

Diagnostic Accuracy of C-Reactive Protein and Erythrocyte Sedimentation Rate in Patients with Acute Scrotum

Seyyed Alaeddin Asgari,^{1*} Gholamreza Mokhtari,¹ Siavash Falahatkar,¹
Mandana Mansour-Ghanaei,² Ali Roshani,¹ Alireza Zare,¹ Mehrangiz Zamani,³
Iradj Khosropanah,¹ Mohammad Salehi¹

¹Department of Urology, Razi Hospital, Gilan University of Medical Sciences, Rasht, Iran

²Department of Obstetrics and Gynecology, Al-Zahra Hospital, Gilan University of Medical Sciences, Rasht, Iran

³Department of Obstetrics and Gynecology, Ekbatan Hospital, Hamedan University of Medical Sciences, Hamedan, Iran

ABSTRACT

Introduction: Our aim was to investigate the diagnostic accuracy of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) in patients with acute scrotum.

Materials and Methods: One hundred and twenty patients with acute scrotum were evaluated and divided into 3 groups: 46 with acute epididymitis (group 1), 23 with spermatic cord torsion (group 2), and 51 with other noninflammatory causes of acute scrotum (group 3). Serum levels CRP and ESR were measured at the time of admission.

Results: Of the patients in group 1, 44 (95.6%) had elevated serum levels of CRP (mean, 67.77 ± 47.80 mg/L). In contrast, only 1 patient in group 2 had a significant increase in the serum level of CRP (mean, 9.0 ± 4.90 mg/L), and the patients in group 3 did not have any significant increase in the CRP levels (mean, 7.0 ± 2.2 mg/L) ($P < .001$). The mean ESR values were 45.9 ± 21.4 mm/h, 14.2 ± 11.2 mm/h, and 8.8 ± 7.5 mm/h, in groups 1 to 3, respectively ($P < .001$). The cutoff points for distinguishing between epididymitis and noninflammatory causes of acute scrotum were 24 mg/L for CRP and 15.5 mm/h for ESR. The sensitivity and specificity values were 93.4% and 100% for CRP and 95.6% and 85.1% for ESR, respectively.

Conclusion: Based on our findings, serum levels of CRP and ESR can provide helpful information for differentiation between epididymitis and other causes of acute scrotum. We recommend CRP and ESR measurements before making a decision of surgical intervention.

KEYWORDS: acute-phase proteins, acute scrotum, C-reactive protein, erythrocyte sedimentation rate, epididymitis, spermatic cord torsion, diagnosis

Introduction

Acute scrotum is defined as a painful inflammation of the scrotum or its components presenting with local signs and systemic symptoms.⁽¹⁾ Its differential diagnoses include

spermatic cord torsion, acute epididymitis, hydrocele, varicocele, trauma, testicular tumors, etc. The most common cause of acute scrotum is epididymitis.⁽²⁾ In practice, early differentiation of spermatic cord torsion from acute epididymitis is of utmost importance. Differentiation of these two conditions is sometimes challenging; diagnosis of spermatic cord torsion must be made

Received January 2005

Accepted September 2005

*Corresponding author: Razi Hospital, Rasht, Iran.

Tel: +98 131 669 0006, E-mail: s-a-asgari@gums.ac.ir

within the first 4 to 6 hours, otherwise it can lead to an irreversible ischemic injury to the testis and loss of gonads,⁽¹⁻³⁾ especially if a complete spermatic cord torsion, ie, a 720-degree rotation, is present.⁽⁴⁾ Physical examination and history can make the diagnosis in two-thirds, but in one-third of patients with acute scrotum, further assessments such as laboratory studies and imaging would be required. Current diagnostic methods are nonspecific, time consuming, and not always available, resulting in loss of the golden diagnostic time.

