

# Tricuspid Valve Infective Endocarditis and Septic Emboli in Drug Addicts: Case Report

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### ABSTRACT

We herein present a case of a 33-year-old woman with Intravenous Drug Use (IVDU) presenting with multiple septic emboli as a result of acute Infective Endocarditis (IE) with large vegetations involving the Tricuspid Valve (TV) cusps. Such presentation may cause severe complications that may be life-threatening. The present case stands out for reinforcing the high virulence of IE pathogens, demonstrated by the systemic embolism and severe valve deterioration. It also emphasizes the importance of a coordinated multidisciplinary management between different specialties from cardiology, infectious disease, and cardiothoracic surgery to address all these challenges related to IE in this group of IVDU. Current recommendations endorse combined therapy of intensive antibiotic regimen, surgical or novel percutaneous intervention when certain criteria is satisfied in complicated cases of infective endocarditis.

Keywords: Intravenous Drug Use; Infective Endocarditis; Tricuspid Valve

#### **INTRODUCTION**

In most cases of intravenous drug user (IVDU) with Infective Endocarditis (IE), Tricuspid Valve (TV) is involved in 90% of cases.<sup>[1]</sup> Poor hygiene, unsafe injection practice and adjuvant particular matters used (talc) may cause cumulative subclinical repetitive damage of right-side heart's valves. Furthermore, septic emboli are another common sequela with septic pulmonary emboli occurring in up to 75% of patients with TV IE.<sup>[2]</sup> Diagnosis of IE can be made on Transthoracic echocardiography (TTE) standard views or modified views, which provide invaluable information about right sided structure (right ventricular inflow, outflow, and TV leaflets). However, other imaging modalities such as Cardiac CT can evaluate the presence of abscess, pseudoaneurysm, and perivalvular extensions of IE affecting the valves. Intravenous antibiotics are the mainstay of management for right-sided IE affecting the TV.<sup>[3]</sup> However, if operative risk assessment is reasonable, then



surgical intervention with vegetation removal, radical debridement of vegetations, and infected tissue and valve repair may be warranted in several circumstances including: bacteremia persisting more than 7 days despite antimicrobial therapy; large persisting TV vegetations (>20mm); right heart failure secondary to severe TV regurgitation; recurrent pulmonary septic emboli with or without right sided heart failure; and right heart failure due to severe TV regurgitations not responding to diuretic therapy.<sup>[4]</sup> In patients with high operative risk, novel approaches with minimal invasive percutaneous aspiration system to debulk TV vegetations has emerged to facilitate reducing the bacterial load (through debulking) and hence allowing for antimicrobial therapeutic effect to be achieved or may act as a bridge to valve surgery.<sup>[5]</sup> We herein present a case of a 33-year-old woman with IVDU presenting with multiple pulmonary infiltrates likely septic emboli because of acute IE of the TV cusps with large mobile vegetations. Such presentation may cause severe complications that may be life-threatening.

