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Case Report

Henoch-Schönlein purpura: a new approach for early diagnose

A. Vasileva[1*], Iv. Chakarov[3], M. Penkova[2], G. Kuyumdzhieva[2], P. Chakarova[1]

[1]Clinic of Pediatrics, UMHAT "Prof. Dr. Stoyan Kirkovich", Stara Zagora, Bulgaria

[2]Department of Gastroenterology, UMHAT "Prof. Dr. Stoyan Kirkovich", Stara Zagora, Bulgaria

[3]Clinic of Childhood Hematology and Oncology UMHAT "Tsaritsa Yoanna-ISUL", Sofia

***Corresponding Author's Email: ani_asken@abv.bg**

Abstract

Injury of the gastrointestinal tract in Schönlein-Henoch disease is one of the most serious potential conditions. Common potential risks of serious late complications are: small bowel perforation, intussusception, gastro-intestinal bleeding and others. Ultrasound diagnosis is effective as first-line screening method in children with an abdominal form of the disease (gastrointestinal symptoms). In the present clinical observation, we present three clinical cases of children with Schönlein-Henoch-abdominal form, in which we studied the new aspects of the changes in the coagulation system, as well as the monitoring of abdominal involvement by ultrasound examination of the small intestines. The results of the ultrasound examination in these patients gives grounds for non-maintenance of the universal treatment with corticosteroids. The study in the dynamics of factor XIII and von Willebrand factor are convincingly informative about the degree of vascular damage and disease activity.

Keywords: Abdominal ultrasound, Factor XIII, Schönlein-Henoch, von Willebrand factor (vWF)

INTRODUCTION

Henoch-Schönlein purpura (HSP) is a vasculitis of small vessels as a result of IgA-mediated inflammation, mainly affecting the skin, gastrointestinal tract, joints, and kidneys. Cutaneous purpura is not associated with thrombocytopenia, it has a pre-selection localization on the extensor surfaces, especially on the lower extremities, symmetrically on the gluteus, often with the manifestation of abdominal pain, sometimes accompanied by blood in the stool. Arthralgia, haematuria, or proteinuria may also occur. Although the prognosis of HSP is generally good, affecting the gastrointestinal tract is one of the most serious potential complications of the disease. It carries risks of later possible complications, such as massive gastrointestinal bleeding, intestinal infarction, perforation of the small intestine, intussusception, peritonitis. Surgical interventions related to complications of GIT are performed in 5-12% of patients with HSP, and in recurrences, this percentage reaches 30% (Martinez-Fontanilla et al., 1984).

Abdominal pain is most often colicky, associated with nausea, vomiting, bleeding from the upper gastro-intestinal tract (GIT). It is possible for hematinous substances to appear in the vomit and for the stool to change to 'resinous'. If the hemorrhages are from the lower floors of the GIT, then they are defined as hematochezia (Saulsbury, 2001; Leung and Chan, 2002). To date, there is no specific serological marker to assist in the diagnosis of HSP and to distinguish it from other diseases with similar clinical manifestations.

Therefore, in clinical practice, there is an urgent need to identify markers indicating gastrointestinal tract involvement when the first or only symptoms are associated with the gastrointestinal tract, to reduce the need for invasive procedures such as laparotomy.

Recently, it has been established that there is a two-way connection between the inflammatory system and the coagulation system. Although even in the acute phase PT and aPTT are within normal limits, the activity of inflammation leads to secondary activation of the coagulation system (Levi and van der Poll, 2005). Anti-inflammatory cytokines and chemokines, polymorphonuclear cells, platelets, endothelial cells, fibrinogen, and fibrin are the important mediators in the activation of inflammation, respectively the coagulation (Levi and van der Poll, 2005; Szaba and Smiley, 2002).

Factor XIII (fibrin-stabilizing factor) decreases significantly during the acute phase of the disease and has been proposed as a prognostic indicator in HSP (Dalens et al., 1983; Kamitsuju et al., 1987).

Thevon Willebrand factor can be used as a specific marker of vascular damage and HSP activity (Sporn et al., 1985). It is a plasma glycoprotein synthesized by megakaryocytes and endothelial cells (Jaffe et al., 1974) isolated from large and small veins, capillaries, aorta, and arteries, which mediate platelet attachment to the subendothelium and platelet aggregation by binding tothedamaged vessel wall (Fretto et al., 1986).

