

A retrospective study of enteroclysis in patients with manifest food allergy

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Abstract

Purpose: The aim of this study was to investigate whether there are typical findings in enteroclysis of patients suffering from food allergy (FA). **Materials and Methods:** Findings of enteroclysis of 26 FA patients were correlated with results of endoscopic and histologic examinations. In two patients allergen provocation was performed during enteroclysis. **Results:** No specific mucosal pathologies were found without provocation. After provocation, low mucosal contrast adhesion was observed. **Conclusion:** Without provocation no specific alterations were found. However, enteroclysis may be used for monitoring of allergen challenge.

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1. Introduction

Frequency of intolerance to food is as high as about 25%. However, less than 5% of the adult population suffers from food allergy (FA), which is defined as an immune-mediated hypersensitivity to ingested allergens. This immunologic reaction to nutritive antigens is mostly an IgE-mediated immediate type of allergy (Type I, Coombs and Gell) [1]. Antigen exposure results in IgE-mediated degranulation of mast cells and eosinophils with a subsequent release of various mediators including histamine, leukotrienes, prostaglandins, and platelet-activating factor at the intestinal surface. Less often, immune complex formation or cell-mediated reactions (Types III and IV) with an abnormal cytokine production of T cells, and in many cases a combination of different types of hypersensitivity, are responsible for FA [2].

Food allergy patients typically suffer from intestinal symptoms such as diarrhea, nausea, vomiting or abdominal pain after the ingestion of nutritive antigens, but also from extraintestinal symptoms concerning respiratory tract (e.g.,

rhinitis, asthma), eyes (e.g., conjunctivitis), and skin (e.g., urticaria) can occur [2]. However, these symptoms may suggest other organic diseases.

Diagnostic workup is based on patients' history with reproducible symptoms after ingestion of nutritive antigens. Diagnosis can be confirmed by skin tests (e.g., Prick), determination of total and specific IgE antibodies in serum (e.g., RAST), determination of methylhistamine in the urine, endoscopy including histology and lavage in stomach, small, or large bowel, measurement of IgE or various mediators in lavage fluid, elimination diet, and double-blind placebo-controlled oral provocation [2–9]. However, in some cases, diagnosis of FA remains difficult and is only possible by a combination of different examination techniques.

The role of enteroclysis in this context has not yet been studied. Typical indications for this technique include obscure intestinal bleeding, chronic abdominal pain, suspected small bowel tumors, evaluation of mucosal alterations in chronic inflammatory bowel diseases, malabsorption, and diarrhea of unknown origin [10]. Due to new techniques such as MRI the incidence of enteroclysis has decreased during the last few years [11]. However, it is the most sensitive radiologic method in evaluation of morphological

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mucosal (e.g., thickened folds, erosions, ulcerations) or functional (e.g., small bowel transition time) disorders in the small bowel. Therefore, it was the aim of this study to evaluate whether there are any typical jejunal or ileal morphologic or functional pathologies of the small intestine in patients with manifest FA and to correlate these findings with those of endoscopic and histologic examinations.

2. Materials and methods

2.1. Patients

Within 1 year, 42 patients with suspected FA underwent enteroclysis due to diagnostic workup. In 26 (62%) of those 42 patients (20 female, 6 male), diagnosis of FA was confirmed by elevated mediator concentrations in the urine (methylhistamine, IgE) or endoscopic lavage fluid (IgE), RAST, or oral provocation tests. These 26 patients were included in the study. Median age was 47 years (range 22–69 years). All individuals reported symptoms after ingestion of nutritive antigens. Patients did not have any comorbidity with celiac disease, chronic inflammatory bowel diseases including Crohn's disease or ulcerative colitis, carcinoma, and intestinal lymphoma. Twenty-four patients underwent colonoscopy and two patients underwent jejunoscopy within 5 days before or after enteroclysis. This study complies with the standards of Declaration of Helsinki and was performed in coordination with our local ethics committee.