An infectious or inflammatory process can alter the serum levels of acute-phase proteins and erythrocyte sedimentation rate (ESR), and so do the inflammatory causes of acute scrotum. This may help early diagnosis; however, the value of these nonspecific inflammatory parameters has not been elucidated yet. In a retrospective study on 104 patients with acute scrotum, it was shown that serum level of C-reactive protein (CRP) is helpful in differentiating epididymitis from noninflammatory conditions like spermatic cord torsion or tumor.⁽¹⁾ However, the literature lacks ample prospective evaluation. We designed a study to investigate the diagnostic efficacy of CRP and ESR in patients with acute scrotum.

Materials and Methods

In a cross-sectional study, we enrolled 120 consecutive patients with an acute scrotum who referred to our emergency clinic from March 2003 to March 2004. All men with an acute scrotum visited within the first 24 hours of pain initiation were enrolled. The exclusion criteria were the existence of one of the following conditions: immunocompromised diseases, administration of immunosuppressives or nonsteroid anti-inflammatory drugs, rheumatoid arthritis, inflammatory bowel diseases, recent surgical operation, acute myocardial infarction, allograft rejection, malignancy, burns, infectious diseases with origins other than the scrotum, anemia, congestive heart failure, multiple myeloma, renal insufficiency, hyperchlostromia, hyperfibrinogenemia, tuberculosis, and endocarditis.

The patients were treated according to history, physical examination, laboratory tests, scrotal ultrasonography, respond to manual detorsion maneuver, and surgical exploration (if required). The final diagnoses were made after appropriate follow-up to evaluate the outcome. In patients

with spermatic cord torsion, preceded by taking serum samples, manual detorsion was attempted and if successful, bilateral orchidopexy was performed immediately. If manual detorsion was not possible or in case of suspicion between epididymitis and spermatic cord torsion, surgical exploration would be carried out. Patients with acute epididymitis were recommended to rest, decrease scrotal temperature, and elevate testes. In addition, appropriate antibiotics and sedatives were started on. Other causes of acute scrotum were treated appropriately.

Patients were divided into 3 groups: 46 with acute epididymitis (group 1), 23 with spermatic cord torsion (group 2), and the remaining 51 had other noninflammatory causes of acute scrotum (group 3; testicular appendix torsion, trauma, tumor, hydrocele, varicocele, etc). Serum levels of CRP and ESR were measured at the time of admission.

Erythrocyte sedimentation rate. As an indirect measurement of an acute-phase plasma protein in serum (fibrinogen), ESR was determined in all patients before therapeutic interventions using modified Westergren method. The Westergren pipet was filled to the "0" mark (+1 mm) with the blood sample which was anticoagulated with tripotassium ethylenediaminetetraacetic acid and diluted by 0.85% NaCl solution. In 1 hour, the distance between the meniscus of the plasma and the top of the sedimented erythrocyte column was recorded in millimeters.⁽⁵⁻⁸⁾

C-reactive protein. Turbidimetric analysis was used to measure serum levels of CRP. The blood sample was centrifuged at 4000 rpm for 10 minutes. The turbidity resulted from the reaction between serum and the specific antibody for CRP was measured using photometrical method.^(1,7,8,9) The reference ranges were less than 8 mg/L for adults and less than 10 mg/L for children.

Statistical analyses. The results of ESR and CRP tests were compared between the 3 groups of patients using 1-way analysis of variance (ANOVA) and Tukey test. Differential diagnosis between acute epididymitis and noninflammatory causes of acute scrotum (including spermatic cord torsion) was considered to determine a cutoff point for ESR and CRP using receiver operating characteristic (ROC) curves. Diagnostic parameters were calculated using routine equations. Continuous variables were demonstrated as means \pm standard deviations

and a *P* value less than .05 was considered significant.