Ultrasound diagnosis is effective as a first-line screening in children with gastrointestinal symptoms (Vasavada, 2004). Ultrasound sensitivity to detect intestinal changes in children with HSP varies from 50-100% with unspecified specificity (Vasavada, 2004; Ozdemir et al., 1995; Bomelburg et al., 1991).

MATERIALS AND METHODS

In the present clinical observation, three clinical cases of children who were diagnosed with the manifestation of a skin rash with the characteristic of the typical HSP rash, as well as with the manifestation of abdominal pain. Based on the new aspects for changes in the coagulation system and the possibilities for monitoring the abdominal involvement by ultrasound examination of the small intestine, a therapeutic regimen that allows not to be used corticosteroids can be chosen.

In addition to routine testing, changes in von Willebrand factor, factor XIII, fibrinogen, and D-dimer levels were monitored.

The ultrasound examination was performed with an ultrasound device HITACHI ARIETTA 70, using a high-frequency probe from 5 to 7 MHz. Standard settings during the study included elevated levels of PRF and total gain. At the basic settings set during the study, only the normally vascularized intestinal wall was free of color or power Doppler signal.

The ultrasound examination was performed in the morning on an empty stomach, and at the beginning of the study, the patient took 50 ml of water to better visualize the internal hypoechoic layers of the intestinal wall of the small intestine-lamina propria. Three of ultrasound-visible five layers of the small intestinal wall were available for measurement.

The normal intestinal wall consists of 5 layers, including the outermost echogenic thin mucosal and serious superficial layers, with submucosa manifesting as a continuous homogeneous echogenic structure less than 2 mm thick, delineated by two hypoechoic layers: inner-lamina propria and externally-muscularis propria (Tio and Tytgat, 1986). An intestinal wall with a thickness equal to or greater than 4 mm is considered thickened. High-resolution ultrasound can detect changes in the intestinal wall in three degrees. Grade I defines the changes as an expression of infiltration of one or more of the surface layers concerning stratification (Siegel et al., 1997). In the absence of a pathological correlation in grade II, the abnormalities are more difficult to explain. Extravascularly, the blood has a different and heterogeneous reflectivity but has a mainly echogenic appearance. Most likely, the additional echogenic layer internal to the submucosa may be secondary, due to deep mucosal and submucosal bleeding (Gorg et al., 2005). This leads to the so-called pseudo-differentiation of the appearance. Such an unusual finding in the absence of coagulation disorder and trauma could be a strongly suggestive hemorrhagic vasculitis. In contrast, the loss of wall differentiation (grade 3) is a relatively unusual pattern that has only been reported in intense infiltrative or necrotic disease processes involving the wall, without affecting the individual layers (Baud et al., 2004).

The established data for elevated von Willebrand factor concentrations are accepted as a reliable index of vascular damage (Bowyer et al., 1989). The possible correlation of vWF: Ag with the size of the affected blood vessel is discussed (Bowyer et al., 1989; Nusinow et al., 1984; Woolf et al., 1987). The von Willebrand factor does not play the role of an acute phase reagent but serves as a marker of vascular damage. Elevated values of vWF: Ag reflect the increased amount of circulating factor released from the endothelium due to vascular damage. Values return to normal when patients are in remission and remain above normal ranges with the continuation of the symptoms. The assessment of the von Willebrand factor can be considered as a reliable test for monitoring disease activity.

Fibrinogen, D-dimer, and FDPs levels are significantly higher during the acute phase of the disease. D-dimer and FDPs are more strongly associated with the overall clinical score of HSP than inflammatory markers such as the number of WBC, ANC, CRP (Yilmaz et al., 2005).

Therefore, they play an important role as indicators of the involvement of the gastrointestinal tract during the acute phase of HSP.

We present three clinical cases of children with Henoch-Schönlein purpura who were admitted for treatment with skin-rash, joint and abdominal syndromes.