2.2. Enteroclysis

Patients gave their informed consent for the examination. The technique of enteroclysis has been described earlier in detail [12]. After administration of local anesthesia to the nose and throat, a nasoduodenal tube was placed past the ligament of Treitz under fluoroscopic guidance. One hundred fifty to 300 ml (median 200 ml) of a 43% barium-containing solution (Micropaque, Guerbet, Germany) were applied with a flow rate of 75 ml/min followed by 750–2200 ml (median 1500 ml) methylcellulose. Each small bowel loop was examined as it became translucent and distended. At least six pictures of different jejunal and ileal segments were documented; usually magnification view was taken from the terminal ileum.

2.3. Allergen provocation

In two male patients (LL and SK), 50 ml allergen solution containing nuts and cereals, respectively, was added to barium and methylcellulose each, and enteroclysis was performed as described above.

2.4. Analysis of examinations

Retrospective analysis of documented pictures of 26 patients with confirmed diagnosis of FA was independently

performed by two radiologists. Small bowel transition time, distention of bowel loops, wall thickening, and mucosal pathologies including mucosal contrast, fold thickening or atrophy, nodular lesions, erosions, and ulcerations were analyzed. Additionally, the examination reports were reviewed. Radiologic findings were correlated with endoscopic and histologic findings of the terminal ileum.

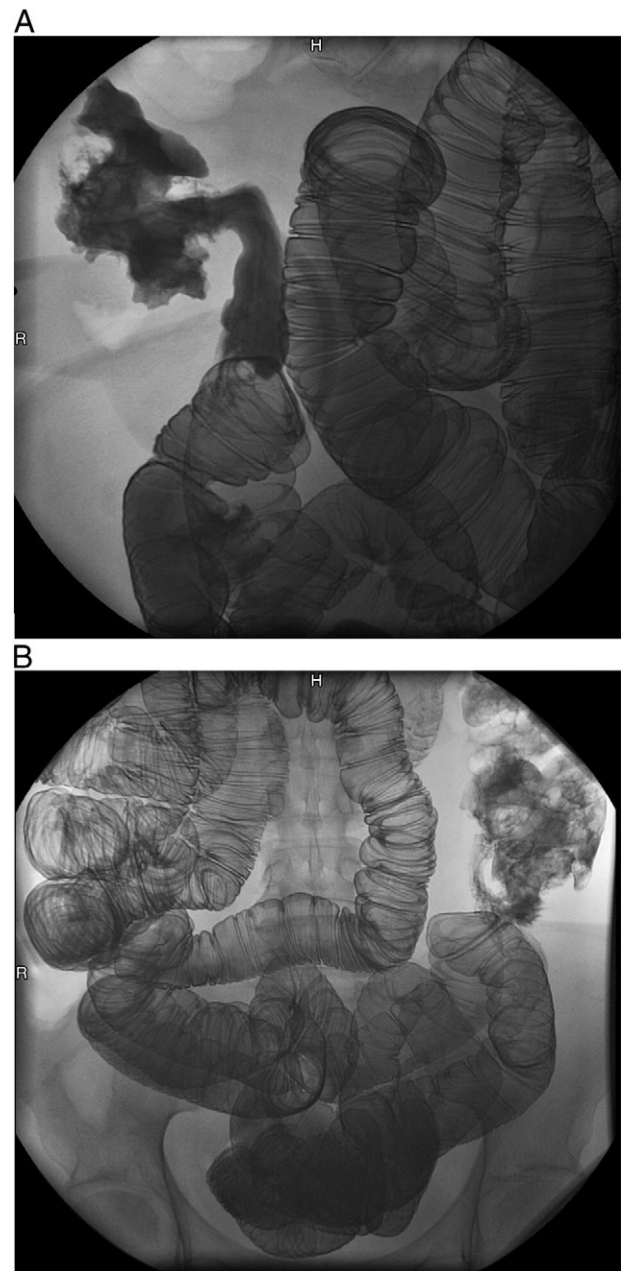


Fig. 1. Enteroclysis of a 58-year-old woman (EM) with manifest FA. Magnification of the terminal ileum in supine position (A) and overview in prone position (B). Normal mucosal pattern is seen in the small bowel. Histology showed lymphofollicular hyperplasia in the terminal ileum. However, endoscopy of the terminal ileum was normal. Small bowel transition time was within normal range.