Results

A total of 120 patients with acute scrotum were investigated and divided into 3 groups based on the final diagnoses (Table 1). Of 46 men with epididymitis, 20 (43.5%) were older than 35 years, and 15 (65.2%) of those with spermatic cord torsion were younger than 20 years. In addition, 1 patient (4.3%) with torsion was older than 35 years (42 years old), while 8 (17.4%) with acute epididymitis were younger than 20 years.

Fever ($> 38.5^{\circ}\text{C}$) was present in 30 men with acute epididymitis (65%; group 1) and in 1 of those with spermatic cord torsion (4.3%; group 2). Irritative urinary symptoms and pyuria were seen in 37 (80.4%) and 31 (67.4%) patients in group 1, respectively, but in none of those in group 2. Leukocytosis was present in 20 (43.5%) and 6 (26%) patients in groups 1 and 2, respectively. The cremasteric reflex was absent in all of the patients in group 2 and in 37 (80%) and 33 (64.7%) of those in groups 1 and 3, respectively. A horizontal position of the testis was found in 19 (82.6%) of the patients in group 2 and 9 (1.9%) of those in group 1. Prehn sign was positive in 10 (21.7%) and 21 (91.3%) patients in groups 1 and 2, respectively.

An at least 4-fold increase in the serum CRP

levels was seen in 44 patients (95.6%) in group 1 (mean, 67.77 ± 47.80 mg/L). In contrast, only 1 patient in group 2 had a significant increase in the serum CRP level (mean, 9.0 ± 4.90 mg/L). The patients in group 3 did not have any significant increase of the CRP levels (mean, 7.0 ± 2.2 mg/L). The mean serum levels of CRP and ESR in the patients are shown in Table 1.

Using the 1-way ANOVA and Tukey test, significant differences were seen in the ESR and the CRP levels between groups 1 and 2 and groups 1 and 3 ($P < .001$; $P < .001$), but not between groups 2 and 3 (CRP, $P = .96$; ESR, $P = .32$). Overall, the patients with epididymitis (group 1) had higher CRP and ESR values than others ($P < .001$; $P < .001$).

According to ROC curves, the best cutoff points for differentiation between epididymitis and noninflammatory causes of acute scrotum (mainly spermatic cord torsion) were 24 mg/L for CRP and 15.5 mm/h for ESR. The values of diagnostic parameters for CRP and ESR are demonstrated in Table 2.

Discussion

Differential diagnosis of acute scrotum by history and physical examination is difficult in one-third of patients, mandating a rapid and accurate diagnostic tool.⁽⁹⁾ In the present study, we evaluated the diagnostic accuracy of CRP and

TABLE 1. Demographic and clinical characteristics of the patients with acute scrotum

	Group 1 (epididymitis)	Group 2 (torsion)	Group 3 (others)
Number of the patients*	46 (38.3)	23 (19.2)	51 (42.5)
Mean age (year)	36.3	16.7	24.4
Age range	1 to 86	9 to 42	5 to 85
Mean ESR (mm/h)	45.9 ± 21.4	14.2 ± 11.2	8.8 ± 7.5
Mean CRP (mg/L)	67.7 ± 47.8	9.0 ± 4.9	7.0 ± 2.2

*Values in parentheses are percents.

TABLE 2. Diagnostic parameters of CRP and ESR for differentiation of acute epididymitis from other noninflammatory causes of acute scrotum*

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
ESR	93.4	100	100	96.1
CRP	95.6	85.1	80	96.9

*Values are percents.

ESR in patients with acute scrotal conditions.