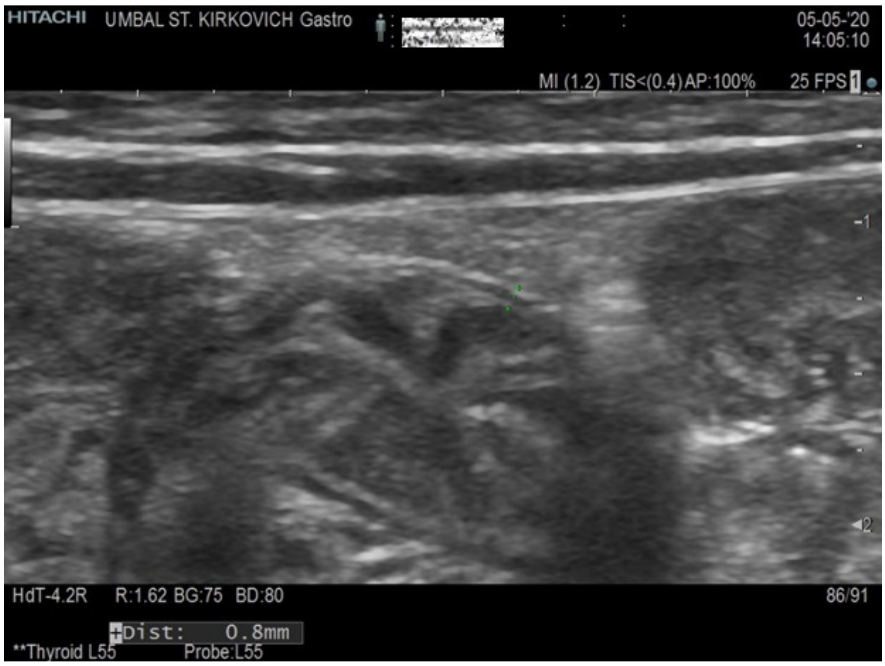

Figure 1. Abdominalultrasoundduringthehospitalization.

Clinical case 1

A child, 5 years of age, admitted to the Clinic of Pediatrics for fever up to 38 C, abdominal pain, and diffuse petechial rash on the buttocks. Treated on an outpatient basis with Klacid and symptomatic agents with a temporary effect. A few days before the current hospitalization, the abdominal pain and skin rash became more intense.

On clinical examination: Pale skin with petechiae and single suffusions on the lower extremities, around the ankles, gluteus, and sparse on the forearms and armpits. Bilateral vesicular breathing. RR 28 / min. Rhythmic heartbeat, HR108 / min. Abdomen-soft, diffusely painful on palpation, without hepato-splenomegaly. Musculo-skeletal system-normal.

The laboratory workup: CRP 248.1 mg / l; Leuc 26.8x10^9 / l; Gran 75.4%. Haemostasis profile: Fibrinogen 3.7 g / l; 4.03g / l; D-dimer-2.21mcg / l; VIII day of hospitalization-Fibrinogen-2.8g / l; D-dimer 0.52mcg / l; vWF: Ag 167.3%; f. XIII 70%. Test for occult hemorr-hages - (+) positive result. AST <200 UI., Blood group A (+) positive.

During the first three days of hospitalization, the child had pronounced abdominal pain, bloody stools, and transient swelling of the left ankle joint.

Abdominal ultrasound: Three of the five ultrasound-described layers of the small intestinal wall are visualized, and the total thickness of the three layers is 0.8 mm-1.1 mm. Figure 1

Ultrasound examination on the 5th day: Three of the five layers of the small intestinal wall described by ultrasound were visualized, as the total thickness of the three layers was 1.1 mm-1.7 mm. The Power Doppler study showed no signal between the individual layers.

On second admission dated 2nd of June 2020, with clinical data for the abdominal-pain syndrome. Three of the five layers of the small intestinal wall described by ultrasound were visualized, and the total thickness of the three layers was 1.8 mm-1.9 mm. The Power Doppler study showed no signal between the individual layers. Figure 2

After the treatment, without the administration of corticosteroids, the abdominal pain and skin rash syndromes underwent a complete reversal.

Clinical case 2

A child, 8 years of age, admitted to the Clinic of Pediatrics for an itchy, punctate, hemorrhagic rash on the lower extremities, spreading to the gluteus and anterior abdominal wall, followed by swelling and pain in the right ankle joint.

