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The role of ulinastatin in pericardial abscess with life threatening conditions

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Abstract
A 34 year old young patient was admitted in medical emergency with history of fever and generalized weakness last 3 days. After 10 minutes of physical examination patient had fainting episode with cardiogenic shock and he was shifted to cardiac ICU. ECG showed low voltage with flat T waves and 2D Echocardiography revealed pericardial abscess without structural heart diseases or coronary heart diseases and no evidence was found for vegetations. Chest X-ray showed cardiomegaly without chamber enlargement. He was treated aggressively for pericardial abscess. Massively raised WBC counts was treated with support of two to three broad spectrum antibiotics and antifungal. Despite of all medical therapy patient did not improved then as per studies and previous papers we started inj Ulinastatin with same antibiotic support. Finally he came out of horrible condition after 3 days.

Keywords: Pericardial abscess, Ulinastatin Staphylococcus aureus

1. Introduction

Pericardial abscess is a serious, life-threatening illness associated with high mortality. Pericardial abscess is an extremely unusual complication of Staphylococcus aureus bacteremia. The mechanism of purulent pericarditis by Staphylococcus aureus is unknown. Possible explanations include hematogenous seeding or direct extension into a pre-existing pericardial cyst or purulent pericarditis occurring in a patient with old pericardial adhesions(1-3). Transthoracic echocardiography and pericardiocentesis confirmed the presence of pericardial fluid collection. Staphylococcus aureus grew in both pericardial fluid and blood. Although an aggressive medical treatment including intravenous antibiotics and percutaneous drainage are required but studies suggest that treatment with ulinastatin may reduce mortality in severe sepsis in humans (2-4). Ulinastatin is a highly selective serine protease inhibitors that act on only a few steps in the multipronged inflammatory response involved in the pathogenesis of sepsis like coagulation (tissue factor pathway inhibitor, activated protein C, thrombomodulin, and antithrombin III), complement cascade (C1 inhibitor), or neutrophil elastase (5, 8, 15).

2. Case Report

A 34 year old young patient was admitted in medical emergency with history of fever and generalized weakness last 3 days. After 10 minutes of physical examination patient had fainting episode with cardiogenic shock and he was shifted to cardiac ICU. ECG showed low voltage with flat T waves and sinus tachycardia. Vital signs on admission showed hypotension (90/46 mm Hg), tachycardia (123 beats per minute), tachypnea (28 per minute), and hypothermia (35°C). His laboratory results showed elevated white blood cell counts (25200/mm 3), with neutrophil 92%, elevated high sensitive C-reactive protein level of 42 mg/dL (reference range, 0-0.5 mg/dL), blood urea nitrogen/creatinine 49/2.5 mg/dL, creatine kinase myocardial band 9.7 U/L (reference range, 0-3.6 U/L), Troponin I 0.08 ng/mL (reference range, 0-0.1 ng/mL). A chest radiograph showed cardiomegaly (Fig-1A). A transthoracic 2D Echocardiography demonstrated concentric left ventricular hypertrophy with fluid collection in the posterolateral wall of the pericardium (Fig-1B) and tamponade physiology with no evidence of valvular vegetation (Fig. 2A). He was treated aggressively for pericardial abscess. Massively raised WBC counts was treated with support of two to three broad spectrum antibiotics and antifungal agent. Pericardial aspiration of the fluid revealed a bloody material and culture showed growth of Staphylococcus aureus. Blood cultures showed staphylococcal bacteremia. Lab analysis of aspiration fluid showed elevated white blood cell counts (>45000/mm3), with polymorphonuclear neutrophil 90%, pH 7.3, glucose 5 mg/dL, lactate dehydrogenase 9878 U/L, albumin 2.25 g/dL and total protein 6.4 g/dL. Percutaneous drainage and empiric antibiotic treatment were started immediately. However, the patient deteriorated due to refractory sepsis and organ failure. Despite of all medical therapy patient did not improved, then as per studies and previous papers we started inj Ulinastatin with same antibiotic support. Finally he came out of horrible condition after 3 days. 2D Echocardiography revealed recovery of tamponade changes (Fig- 2B).

