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Evaluation of Our Food Protein Induced Proctocolitis Cases: A Single Center Experience

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Abstract

Aim: The purpose of this study was to determine clinical characteristics, laboratory findings and course in infants diagnosed with allergic proctocolitis.

Materials and methods: Thirty-four patients diagnosed with food protein-induced proctocolitis in our clinic between 2013 and 2016 were evaluated retrospectively. Files were reviewed in terms of symptoms, clinical features, laboratory findings and responses to treatment.

Results and discussion: Sixteen (47%) patients were female. Mean age was 3.3 ± 2.3 months (1-10 months). Eleven (32.3%) cases presented with pronounced rectal bleeding and 23 (67.6%) with bloody spots or streaks in stool. In terms of nutrition, 76.4% of babies were receiving breast milk alone, and the remainder received breast milk with supplementary formula. Mean peripheral eosinophil rate was $8.6 \pm 6.3\%$. Response was achieved solely by removal of milk and dairy products from the mother's diet in 25 (73.5%) cases, while multiple allergen food (eggs, nuts, fish etc.) elimination was applied to mothers in 8 (23.5%) and breast milk was discontinued for 3 months in one case. Symptoms resolved in a mean 6.4 ± 5.9 days (1-25) following of elimination diet.

Conclusion: Our study shows that allergic proctocolitis in infancy frequently appears in exclusively breastfed babies, that the condition has a benign course and that cow's milk protein plays an important role in the etiopathogenesis.

Keywords: Allergic proctocolitis; Food allergy; Food protein-induced proctocolitis; Infant; Rectal bleeding

Food protein-induced proctocolitis is also known as allergic proctocolitis (AP) and results from a non-IgE-mediated allergic reaction. AP is a widespread clinical entity, although the exact prevalence is still unclear [3]. AP manifests with mucus or blood in the stool, and particularly in healthy appearing infants who are exclusively breastfed [4,5]. However, it may also manifest with diarrhea, vomiting, irritability, abdominal distension and delayed growth [6]. Diagnosis is based on history, clinical findings, improvement after dietary therapy and the "challenge" test [7,8]. The purpose of this study was to examine clinical features and laboratory characteristics including mean platelet volume (MPV) and the neutrophil-to-lymphocyte ratio (NLR) in patients diagnosed with AP, in the light of the current literature.

Materials and Methods

The records of patients monitored in our clinic with a diagnosis of AP between January 2013 and April 2016 were evaluated respectively. Diagnosis of AP in presentations with rectal bleeding was based on resolution of symptoms following elimination diet and recurrence of symptoms with an oral food challenge, following exclusion of other potential causes such as infection, necrotizing enterocolitis, Hirschsprung's disease and volvulus. Patients' demographic characteristics, type of rectal bleeding (streaks/pronounced rectal bleeding), presence of accompanying extraintestinal findings (atopic skin findings/wheezing), nutrition history (breast milk/formula), history of antibiotic use in other health centers where patients presented due to rectal bleeding, responses to and durations of elimination diet, presence of anal fissure at physical examination, complete blood count, C-Reactive protein (CRP), erythrocyte sedimentation rates (ESR), absolute eosinophil count, MPV, NLR values and stool microscopy and culture results were recorded. A control group consisting of 30 patients matched with the control group in terms of age and sex was established, and MPV and NLR were compared.

The data obtained were transferred onto and analyzed on SPSS 16.0 software. Continuous variables were expressed as mean \pm standard deviation and categorical variables as number and percentage (%). The Mann-Whitney U test was used to

Introduction

The prevalence of food allergies is increasing worldwide and is becoming a major public health problem [1]. The prevalence of allergic reactions to food proteins in infants is 2% to 8% [2].

compare non-normally distributed numeric variables. $p < 0.05$ was regarded as statistically significant. Approval for the study was taken from the Suleyman Demirel University ethics committee of clinical research.

