9). Our patient had no evidence of prominent eosinophilia on the mucosal biopsy of the small bowel but did, how-

ever, have a picture of gluten enteropathy. Peripheral eosinophilia at the time of the most severe malabsorption was mild. After marked clinical response to gluten elimination, obstructive symptoms occurred, accompanied by intense peripheral eosinophilia. At that time the findings were eosinophilic infiltrates of the muscular layers of the gut wall. Specimens of the ileal mucosa were free of eosinophilic infiltrate. It would be logical to consider this a case of eosinophilic gastroenteritis with predominant muscular involvement, accompanied by dermatitis herpetiformis and its associated mucosal abnormality. It must be noted, however, that Leinbach and Rubin described varying mucosal abnormalities, including a picture resembling gluten enteropathy occurring in eosinophilic gastroenteritis (10). Klein mentioned cases of eosinophilic gastroenteritis with possible response to gluten restriction (9). It is possible that the severity of the malabsorption syndrome in our patient might very well have been due to additive effects of the two entities occurring together.

Eosinophilic gastroenteritis is considered to be allergic in nature (6, 9, 11). The fact that our patient was asthmatic and had an episode of bowel obstruction apparently related to his ingestion of a known allergen would tend to support this. This concept has been brought into serious question, however, by Leinbach and Rubin, who found no consistent evidence of direct allergic response in this disorder. It is their feeling that eosinophilic gastroenteritis represents an ongoing condition with periodic exacerbation by specific substances in the diet, but which is not directly caused by the dietary intake (10).

The possible relationship between eosinophilic gastroenteritis and dermatitis herpetiformis is obscure at this time. Although the present case may represent a coincidental occurrence, the possibility of a common underlying factor does exist. The known iodide sensitivity in many patients with dermatitis herpetiformis suggests a hypersensitivity response, as does the occurrence of asthma in eosinophilic gastroenteritis. Dermatitis herpetiformis, a skin disease, and eosinophilic gastroenteritis, an intestinal disorder, both have eosinophilic infiltration as one of their main histological characteristics. The association of dermatitis herpetiformis and the celiac syndrome has been considered an expression of a common genetic factor, since the intestinal mucosal lesion has been found in unaffected relatives of patients with the skin disease (5, 11).

Asthma and the allergic diathesis are also thought to have a genetic basis, but to date no evidence exists to link all the three entities in this case on a hereditary basis. The possibility of discovery of more cases associating these three abnormalities may shed some light on the underlying etiology, but at this time the concurrence must be considered coincidental.

SUMMARY

We have presented a case of eosinophilic gastroenteritis with dermatitis herpetiformis and gluten enteropathy and considered both the possible interrelationship of these conditions and their similarities. We have suggested that this particular case represented eosinophilic gastroenteritis with dermatitis herpetiformis occurring independently with a severe malabsorption syndrome being produced by the additive effects on the gut. The possibility of a common underlying factor was considered.

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