## **CASE REPORT**

A 33-year-old female with a past medical history of polysubstance intravenous drug abuse (chronic history of heroin abuse since the age of 19-year and crystal meth usage 1 week ago), and history of COVID 19 pneumonia presented to the Emergency Department (ED) with lethargy, and fever. The patients were found to be responding to only pain stimuli/ sternal rub and complete history was obtained from the next of kin. Vitals in the ED was sinus tachycardia (111 bpm), Temperature (39°C), respiratory rate 33/min and blood pressure (100/59 mm Hg), all indicating a Systemic Inflammatory Response Syndrome (SIRS). On physical examination, the patient was obtunded, and difficult to arouse. On chest and heart examination revealed bibasilar rales and 2/6 systolic murmur was heard best at the left lower sternal border on auscultation were noted. Right sided third heart sound was audible, and bilateral lower limb edema +2 and raised JVD was noted. Chest X-ray (Figure 1) showed bilateral hazy patchy opacities with a suspecting diagnosis of a community acquired pneumonia. ECG (Figure 2) demonstrated a prolonged PR interval with no ST and T wave changes. Brain CT without contrast showed no CT evidence of acute intracranial hemorrhage, midline shift, or mass effect. Labs on admission showed: WBC 20.8 (77.5% Neutrophils) (reference 4-11 103/uL); RBC 2.06 (reference 3.8-5.20 106/uL); Hgb 5.8 g/dL (references 12-15 g/dL); hematocrit 16.3% (reference 35-45%); MCV 79 (reference 80-100L); RDW 15.2%; Reticulocyte 3.16% (reference 0.3-2%). Blood gas analysis showed pH: 7.52, pO2: 57mmHg, pCO2: 24 mmHg, HCO3: 19.4 and saturation: 92.9%. Complete metabolic panel included Na 123, (reference 135-147 mmol/L0; Chloride 91 (reference 98-107 mmol/L); Potassium 4.6 (reference 3.5-5.1 mmol/L); calcium 6.8 mg/dL(reference 8.4 -10.2 mg/Dl); anion gap 12.4 mmol/L (reference 4-13 mmol/L); phosphorus 5.6 mg/dL (reference 2.8 to 4.5 mg/dL); serum osmolarity 297.9 mOsm/kg (reference: 285-305 mOsm/kg); creatinine 2.95 (reference 0.52-1.04 mg/dL); BUN 102 (reference 7-17 mg/dL); Glomerular Filtration Rate (GFR) 18 ml/min/1.732, liver function was unremarkable except for low albumin levels (Albumin 1.8 g/dL, reference 3.5-5.0 g/dL); Total bilirubin 1.4 mg/dL (reference 0.2-1.3 mg/dL), Direct bilirubin 0.7 mg/dL (reference 0.0-0.3 mg/dL); LDH 441 U/L (reference 135-225 U/L); lactic acid 1.40 mmol/L (reference 0.3-1.3mmol/L); and BNP 608 pg/ml (reference 0-98 pg/ml). COVID-19 test was negative. Serological results for HIV were negative while positive for HCV infection. Blood smear shows what appears to be Howell-Jolly bodies. Coagulation profile included PT 12 (reference 9.4-11.6 seconds); INR 1.17 (reference 0.8-1.2); and aPTT 30.2 sec (reference 23-35 seconds). Hyperfibrinogenemia was noted to be secondary to severe sepsis. Iron studies



included: % SAT 26.9 (reference 11 - 46 %); Iron levels 36 ug/dL (reference: 49 - 181 ug/dL); Total Iron Binding Capacity (TIBC) 136 ug/dL, (reference 261 - 462 ug/dL); and Transferrin 107 mg/dL (reference: 206 -381 mg/dL). Inflammatory markers, ferritin was 1628 ng/ml (reference 6.24-37 ng/ml). Baseline troponin was unremarkable. A full urinary toxicology screen was positive for Amphetamine, and negative for the remainder of substances including Barbiturates, Benzodiazepines, Cocaine, Opiates, Methadone, Phencyclidine, Tetrahydrocannabinol (THC). Serology for ANAs, dsDNA, c-ANCA, p-ANCA were negative and Hgb Electrophoresis to rule out sickle cell trait or disease was also unremarkable. The patient was admitted to the intensive care unit and sepsis protocol was activated. Because of fever, all the routine cultures, including blood, urine, and sputum, were obtained prior to starting empiric intravenous antibiotics including Vancomycin 1 gm every 24 hours and Piperacillin/tazobactam 3.375gm every 8 hours. Patient received 2 L of NS and 2 Units of Packed Red Blood Cells (PRBCs). Patient was closely monitored to maintain mean arterial pressure > 65mmHg for adequate cerebral perfusion. Hemoglobin improved post transfusion to 7.3 g/dL and the low platelets was attributed to ongoing hemolysis given the high LDH and low indirect bilirubin and low haptoglobin <10. Given the extensive intravenous drug use history, the patient underwent Two-dimensional echocardiography (Figure 3) which was significant for the findings of thickened TV leaflets with an attached large mobile mass (Size 3.62 x 1.6 cm Vegetations) along with severe TV regurgitations. Right ventricular systolic pressure was estimated from tricuspid valve regurgitation to be 53 mmHg. Right atrial dilation was reported. The left and right ventricles were of normal size, wall thickness, and function and no demonstrated segmental wall motion abnormalities. Left ventricular ejection fraction was 60%. No other valves abnormalities were noted or any vegetations involving left side heart valves. Urine cultures were negative. However, Blood cultures times 2 prior to empiric antibiotics showed gram positive cocci in clusters with culture sensitivity showing a minimum inhibitory concentrations' µg/mL sensitive for Oxacillin. Hence Vancomycin was change to intravenous Oxacillin 1gm every 12 hours. Patient met the Dukes Criteria for definite IE. The patient in hospital course remained borderline (with BP 100/68 and HR 120), she remained oliguric, and her renal function continued to worsen (creat 3.22 and BUN 112, Fe NA <0.2 (i.e., prerenal injury), and Phosphorus 7.8 mg/dL). Kidney ultrasound was unremarkable showing preserved cortical thickness bilaterally, within normal echogenicity, no perinephric fluid collection, and no evidence of suspicious renal mass, hydronephrosis or large obstructing renal stones. Abdominal ultrasound showed an enlarged spleen measuring up to 14.5 cm with There is an isoechoic rounded lesion adjacent to the splenic hilum measuring up to 2.8 cm most likely accessory spleen. Hemodialysis sessions were initiated, and phosphate binder (Sevelamer) was added at a dose of 800mg three times daily. Despite the Intensive Intravenous (IV) antibiotic therapy, and ongoing hemodialysis sessions, the systemic sepsis remained unrelenting, and patient was in distress (Acute Hypoxic Respiratory Failure) and a follow up Chest X ray showed (Figure 4) bilateral hazy and consolidative patchy opacities, right greater than left, with moderate right and trace to small left-sided pleural effusions. As the patient is with acute kidney injury, lung perfusion scan was performed showing (Figure 5) heterogenous activity bilaterally throughout the lungs with multifocal mismatched segmental perfusion defects (i.e., high probability for multifocal bilateral pulmonary emboli). Chest CT scan (Figure 6) was performed without intravenous contrast (given the Acute kidney injury) and demonstrated enlarged pulmonary trunk with a pulmonary embolus visualized in the left posterior basal artery. Additionally, bilateral consolidations, right greater than left, with mild to moderate pleural effusion on right and multiple peripheral pulmonary nodules, cavities, and wedge-shaped consolidations were noted. A