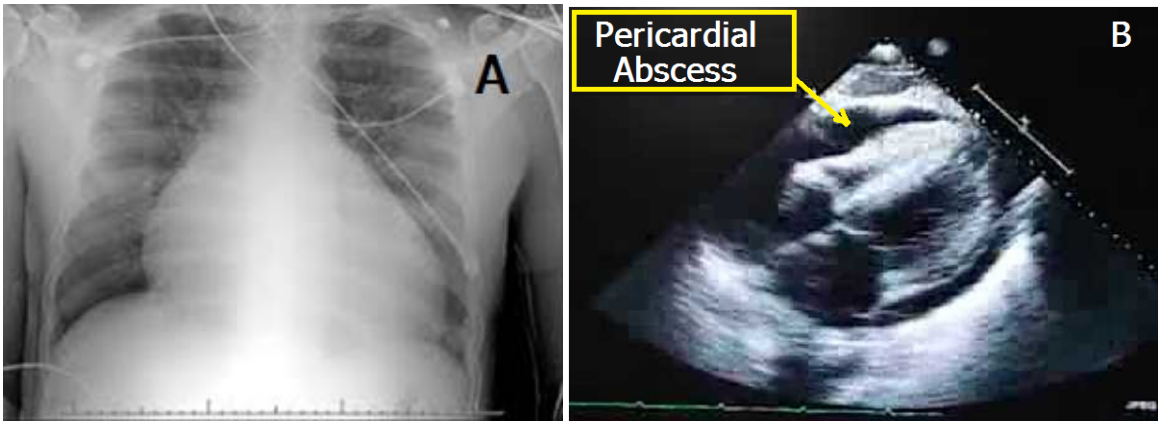

Fig 1: A (Chest X-Ray showed Cardiomegaly), **B** (2D Echo showed pericardial abscess with RV Collapse.)

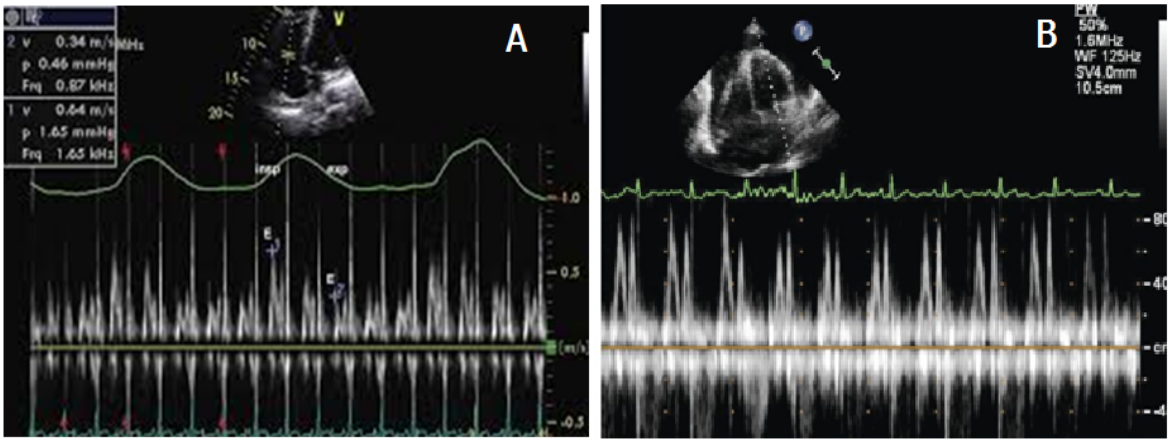

Fig 2: A (2D Echo doppler showed Tricuspid valve Tamponade variation with inspiration. **B** (Recovery of Tamponade TV variation with respiration.)

3. Discussion

Pericardial abscess is a rare sequale of Staphylococcus aureus bacteremia. The mechanism of pericardial abscess by Staphylococcus aureus is unknown. Possible explanations include hematogenous seeding or direct extension into a pre-existing pericardial cyst or purulent pericarditis occurring in a patient with old pericardial adhesions. Other microorganisms causing pericardial abscess include Mycobacterium tuberculosis, Gram-negative bacilli, Streptococcus species, and Aspergillus. Because delayed diagnosis of pericardial abscess may lead to debilitating complications, early echocardiography is important. Tomography provides useful information on the extent of the pericardial abnormality when the echocardiographic picture is not clear. Pericardial abscess is a serious, life-threatening illness associated with high mortality. The primary treatments for pericardial abscess include percutaneous or surgical drainage and pericardiectomy with prompt administration of appropriate antibiotics (1-4).