On clinical examination: Pale pink skin with the presence of a hemorrhagic rash on the lower extremities, gluteus, and anterior abdominal wall, with the character of palpable purpura, single suffusions on the lower legs. Bilateral vesicular breathing. RR 24 / min. Rhythmic heartbeat, HR 90 / min. Abdomen-soft, with slight palpatory pain periumbilical, accelerated intestinal peristalsis, without organomegaly.

The laboratory workup: CRP 52.8 mg / l; Leuc 11.8x 10^9 / l; haemostasisprofile: day I of hospitalization-

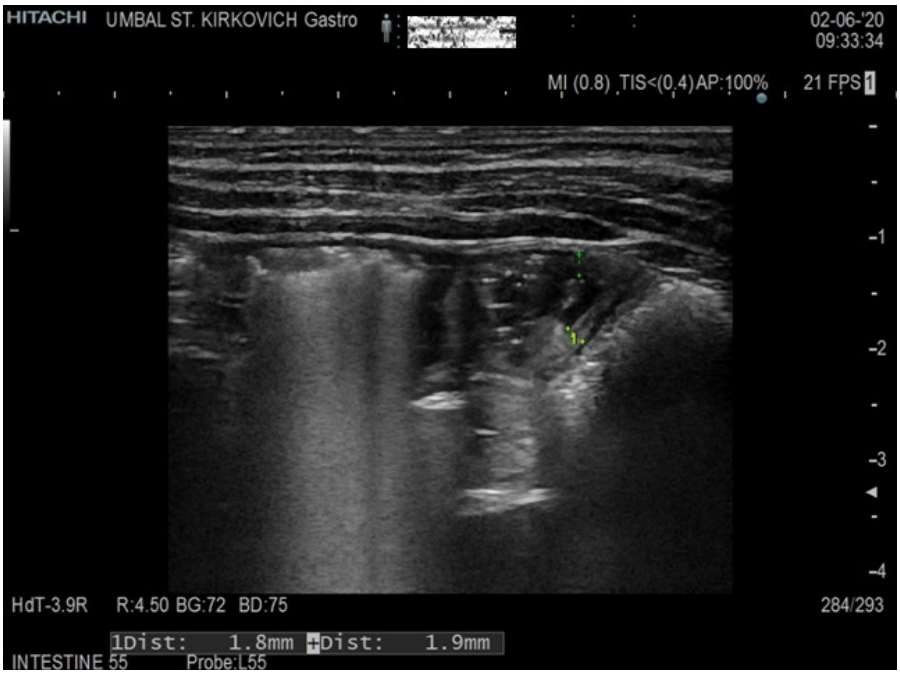

Figure 2. Abdominal ultrasound.

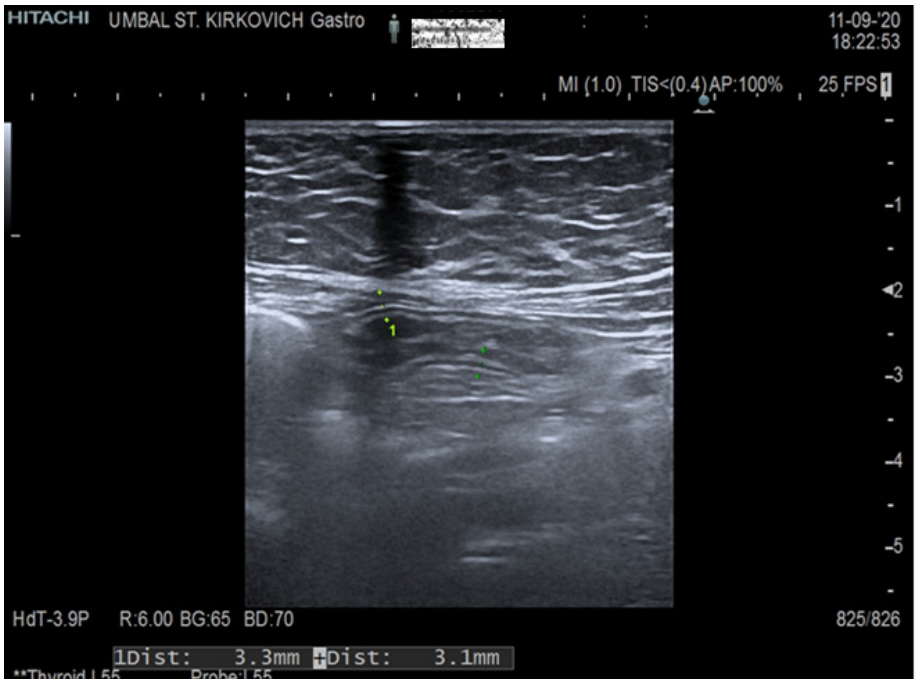

Figure 3. Abdominal ultrasound of patient number two.