Acute-phase proteins comprise a large heterogeneous group of proteins, mainly synthesized in the liver, and their serum concentrations usually increase or decrease by at least 25% in acute conditions. Several stimuli can lead to an acute phase such as infections, physical or chemical traumas, surgical operations, tissue ischemia, and advanced carcinomas. Sophisticated mechanisms including the release of a series of mediators are behind this acute response. Acute-phase proteins are capable of direct neutralization of inflammatory factors, reduction of tissue damage, and contribution to reconstruction of tissue.^(1,10) Serum levels of some proteins such as albumin, pre-albumin, and transferrin (negative group), decrease while some others such as CRP, haptoglobin, and fibrinogen (positive group) increase. In 1991, Young and associates suggested that the serum levels of CRP are helpful in 6 clinical conditions: monitoring the response to antibiotic treatment; in obstetric patients with premature rupture of membranes, a rise in CRP can give early warning of intrauterine infections; differentiation between active disease and infections in patients with systemic lupus and ulcerative colitis where the level of response to active disease has been previously established; as a measure of disease activity and response to disease-modifying drugs in rheumatoid arthritis; early detection of complications in postoperative patients; and in differentiating between infection and graft-versus-host disease in bone marrow transplant patients.⁽¹¹⁾

Acute-phase proteins and their indicators such as CRP and ESR were then considered in the differential diagnoses of acute scrotum including epididymitis, spermatic cord torsion and other noninflammatory causes. Acute scrotum is most often diagnosed by history, physical examination, laboratory studies, and imaging. Age is a major parameter as spermatic cord torsion usually occurs during adolescence, often in men younger than 20 year, whereas epididymitis is mostly seen in men older than 35 years.⁽²⁾ In our study, 43.5% of men with epididymitis were older than 35 years and 65.2% of those with spermatic cord torsion were younger than 20 years. Acute epididymitis is accompanied by fever in 18% to 33%, pyuria in 24% to 74%, and leukocytosis in 17% to 72% of cases.^(2,3) The above factors, albeit strongly indicative of epididymitis, are not

pathognomonic. Pyuria and bacteriuria are rarely seen in cases of torsion, but since they are nonspecific signs, even by a positive urine culture for infection one cannot rule out spermatic cord torsion. In our study, fever and leukocytosis were present in 4.3% and 26% of men with spermatic cord torsion, respectively. Thus, it seems that such classic indicators of inflammation are less accurate diagnostic parameters than CRP and ESR. Of 46 men with epididymitis, 20 (43.5%) were older than 35 years, and 15 (65.2%) of those with spermatic cord torsion were younger than 20 years. In addition, 1 patient (4.3%) with torsion was older than 35 years (42 years old), while 8 (17.4%) with acute epididymitis were younger than 20 years.

A severely tender testis is typically seen in spermatic cord torsion, and on physical examination, the horizontal position of the testis is a common finding. The cremasteric reflex is absent, spermatic cord is thick, and epididymis may be palpable at initial stages. However, progression of inflammation and the subsequent enlargement of scrotum preclude palpation of epididymis. Moreover, if a 360-degree torsion occurs, epididymis is placed posteriorly. The cremasteric reflex was absent in all of our patients with spermatic cord torsion and in 80% with epididymitis. A horizontal position of the testis was found in 82.6% of the patients with torsion and only 1.9% with acute epididymitis. Prehn sign is another diagnostic factor in the differential diagnoses of spermatic cord torsion and epididymitis. A positive Prehn sign is in favor of epididymitis, but it is not reliable in most of cases. A positive result was seen in 21.7% and 91.3% of our patients with epididymitis and spermatic cord torsion, respectively.

Doppler ultrasonography is usually used to assess blood circulation in the spermatic cord and the testis, reported to have a 89% sensitivity and a 100% specificity for diagnosis of spermatic cord torsion. However, it is operator dependent; not always available; and not reliable in incomplete torsions, pediatric cases, and torsions in their initial stages.^(1,12,13) Radionuclide imaging reveals a photopenic feature in torsion and an increased flow and infiltration of radioactive substance in epididymitis. It is the study of choice in the diagnosis of acute scrotum, yet even with more limitations than ultrasonography⁽²⁾; anatomic assessment is not possible and an inflammation and hyperemia in the scrotal wall can result in

false-positive findings for spermatic cord torsion.