Ulinastatin is a highly selective serine protease inhibitors that act on only a few steps in the multipronged inflammatory response involved in the pathogenesis of sepsis like coagulation (tissue factor pathway inhibitor, activated protein C, thrombomodulin, antithrombin III), complement cascade (C1 inhibitor), or neutrophil elastase [5, 8, 15]. Another prospective, double-blind, randomized, placebo-controlled trial of ulinastatin in patients with severe sepsis showed that intravenous administration of ulinastatin in a dose of 200,000 units twice daily for 5 days was associated with a reduction in 28-day all-cause mortality (the primary end-point) to 7.3 versus 20.3 % in the placebo control group. A few small studies, published in Chinese-language journals, have shown lower mortality in patients treated with ulinastatin [14, 16, 17,]. A small Korean study showed that mortality was lower in patients with severe sepsis treated with ulinastatin (18.6 vs. 27 % in the control group) [13].

In contrast, ulinastatin inhibits a wide variety of pro-inflammatory serine protease enzymes including trypsin, thrombin, kallikrein, plasmin, cathepsin, neutrophil elastase, neutrophil protease-3, and coagulation factors IXa, Xa, XIa, and XIIa [18]. Although the exact mechanism of action of ulinastatin in sepsis is not clear, it is likely that it may attenuate the inflammatory response by acting at multiple sites. In animal models of sepsis, exogenously administered ulinastatin has been shown to reduce levels of TNF-α, IL-1, IL-6, cytokine-induced neutrophil chemoattractant-1 (CINC-1), myeloperoxidase, free oxygen radicals, high mobility group box 1 (HMGB1), interleukin (IL)-6, interleukin-8 (IL-8), malondialdehyde and soluble intercellular adhesion molecule-1 (sICAM-1) in serum and in organs like lung, kidney and intestine of rats with lipopolysaccharide induced SIRS [9, 12, 18, 20]. Ulinastatin also decreases phosphorylation of p38 mitogen activated protein kinase (p38-MAPK) which in turn attenuates activation of NF-κB and down regulates expression of the TNF-α gene. Studies in humans too have shown that patients with sepsis treated with intravenous administration of ulinastatin have lower serum

levels of pro-inflammatory markers like TNF-α, IL-1β, IL-4, IL-6 and C-reactive protein, while levels of anti-inflammatory cytokine IL-10 was significantly higher [14, 17, 21, 23]. It also reduces thrombomodulin levels and decreases endothelial dysfunction [24].

Besides reduction in 28-day all-cause mortality, ulinastatin also showed beneficial effects on some secondary end-points in the present study like new-onset organ dysfunction. Although the duration of vasopressor use was similar in the two groups, ventilator-free days were significantly higher in the ulinastatin group (19.4 vs. 10.2 days), suggesting faster recovery from severe sepsis. This also translated into a shorter mean hospital stay in the ulinastatin group. No infusion-related adverse effects were seen in the present study. Adverse effects with ulinastatin are rare and were reported in 0.84 % of patients in a Japanese study [25]. These included increased transaminases (0.36 %), eosinophilia or leucopenia (0.16 %), rash (0.13 %), gastrointestinal symptoms (0.08 %), fever (0.02 %), and local irritation at the injection site (0.02 %). These were reported in less ill patients with pancreatitis or when the drug was used prophylactically in patients undergoing endoscopic retrograde pancreatography, for which the drug is licensed in Japan.

4. Conclusion

Pericardial abscess is a rare adverse condition of Staphylococcus aureus bacteremia and presented life threatening condition. In that particular situation with refractory of multiple broad spectrum antibiotics, ulinastatin have good role in control of sepsis and recovery of multiorgan failure status. Studies suggest that ulinastatin have key role in patients with severe sepsis investigated a novel therapy directed against the systemic inflammatory response. We found that 5-day treatment with intravenous administration of ulinastatin in patients with severe sepsis, when started within 48 h of organ dysfunction, resulted in a reduction in 28-day all-cause mortality. We also found a reduction in new onset of organ dysfunction, days of mechanical ventilation and hospital stay.

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6. References

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