Fibrinogen-3.93g/l; D-dimer-2.9mcg/l; XII day of hospitalization - Fibrinogen - 3.56g/l; D-dimer 0.8 mcg/l. vWF: Ag- 156.9% Blood group- A (+) positive; occult bleed ingtest - (+) positiveresult.

Abdominal ultrasound: Visualization of three of the ultrasound-described 5 layers of the small intestinal wall was achieved, as the total thickness of the three layers - mucosa, submucosa, and muscularis propria did not exceed in any of the measurements a value above 3.3 mm. The Power Doppler study showed no signal between the individual layers. Figure 3

During the stay in the clinic, the child was permanently

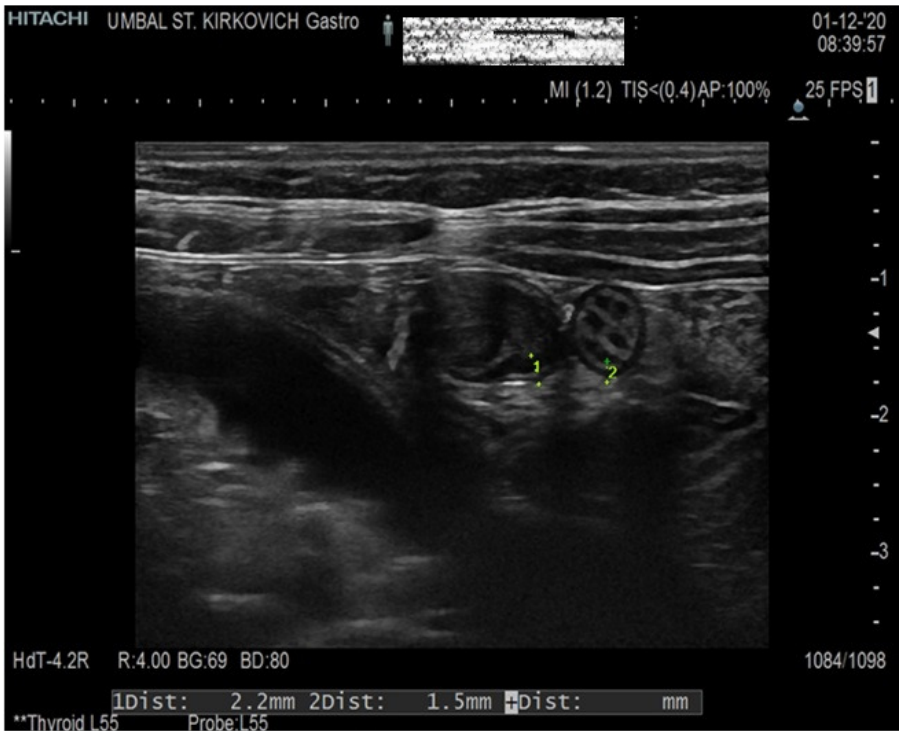

Figure 4. Abdominal ultrasound of patient number three.