Results

The records of 41 patients with AP were retrieved in this period, and these were investigated retrospectively. Five patients whose files were incomplete were excluded, and the study was completed with 36 patients. Characteristics of cases are shown in **Table 1**.

Table 1: Characteristic features of cases (n: 33).

Variables	n (%)
Age (months)	3.2 ± 2.3
F/M	17 (47.3) /19 (52.7)
Time to resolution of symptoms (days)	6.1 ± 5.9
Presentation symptoms	
Pronounced rectal bleeding	11 (30.5)
Streak/spot type bleeding	25 (69.5)
Accompanying GIS symptoms (vomiting, diarrhea with mucus)	5 (13.8)
Extraintestinal findings (atopic skin findings, wheezing)	16 (44.4)
Laboratory results	
Peripheral eosinophilia (>6%)/Absolute eosinophil count (>450 mm ³)	22 (61.1)
Thrombocytosis (450,000-700,000/mm ³)	12 (33.3)
Anemia (Hb below normal value)	4 (11.1)
Mean MPV	8.2 ± 0.99 fL
NLR	38.5 ± 20.2%

Seventeen (47.3%) patients were female and 19 (52.7%) male. Mean age at presentation was 3.2 ± 2.3 months (1-10). Eleven (30.5%) patients presented with pronounced rectal bleeding and 25 (69.5%) with stripe/spot type blood in stool. In addition, extra-intestinal findings such as skin rash and/or wheezing were present in 16 (44.4%) cases. Vomiting and/or diarrhea with mucus as accompanying gastrointestinal system symptoms were present in 5 (13.8%) cases.

In terms of nutrition, 77.7% of infants were receiving only breast milk, with the remainder receiving formula support in addition to breast milk. Seven (19.4%) had a history of antibiotic therapy with diagnosis of amebic dysentery at other health centers.

All patients were healthy in appearance, and growth and development were normal. Systemic examination was normal in all cases except for presence of anal fissure in 8 (22.2%) patients.

Eosinophilia was present in 22 (61.1%) patients. Mean eosinophil rate at complete blood count was 8.6 ± 6.3%, ranging from 2% to 26%. Mean absolute eosinophil count was 904 ± 727/mm³ (162-3075). Hemoglobin levels were slightly below normal only in 4 (11.1%) patients. Mild thrombocytosis (<700,000/mm³) was determined in 12 (33.3%) patients. Patients' mean MPV value was 8.2 ± 0.99 fL. This did not differ statistically significantly compared to the control group ($p=0.95$). Mean NLR value in the study group was 38.5 ± 20.2%. No statistically significant difference was again determined compared to the control group ($p=0.33$). No elevation in CRP or ESR, leukocytosis or pathogen in stool culture was observed in any patient.

Eosinophil in stool smear was investigated in 7 (19.4%) patients, and all were positive (**Figure 1**). Histopathology was compatible with eosinophilic proctocolitis in 2 patients whose undergoing rectal biopsy.

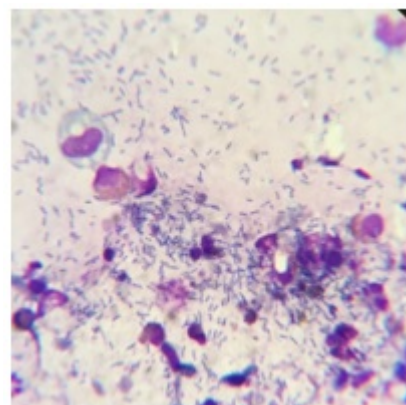


Figure 1: Eosinophil in stool examination at microscopic.

Symptoms resolved entirely with elimination of cow's milk and milk products from the mother's diet in 27 (75%) cases, while symptoms resolved with elimination of various allergenic foods (eggs, nuts and fish) in 8 (22.2) cases.

Table 2: Treatment regimens leading to resolution (n:33).

