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Determination of Acute and Chronic Urticaria Based on C-Reactive Protein or Mean Platelet Volume Levels

KEYWORDS: Urticaria; Mean Platelet Volume; C-Reactive Protein; Child

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ABSTRACT *The aim of the present study is to investigate the relationships of mean platelet volume (MPV) and C-reactive protein (CRP) levels in acute and chronic urticaria. We retrospectively evaluated 93 children with acute urticaria, 89 children with chronic urticaria and 103 healthy children as controls. Although MPV was found to be significantly higher in the chronic urticaria group than in the control group (median 7.5 vs. 7.15 fL, $p < 0.05$), CRP was significantly higher in children with acute urticaria (median 0.38 vs. 0.33, $p < 0.05$). No significant differences in platelet counts, platelet distribution width, mean platelet volume/platelet count ratio and neutrophil/lymphocyte ratio ($p > 0.05$) were found between urticaria patients and controls. Thus, acute and chronic urticaria may be discriminated by evaluating CRP and MPV levels before the end of 6 weeks in patients with urticaria.*

INTRODUCTION

Urticaria is characterized by the appearance of pruritic, erythematous, cutaneous elevations that blanch with pressure, indicating the presence of dilated blood vessels and edema (Kaplan, 2009). Urticaria is conventionally classified by symptom duration into acute (total duration, <6 weeks) and chronic (>6 weeks) subtypes (Zuberbier et al., 2009).

The binding of an antigen (allergen) to antigen-specific IgE on mast cells and basophils causes cell degranulation, resulting in the release of histamine and other vasoactive mediators responsible for clinical symptoms in urticaria. However, in most of the patients with chronic urticaria, mast cell triggering specific allergen cannot be defined (Hide et al., 1993). In recent years, autoimmune mechanisms have been thought to play a role in the development of chronic urticaria. Researchers have demonstrated autoantibodies against the high-affinity IgE receptors (FcεRI), which directly activates the α subunit of FcεRI and triggers the release of histamine in the absence of IgE (Grattan et al., 1991). However, these autoantibodies could be detected in only 25% of the patients with chronic urticaria (Hide et al., 1993). Another reason to suspect autoimmune mechanisms in the development of chronic urticaria is the determination of positive autologous serum skin test (ASST) response. Nonetheless, ASST is positive in only 60% of the patients with chronic urticaria (Sabroe et al., 1999).

It was shown in a study that the extrinsic pathway of the clotting cascade was activated and the level of fragment F (1+2), an indicator of thrombin production, was increased in patients with chronic urticaria (Asero et al., 2007). Thrombin is a serine protease which promotes platelet activation (Lundblad et al., 2005). Mean platelet volume (MPV) is a routine blood count parameter showing platelet volume. Researchers have indicated the increase of MPV during platelet activation (Vagdatli et al., 2010).

Interleukin 6 (IL-6) plays a key role in the release of several acute phase reactants, including C-reactive protein (CRP) (Kasperska-Zajac, 2012). A relationship has been found between chronic urticaria activity scores and the levels of CRP and serum IL-6 in a study, and systemic inflammation has been reported to have a role in the pathogenesis of chronic urticaria (Kasperska-Zajac et al., 2007). Acute urticaria may be accompanied with the signs of inflammation such as low grade fever and leukocytosis. Elevated IL-6 and CRP levels have also been reported in acute urticaria (Fujii K et al., 2001). Some studies have also indicated that MPV may be used as an inflammatory marker in inflammatory diseases such as attacks of familial Mediterranean fever (FMF) (Makay et al., 2009) and psoriasis (Canpolat et al., 2010).

In our study we aimed to determine the relationships between CRP and MPV in children with acute and chronic urticaria.

MATERIALS AND METHODS

In our study, children presented to the Pediatric Allergy and Asthma Polyclinic of Inonu University between 1 January 2009 and 1 January 2014 with a primary complaint of urticaria were enrolled.

Urticaria was considered acute if symptoms were present for <6 weeks and chronic if they were present for >6 weeks. Patients with physical urticaria and other types of chronic urticaria were excluded. Age- and gender-matched healthy children who presented to the outpatient clinic for

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regular visits were enrolled as the control group. Demographic characteristics, complete blood counts and CRP levels were obtained from the patients' records. MPV and CRP levels of the patients with acute and chronic urticaria were compared with the control group.

Statistical analysis

The Kruskal–Wallis test was used for group comparisons because the data were not normally distributed. Conover–Inman post-hoc testing for multiple pairwise comparisons between groups was performed following a significant Kruskal–Wallis test. To obtain summary statistics for numerical variables, median, minimum and maximum values were used. Categorical variables were defined as numbers and percentages, and Pearson's chi-square test was used for comparisons. P values <0.05 were considered significant for all comparisons.

RESULTS

Ninety-three children were included in the acute urticaria (45 females, median age 5 years) and 89 in the chronic urticaria (39 females, median age 6 years) groups. One hundred and three healthy children were enrolled as the control group (43 females, median age 5 years). Demographic characteristics of the patients with acute and chronic urticaria are shown in Table 1.