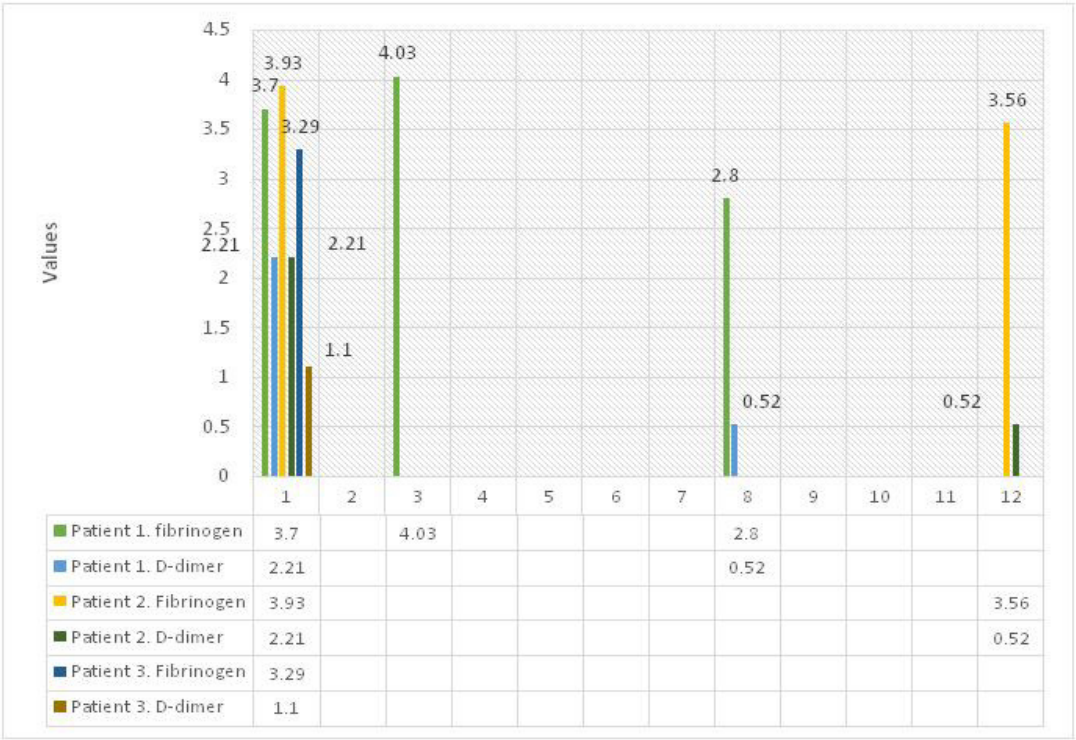

Figure 5. Graphical representation of fibrinogen and D-dimer values

afebrile, there was a double push of the skin-rash syndrome, with the manifestation of transient abdominal pain. As a result of the antibiotic treatment and the orally administered NSAIDs, the skin rash, joint, and abdominal-pain syndromes underwent a complete reversal. Corticosteroids have not been administered.

Clinical case 3

A child, 5 years of age, was admitted to the Clinic of Pediatrics on the occasion of the appearance of punctate, hemorrhagic rash on the lower extremities and buttocks, and swelling of the feet.

On clinical examination: Pale pink skin with petechiae and suffusions on the lower extremities and gluteus. Bilateral vesicular breathing. RR 24 / min. Rhythmic heartbeat, HR 108 / min. Abdomen - soft, palpably painless, without organomegaly, physiological intestinal peristalsis. Musculoskeletal system-normal.

The laboratory workup: CRP 0.6 mg/l; Leuc 12.03 x 10^9/l; Haemostasis profile: Fibrinogen 3.29 g/l; D-dimer-1.1mcg/l; VIII day of hospitalization-Fibrinogen-2.8g/l; D-dimer 0.52mcg/l; vWF: Ag 135%; f. XIII 100%. Test for occult hemorrhages - (+) positive result. AST <200 UI., Blood group A (+) positive.

Abdominal ultrasound: Three of the5 layers of the intestinal wall, were available for an ultrasound examination. The thickness of the three layers was established in the range from 1.5 to 2.2 mm. Figure 4

During the stay in the clinic, the child was permanently afebrile. As a result of the treatment, without the use of corticosteroids, the skin-rash syndrome underwent a complete reversal, without new pushes. The changes in fibrinogen and D-dimer levels in the three clinical cases are presented in figure 5.

The evaluation of fibrinogen and D-dimers are related to disease activity, together with the application of the HSP clinical evaluation system.

DISCUSSION

Henoch-Schönlein vasculitis is a disease that can lead to unpredictable complications, especially from the digestive system: appendicitis, hemorrhagic terminal ileitis, intramural hematoma, intestinal intussusception. Although the prognosis of HSP is generally good, gastro-intestinal involvement remains the most serious potential complication.