A definite diagnosis of spermatic cord torsion is ultimately made by operative exploration, and prompt exploration is necessary when torsion is suspected. We considered surgical operation as the gold standard and assessed the CRP and ESR values obtained preoperatively in association with the final diagnoses. Based on our findings, ESR and especially CRP have high sensitivities, specificities, and predictive values for differentiation between epididymitis and noninflammatory causes of acute scrotum including spermatic cord torsion. Of 46 patients with acute epididymitis, only 2 had a CRP value less than the cutoff point (24 mg/L) and 2 had an ESR less than 15.5 mm/h. Consonant with the only similar study performed worldwide,⁽⁹⁾ a 4-fold increase in serum CRP levels was seen in 2 patients with epididymitis, while a significant increase was seen in only 1 patient with torsion and no one with other causes. Both CRP and ESR had high diagnostic values (Table 2).

Conclusion

While most diagnostic tests are not precise enough or otherwise not practicable in the limited golden time for the diagnosis of acute scrotum causes, serum levels of CRP and ESR can provide helpful information easily and rapidly. Our findings revealed that with high sensitivity and specificity, these tests can differentiate acute epididymitis from noninflammatory causes, especially spermatic cord torsion. We suggest CRP and ESR be measured before making a decision of surgical exploration. However, further study is warranted to prove their value and rely on them without a concern of missing spermatic cord torsion.

References

1. Doehn C, Fornara P, Kausch I, Buttner H, Friedrich HJ, Jochem D. Value of acute-phase proteins in the differential diagnosis of acute scrotum. *Eur Urol.* 2001;39:215-21.
2. Schneck FX, Bellinger MF. Abnormalities of the testes and scrotum and their surgical management. In: Walsh PC, Retik AB, Vaughan ED Jr, et al, editors. *Campbell's urology.* 8th ed. Philadelphia: WB Saunders; 2002. p. 2379-82.
3. Gerber GS, Brendler CB. Evaluation of the urologic patient: history, physical examination, and urinalysis. In: Walsh PC, Retik AB, Vaughan ED Jr, et al, editors. *Campbell's urology.* 8th ed. Philadelphia: WB Saunders; 2002. p. 95-7.
4. Kogan SJ, Hadziselimovic F, Howards SS, Huff D, Snyder III HM. Pediatric andrology. In: Gillenwater JY, Grayhack JT, Howards SS, Mitchell M, editors. *Adult and Pediatric Urology.* 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2002. p. 2572-81.
5. Dinarello CA, Wolff SM. The role of interleukin-1 in disease. *N Engl J Med.* 1993;328:106-13.
6. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. *N Engl J Med.* 1999;340:448-54.
7. Kushner I, Gewurz H, Benson MD. C-reactive protein and the acute-phase response. *J Lab Clin Med.* 1981;97:739-49.
8. Pepys MB, Baltz ML. Acute phase proteins with special reference to C-reactive protein and related proteins (pentaxins) and serum amyloid A protein. *Adv Immunol.* 1983;34:141-212.
9. Pakzad P. Principles and interpretation of clinical serologic tests. 1st ed. Tehran: Nour-e-Danesh; 2001. p. 178.
10. Feingold KR, Soued M, Serio MK, Moser AH, Dinarello CA, Grunfeld C. Multiple cytokines stimulate hepatic lipid synthesis in vivo. *Endocrinology.* 1989;125:267-74.
11. Young B, Gleeson M, Cripps AW. C-reactive protein: a critical review. *Pathology.* 1991;23:118-24.
12. Pepys MB, Baltz ML. Acute phase proteins with special reference to C-reactive protein and related proteins (pentaxins) and serum amyloid A protein. *Adv Immunol.* 1983;34:141-212.
13. Baker LA, Sigman D, Mathews RI, Benson J, Docimo SG. An analysis of clinical outcomes using color doppler spermatic cord ultrasound for spermatic cord torsion. *Pediatrics.* 2000;105:604-7.