Although MPV level was significantly higher in the chronic urticaria group than in the control group (median 7.5 vs. 7.15 fL, $p < 0.05$ years), no difference was found between the MPV level of patients with acute urticaria and the healthy controls (median 7.4 vs. 7.15, $p > 0.05$).

Although CRP level was significantly higher in children with acute urticaria ($n = 69$) than in the healthy controls ($n = 106$) (median 0.38 vs. 0.33 mg/dl, $p < 0.05$), no significant difference was observed between the patients with chronic urticaria ($n = 50$) and the healthy controls with respect to CRP (median 0.31 vs. 0.33, $p > 0.05$).

WBC count was higher in patients with acute urticaria than in the healthy controls (median 8800/mm^3 vs. 8150/mm^3, $p < 0.05$). However, there was no difference in WBC counts between the children with chronic urticaria and the healthy controls (median 7600/mm^3 vs. 8150/mm^3, $p > 0.05$)

No significant difference was found in patients with either type of urticaria when compared with the healthy controls with respect to platelet counts, platelet distribution width (PDW), MPV/platelet count ratio and neutrophil/lymphocyte ratio ($p > 0.05$).

DISCUSSION

In our retrospective study, we determined that MPV level was significantly higher in the chronic urticaria group than in the control group, whereas no difference was found between the MPV levels of patients with acute urticaria and the healthy controls. Although CRP level was significantly higher in children with acute urticaria than in the healthy controls, the levels were similar in patients with chronic urticaria and the healthy controls.

Autoimmune and inflammatory mechanisms are thought to be involved in the pathogenesis of chronic urticaria. Researchers have reported that 86% of the patients with chronic urticaria tested positive on autologous plasma skin test (APST), whereas 53% of them were positive on ASST (Asero et al., 2006). They determined that the difference between ASST and APST results suggested a possible role of platelet-derived clotting factors in plasma which were causing the skin reactions; they pointed out that thrombin was the responsible agent. Thrombin is a serine protease which promotes platelet activation (Lundblad et al., 2005). MPV is a routine blood count parameter which shows platelet volume. Researchers have indicated the increase in MPV during platelet activation (Vagdatli et al., 2010).

Researchers have stated that MPV was the most common abnormal laboratory parameter in patients with chronic urticaria (Confino-Cohen et al., 2012). In another study, researchers have reported increased levels of MPV and PDW in chronic urticaria patients when compared with those in the controls (Chandrashekar et al., 2014). The only study which has evaluated the role of MPV in children with chronic urticaria showed lower MPV levels and higher platelet counts in children with chronic urticaria than in healthy children (Akelma et al., 2015). In our study, higher MPV levels were detected in children with chronic urticaria than in the healthy controls, which was compatible with studies conducted in adults. No difference was also found between the groups with respect to PDW and platelet counts.

Resarchers have demonstrated that procalcitonin levels were within normal limits in most chronic urticaria patients and slightly elevated in some severe cases, whereas CRP levels were higher in severe chronic urticaria patients than in the healthy controls (Kasperska-Zajac et al., 2013). Some authors suggested that CRP could be used as an indicator of disease activity in chronic urticaria (Takahagi et al., 2010). Researchers have determined elevated CRP and IL-6 levels in acute urticaria patients, which dropped to their normal ranges after the improvement of the urticaria symptoms (Fujii et al., 2001). In our study, WBC counts and CRP levels were found higher in acute urticaria patients than in the healthy controls, whereas no difference was found for patients with chronic urticaria.

MPV may be influenced by inflammation (Yuksel et al., 2009). Researchers have reported lower MPV levels in patients with Crohn's Disease (Liu et al., 2012), whereas another study found higher MPV levels in rheumatoid arthritis subjects than in the healthy controls (Yazici et al., 2010). Researchers have suggested that high-grade inflammatory diseases such as active rheumatoid arthritis or attacks of FMF are accompanied by low levels of MPV (Gasparyan et al., 2011). In addition, low grade inflammatory diseases may present with high MPV levels. By virtue of low levels of CRP in patients with chronic urticaria, we thought that MPV level was increased in those patients because of the activation of coagulation cascade, which was unrelated with the inflammation.

CONCLUSION

In our study, significantly higher CRP levels were found in patients with acute urticaria, whereas chronic urticaria patients showed higher MPV levels than those in the healthy controls. It was thought that MPV level was increased in chronic urticaria because of the activation of coagulation cascade, which was unrelated with the inflammation. To establish the autoimmune diseases associated with chronic urticaria earlier, acute and chronic urticaria may be discriminated by evaluating CRP and MPV levels in the first 6 weeks after presentation in patients with urticaria.

Table 1. Demographic characteristics of the patients

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with acute and chronic urticaria

	Acute urticaria (n =93)	Chronic urticaria (n = 89)
Age [years; median (minimum–maximum)]	5 0.5–17	6 1–17
Gender [Female; *n*(%)]	45 (48.4)	39 (43.8)
Total IgE [IU/mL; median (minimum–maximum)]	63.1 (n = 78) 1.2–1498	144 (n = 78) 1.56–2000
Eosinophils [count/mm^3; median (minimum–maximum)]	200 0–1400	200 0–1200

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