Decreased factor XIII levels during the acute phase of HSP may be a prognostic factor in HSP (Dalens et al., 1983; Kamitsuju et al., 1987), and von Willebrand factor levels may be used as a specific marker of vascular damage and disease activity (Sporn et al., 1985). In recent years, various authors have reported an increase in plasma vWF antigen. (Nusinow et al., 1984; Lie, 1988). Accumulated data on elevated von Willebrand factor concentrations are considered a reliable index of vascular damage.

The results obtained from the tests performed on our patients correlate with those of the evidence described above. Ultrasound is effective as a first-line screening method in children with gastrointestinal symptoms (Vasavada, 2004). It is an indisputable fact that intestinal sonography is the most sensitive method for detecting intramural bleeding and can reduce the diagnostic exposure of children. Gastrointestinal manifestations of HSP are associated with edema and intramural hemorrhage. When gastrointestinal symptoms are predominant and precede skin lesions, the clinical manifestation can mimic many diseases with a clinical picture of acute surgical abdomen. Therefore, laparotomies are often performed (Martinez-Fontanilla et al., 1984).

In these cases, the diameter of the intestinal wall (1.5 cm) is used as a distinguishing factor (Gedalia, 2004). The target mark is defined as a thickened intestinal wall having three concentric circles of strong, weak, and strong attenuation (Balthazar, 1991).

It is an indisputable fact that intestinal sonography is the most sensitive method for detecting intramural bleeding in HSP and can reduce the diagnostic exposure of children. The findings demonstrate demarcated hypoechoic to aehogenic crescent-shaped areas, thickened intestinal walls, and a cockade phenomenon emphasizing intramural bleeding and edema (Bomelburg et al., 1991). Another advantage of ultrasound in the early detection of intussusception in patients with HSP, which is a common surgical complication (Choong et al., 1998). Other rare complications may be ileal perforation (Chao and Huang, 1996)or ileal stricture, manifested by chronic intestinal obstruction (Cream et al., 1970). Although a rare complication may be acute pancreatitis. Ultrasonographic findings (Bomelburg et al., 1991) can help rule out abdominal surgery and establish a correct diagnosis even in the absence of typical skin lesions. Serial ultrasonography makes it possible to report the progressive reduction of wall thickening, mucosal thickening, and recurrence of peristalsis and visualization of small intestinal folds (Couture et al., 1992).

Ultrasonographic findings (Bomelburg et al., 1991) can help rule out a surgical abdomen, establish a correct diagnosis even in the absence of typical skin lesions, and prevent unnecessary surgery, especially in cases where purple skin lesions appear after gastrointestinal symptoms. Sonography is useful in follow-up examinations of patients with HSP. Serial ultrasono-graphy makes it possible to account for the progressive reduction of thickening of the mucosal walls, the recurrence of peristalsis, and visualization of the small intestinal folds (Allen et al., 1960).

CONCLUSION

Monitoring of the ultrasound examination in patients with abdominal HSP gives grounds for non-maintenance of universal treatment with corticosteroids. The study in the dynamics of factor XIII and von Willebrand factor is convincingly sufficiently informative about the degree of vascular damage and disease activity. Therefore, the use

of factor XIII is a good alternative, especially in cases of delayed onset, severe abdominal pain, when symptoms do not improve even after treatment with corticosteroids and intravenous immunoglobulins.

REFERENCES

Allen DM, Diamond LK, Howell DA (1960). Anaphylactoid purpura in children(Schönlein-Henoch syndrome): Review with a follow-up of the renal complications. *Am J Dis Child; 99:147-68.*

Balthazar EJ (1991). CT of the gastrointestinal tract: principles and interpretation. AJR; 156:23-32.

Baud C, Saguintaah M, Verac C, et al (2004). Sonographic diagnosis of colitis in children. EurRadiol; 14:2105-19.

Bomelburg T, Claasen U, von Lengerke HJ (1991). Intestinal ultrasonographic findings in Schonlein-Henoch syndrome. *Eur J Pediatr 150:158-60.*

Bowyer SL, Ragsdale CG, Sullivan DB (1989). Factor VIII related antigen and childhood rheumatic disease. *J Rheumatol; 16:1093-7.*

Chao HC, Huang JL (1996). Ileal perforation in Henoch-Schönlein purpura: report of one case. *Acta Paediatr Sin; 37:455-7.*

Choong CK, Kimble RM, Pease P, Beaslley SW (1998). Colocolic intussisception in Henoch-Schönlein purpura. *Pediatr Surg Int; 14:173-4.*

Couture A, Veyrac C, Baud C, Galifer RB, Armelin I (1992). Evaluation of abdominal pain in Henoch-Schönlein syndrome by high-frequency ultrasound. *PediatrRadiol; 22:12-7*

Cream JJ, Gumpel JM, Peachey RDG (1970). Schönlein-Henoch-purpurainadults. Q J Med; 39:461-83.