Treatment regime	n (%)
Elimination of cow's milk+milk products from the mother's diet	27 (75)
Elimination of multiple allergen foods (eggs, nuts, fish and meat) from the mother's diet	8 (22.2)
Discontinuation of mother's milk	1 (2.7)
Mother's milk+elementary formula during the supplementary nutrition period	25 (69.4)
Mother's milk + extensively hydrolyzed formula	17 (68)
Mother's milk+ amino acid-based formula	8 (32)

In one case, breast milk had to be discontinued since symptoms failed to improve despite multiple allergen food elimination from the mother's diet. The symptoms then improved, but rectal bleeding recurred when breast milk was

again given after 1 week. Breast milk was therefore discontinued for 3 months. Twenty-five (69.4%) patients started on formula and supplementary foods in addition to breast milk during monitoring were started on elementary formulas. Seventeen (68%) of these were given extensively hydrolyzed formula and 8 (32%) were given amino acid-based formula (**Table 2**).

Mean time to improvement of symptoms following commencement of elimination diet was 6.1 ± 5.9 days (1-25), and this diet was maintained for at least 6 months in all cases. Allergen foods were reintroduced at the end of 6 months. Elimination diet was maintained until at least 1 year of age in cases in which symptoms persisted.

In terms of patient distribution by years, the number of diagnosed cases increased over the years (**Figure 2**).

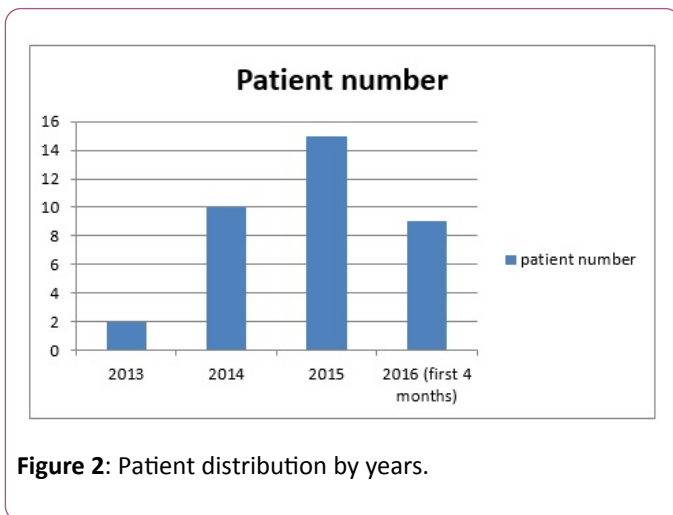


Figure 2: Patient distribution by years.

Discussion

AP is one of the most common causes of rectal bleeding in the form of spots or streaks inside the stool in early infancy and may manifest, albeit rarely, as pronounced rectal bleeding [9]. In agreement with the literature, the most common cause of presentation in our study was bloody streaks or spots.

Findings usually appear between 2 and 8 weeks [10]. Mean age at diagnosis in our cases was 3.2 ± 2.3 months, with 16 (44.4%) cases presenting before 8 weeks. We attribute the later age at diagnosis compared to that in the literature to patients having spent time in primary and secondary health institutions before diagnosis and thus presenting to us late.

These infants have a healthy appearance despite diarrhea and rectal bleeding, and delayed growth and interrupted weight gain are not generally to be expected [11]. Our cases were also infants with a healthy appearance, and no growth delay was observed in any patients. Fissure or erythema accompanying AP may be determined at anal examination [12]. Fissure was determined in 22.2% of our cases. Frequent defecation and stool pH alteration may play a role in fissure development.

A history of taking antibiotic therapy with a diagnosis amebic dysentery at other health centers based on bloody

stool was present in 7 (19.4%) cases. This may threaten the baby's health by compromising the intestinal flora and also result in unnecessary economic costs.

More than 60% of infants diagnosed with AP are exclusively breastfed babies, the remainder also receiving supplementary foods containing cow's milk protein or soya [5]. The great majority of our cases (77.7%) were exclusively breastfed babies.