3. Results

Retrospective analysis of mucosal pathologies revealed no differences between the two independent observers and the examination reports. Despite several gastrointestinal complaints including diarrhea, nausea, vomiting, and abdominal pain after the ingestion of nutritive antigens, in none of the 24 patients with manifest FA could morphological changes of jejunal or ileal mucosa be detected, if no allergen challenge was performed (Fig. 1). Transition time from the duodenum to the cecum was able to be retrospectively determined in 14 of 26 patients and ranged from 3 to 21 min (median 10 min). Endoscopic and histologic reports were available in all patients. Endoscopy showed atrophy of the terminal ileum in three patients, but was not confirmed histologically. Lymphofollicular hyperplasia in the terminal ileum was histologically found in 10 (38%) of 26 cases, but could not be visualized by enteroclysis and only in three cases by endoscopy (Table 1, Fig. 2). In those patients median transition time was 9 min (range 3–18 min). In one patient (WM), mucosal alterations of the descending

colon were suspected, but could not be confirmed endoscopically or histologically.

In one patient undergoing allergen provocation (LL) during enteroclysis, transition time was 10 min and low mucosal barium adhesion of the jejunum was observed a few minutes after ingestion of the allergen (Fig. 3). He reported typical symptoms during examination similar to those after ingestion of food including abdominal pain. Clinically, the abdomen became distended during the examination. Endoscopy revealed slight jejunal edema which was confirmed histologically. The other individual (SK) also showed low mucosal contrast adhesion and thickened wall in the jejunum under provocation.

4. Discussion

Very few data have been published about transition time in enteroclysis. Normal mean transition time has been reported to be 9.3 min with a range from 5 to 18 min and a standard deviation of 0.9 min. In patients with hypermotility,

Table 1

Analysis of small bowel transition time, distention, jejunal and ileal mucosal alterations including thickened folds, nodular lesions, erosions, or ulcerations, and endoscopic and histologic findings in the terminal ileum of 26 patients with confirmed diagnosis of FA

Patient	Age (years)	Small bowel pathology ^a	Transition time (min)	Endoscopical findings of the terminal ileum	Histological changes in the terminal ileum
ER	56	No	18	Lymphofollicular hyperplasia	Lymphofollicular hyperplasia Eosinophil granulocytes
SR	57	No	13	None	None
OL	49	No	3	Atrophy	Lymphofollicular hyperplasia
DI	40	No	nd	Jejunum: none ^b	Jejunum: none ^b
EM	58	No	11	None	Lymphofollicular hyperplasia
MG	58	No	6	None	Lymphofollicular hyperplasia Eosinophil granulocytes
SC	37	No	16	Lymphofollicular hyperplasia	None
FI	39	No	nd	None	None
FH	42	No	nd	None	Lymphofollicular hyperplasia
SK	53	No	nd	None	None
BG	57	No	nd	None	Lymphofollicular hyperplasia
KI	69	No	nd	None	None
NB	33	No	11	None	None
DW	60	No	11	None	Lymphofollicular hyperplasia
FB	24	No	9	None	Lymphofollicular hyperplasia
BE	47	No	nd	Atrophy	Lymphofollicular hyperplasia
SW	41	No	9	Lymphofollicular hyperplasia	Lymphofollicular hyperplasia
HR	69	No	nd	None	None
BM	43	No	nd	Atrophy	None
DS	43	No	7	None	None
ML	27	No	21	Lymphofollicular hyperplasia	None
BH	47	No	nd	None	None
SA	68	No	nd	None	None
WM	40	No	9	None	None
LL	22	Low mucosal contrast adhesion ^c	10	Lymphofollicular hyperplasia Slight edema in jejunum ^b	None in the terminal ileum; slight edema in the jejunum ^b
SK	58	Low mucosal contrast adhesion ^c	nd	None	None

nd=not documented.

^a Independent results of Observer 1 and 2 and report analysis revealed no differences.

^b For patients DI and LL, additional jejunoscopy was performed; therefore endoscopical and histological findings concern the jejunum.

^c For patients LL and SK, alterations were found after allergen provocation.