Dalens B, Travade P, Labbé A, Bezou MJ (1983;. Diagnostic and prognostic value of fibrin stabilizing factor in Schönlein-Henoch syndrome. *Arch Dis Child 58:12-4.*

Fretto LJ, Fowler WE, McCaslin DR, Erickson HP, McKee PA (1986). Substructure of human von Willebrand factor. *J Biol Chem 261:15679-89.*

Gedalia A (2004). Henoch-Schönlein purpura. *CurrRheumatol Rep; 6:195-202.*

Gorg C, Wollenberg B, Beyer J, et al. (2005). High-resolution ultrasonography in gastrointestinal graft-versus-host disease. *Ann Hematol; 84:33-9.*

Jaffe EA, Hoyer LW, Nachman RL (1974). Synthesis of von Willebrand factor by cultured human endothelial cells. *Proc Natl Acad Sci USA 71:1906-9.*

Kamitsuju H, Tani K, Yasui M, Taniguchi A, Tiara K, Tsukada S, et al. (1987). Activity of blood coagulation factor XIII as a prognostic indicator in patients with Henoch-Schönlein purpura. Efficacy of factor XIII substitution. *Eur J Pediatr; 146:519-23.*

Leung AK, Chan KW (2002). Evaluating the child with purpura. *Am Fam Physician. 2001; 64:419-428. Erratum in: Am Fam Physician 65:1751.*

Levi M, van der Poll T (2005). Two-way interactions between inflammation and coagulation. *Trends Cardiovasc Med 15:254-9.*

Lie JT (1988). Classification and immunodiagnosis of vasculitis; a new solution or promise unfulfilled? *J Rheumatol; 15:728-31.*

Martinez-Fontanilla LA, Haase GM, Ernster JA, Bailey WC (1984). Surgical complications in Henoch-Schönlein Purpura. *J Pediatr Surg 19:434-6.*

Nusinow SR, Federici AB, Zimmerman TS, Curd JG (1984). Increased von Willebrand factor antigen in the plasma of patients with vasculitis. *Arthritis Rheum*; *27:1405-10.*

Ozdemir H, Isik S, Buyan N, et al. (1995). Sonographic demonstration of intestinal involvement in Henoch-Schönlein syndrome. *Eur J Radiol; 20:32-4.*

Saulsbury FT (2001). Henoch-Schönlein purpura. *CurrOpin Rheumatol 13:35-40.*

Siegel MJ, Friedland JA, Hildebolt CF (1997). Bowel wall thickening in children: differentiation with US. *Radiology; 203:631-5.*

Sporn LA, Chavin SI, Marder VJ, Wagner DD (1985). Biosynthesis of von Willebrand protein by human megakaryocytes. *J Clin Invest 76:1102-6.*

Szaba FM, Smiley ST (2002). Roles for thrombin and fibrin(ogen) in cytokine/chemokine production and macrophage adhesion in vivo. *Blood 99:1053-9.*

Tio TL, Tytgat GN (1986). Endoscopic ultrasonography of normal and pathologic upper gastrointestinal wall structure: comparison of studies in vivo and in vitro with histology. *Scand J Gastroenterol Suppl; 123:27-33.*

Vasavada P (2004). Ultrasound evaluation of acute abdominal emergencies in infants and children. *Radiol Clin North Am; 42:445-56.*

Woolf AD, Wakerley G, Wallington TB, Scott DGI, Dieppe PA (1987). Factor VIII related antigen in the assessment of vasculitis. *Ann Rheum Dis; 46:441-7.*

Yilmaz D, Kavakli K, Ozkayin N (2005). The elevated markers of hypercoagulability in children with Henoch-Schönlein purpura. *PediatrHematol Oncol; 22:41-8.*