AP developing in association with food proteins is a non-IgE-mediated allergic reaction, the most common cause of which is cow's milk protein [2]. However, AP has also been associated with food proteins such as eggs, soya, fish and meat [13]. No clinical improvement was observed in 25% of our patients with elimination of cow's milk and milk products only from the mother's diet, and additional elimination of eggs, nuts, fish and meat was required.

There is no sensitive laboratory test capable of use in the diagnosis of AP. Skin tests and specific IgE levels are also negative. Anemia or hypoalbuminemia are rarely determined, while peripheral eosinophilia is observed in approximately half of patients [6,14]. Most babies' results are also normal [4,10]. Mild anemia develops in infants with continued bleeding, but is rarely significant at initial examination [15]. Eosinophilia was observed in 61.1% of our cases, and hemoglobin values were slightly below normal in 11.1%. Reports of thrombocytosis in cases of AP have found in the literature [16]. Mild thrombocytosis was determined in 12 (33.3%) of our cases, and this was interpreted as a nonspecific inflammation finding of AP.

The NLR is an easily available and economical method that can be used in the diagnosis of disease with an inflammatory component [17,18]. Previous studies have reported a change in favor of neutrophils in gastrointestinal bleeding in Henoch-Schönlein purpura and in diseases such as allergic rhinitis, asthma and juvenile idiopathic arthritis [19,20]. We also investigated the NLR in our patients and determined a change in favor of lymphocytes, similarly to the control group. Similarly, mean MPV in the study group did not differ significantly from that in the control group. To the best of our knowledge, there are no previously published reports concerning MPV or NLR in patients with AP. It is not therefore possible to discuss these results in the light of the literature.

Endoscopic and colonoscopic examinations are not recommended for diagnosis [21]. Rectal biopsy was performed in only two patients in our study. Histopathological examination revealed eosinophilic proctocolitis. Investigation of eosinophils in the stool smear is a more specific and easier method for the diagnosis of AP colitis. Eosinophils are believed to be directly responsible for the tissue injury in this disease [22]. In the current study, stool smear was performed with seven patients, and eosinophil was determined in all these cases.

The basic approach in the treatment of AP consists of eliminating the responsible food allergen from the diet [23]. Most exclusively breastfed infants improve when cow's milk and milk products are eliminated from the mother's diet.

Improvement in refractory cases can also be achieved with the elimination of allergen foods such as soya, egg and fish. If the mother is not compliant with the diet, if the allergen protein cannot be identified and eliminated or if the baby is receiving cow's milk-based formula, then the diet can be adjusted to fully hydrolyzed or amino acid-based. In our study, amelioration was achieved in the majority of babies (75%) with the elimination of milk and milk products from the mother's diet, while in some (22.2%) clinical improvement was achieved with the elimination from diet of eggs, nuts, fish and meat. In one case, who was refractory to diet, breast milk was discontinued for 3 months. Twenty-five patients (69.4%) receiving additional formula and complementary nutrition during monitoring were started on elementary formula in addition to breast milk. Healing was achieved with extensively hydrolyzed formula in 17 (68%) of these and with amino acid-based formula in 8 (32%).

Improvement in rectal bleeding may be anticipated within 72-96hrs at latest following elimination of the relevant allergen foodstuff [2]. Mean time to resolution of symptoms following commencement of elimination diet in our cases was 6.1 ± 5.9 (1-25) days. We think that the mean was raised by the case that failed to respond to mother's diet, that received multiple allergen food stuff elimination and in which breast milk had to be interrupted.

Conclusion

In conclusion, the current study showed that AP is frequently seen in extensively breastfed infants with a healthy appearance. The allergen most commonly involved was cow's milk protein, and almost all cases resolved at approximately 1 year of age. Good response is achieved to elimination diet, and breast milk may rarely need to be interrupted. To the best of our knowledge, this is the first study to investigate MPV and the NLR in babies with AP. Although no difference was determined compared with the control group, we think that our results can contribute to the literature and that it will be useful for these parameters to be evaluated in further, wider series.

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Conflict of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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