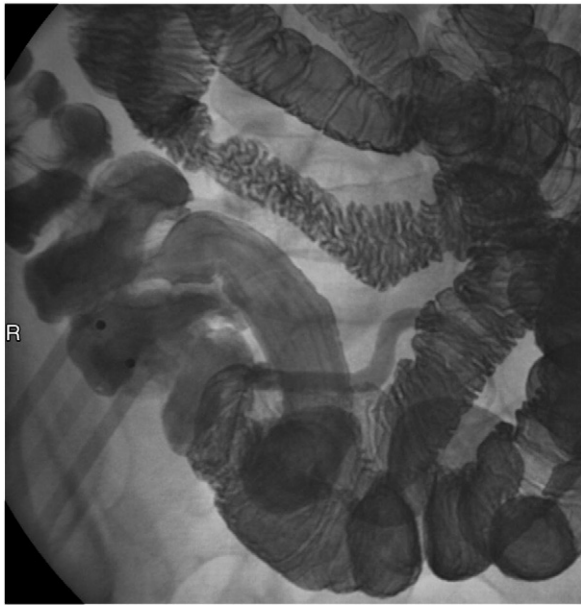


Fig. 2. Enteroclysis of a 42-year-old woman (FH) with manifest FA. Magnification of the terminal ileum. Lymphofollicular hyperplasia in the terminal ileum was histologically found in this patient, but could neither be visualized by enteroclysis nor by endoscopy.

it ranges from 3 to 6 min with a mean of 4.2 min [10]. In those cases in our study where small bowel transition time was documented, the median was 10 min and therefore within the normal range. However, in one female after 3 min the cecum was reached and in one examination transition time was prolonged (Table 1). Hypermotility can be found in various diseases including irritable bowel syndrome, hyperthyroidism, lactose intolerance, mastocytosis, and malabsorption, whereas hypomotility has been reported in pseudo-obstruction, scleroderma, diabetes, and amyloidosis [10]. Therefore, changes in jejunal and ileal transition in our patients can be viewed as a nonspecific sign.

The presence of lymphofollicular hyperplasia (LFH) in the colon or ileum has been reported to be a frequent endoscopic finding in symptomatic children suffering from FA. It has been proposed to be a related condition of delayed-type food hypersensitivity and a hallmark histologic lesion in patients with non-IgE-mediated FA [13,14]. Hence, it can also be found in other intestinal diseases including ileitis and in rare cases in patients with a lack of IgA or intestinal lymphoma [10]. In enteroclysis, LFH can be sometimes detected in these diseases; sometimes it is incidentally found. In 38% of our patients, lymphofollicular hyperplasia was evident histologically. These patients showed normal enteroclysis, and in six of 10 cases normal endoscopic findings of the terminal ileum. In three individuals, LFH was suspected endoscopically, but could not be confirmed histologically. LFH is characterized by a tiny nodular pattern. The small size of the lesions might be the reason why they were not detectable in enteroclysis and only in a few cases in endoscopy in our patients (Figs. 1A and 2).

Limitations of this study were the retrospective character, the small number of patients ($N=26$), and the fact that transition time has been documented in only 56% of the cases.

Although in enteroclysis no mucosal alterations were detectable without allergen challenge, in two individuals provocation with an allergen solution led to a low mucosal contrast adhesion which can be a sign of mucosal hypersecretion. This might be assessed as an answer to the ingested allergen and therefore it seems to be possible to monitor provocation tests using enteroclysis.

It has been reported in one case that monitoring of food challenge is possible by MRI [15], but until now, no further examinations on the value of this technique in diagnostic workup of FA patients have been performed. The correlation of radiologic findings of the jejunum and ileum with MRI or modern endoscopic imaging modalities like capsule endoscopy or push-and-pull enteroscopy could be a promising purpose for future studies.

Food allergy remains a clinical diagnosis based on patients' history and clinical tests. Further studies on this field should clarify whether new techniques including MR enteroclysis show typical small intestinal alterations and might therefore be a valuable tool in FA. Enteroclysis without allergen challenge seems to have no great yield in diagnostic workup of FA. However, it remains an important tool in order to exclude other small intestinal disorders as chronic inflammatory bowel diseases, which can show similar symptoms like FA. Monitoring of allergen provocation tests using enteroclysis seems to be possible and should be evaluated in further studies.



Fig. 3. Enteroclysis of a 22-year-old man (LL) with manifest FA. Magnification of the jejunum. A few minutes after provocation with an allergen, low jejunal contrast adhesion was observed and the patient reported abdominal complaints.

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