Feeding vessel sign (a distinct vessel leading directly into the center of a nodule) indicative of septic pulmonary emboli was also demonstrated on Chest CT. Thoracocentesis of 732 ml serosanguinous colored fluid was removed without difficulties to improve the patient breathing. Due to native right sided septic emboli, treatment focused on antimicrobial rather than therapeutic anticoagulation as it increases the risk of bleeding including intracranial bleeding and does not treat septic emboli. Beside the antibiotics and scheduled hemodialysis sessions, the patient was maintained on the following regimen: oxygen supplementation for a goal of SPO2 >92%, proton pump inhibitors pantoprazole 40 mg intravenously daily , Heparin 5000 Units/ml subcutaneously twice daily was initiated for DVT prophylaxis, albumin human 25% 12.5 gm intravenously every 12 hours, Furosemide 40 mg intravenously twice daily, metoprolol tartrate 100 mg orally twice daily, epoetin alfa 4000 units/ml subcutaneously scheduled 3 days per week for the persistent anemia in setting of acute renal failure, and Lorazepam 2 mg intravenously per need for withdrawal symptoms. Addiction medicine evaluation and aspiration precautions were also put in place. Repeat echocardiogram within one week of hospital stay (Figure 7), showed a normal Left ventricular size and wall thickness. Mildly hypokinetic mid anteroseptal segment and LVEF of 50%. No left ventricle thrombus noted on this study. The right ventricle had normal systolic function and showed mild to moderately dilation. Large sized TV mobile vegetation on follow up echo measured 2.5 x 1.9 cm. The IVC was dilated and collapses <50% with inspiration, indicating right sided volume overload. No other intracardiac masses noted in any heart chamber. Left heart valves were not involved with vegetations. Patient remained afebrile, with hemodynamics including BP 125/86 mmHg, HR 85 beats/minutes, temp 97.7 F, RR 20/minutes, and O2 saturation 92% on 2.5 L of oxygen via nasal canula. A synopsis of the blood work during hospital stay is shown in (Figure 8). Because the CT images were not able to exclude a fungal pneumonia, the antifungal agent Micafungin 100 mg IV q24h was added. Given the clinical condition of the patient as a poor surgical candidate with multiple pulmonary emboli with right ventricle dilation and right heart strain, persistent positive blood cultures and bacteremia more than 7 days in the setting of TV IE, persistence of bibasilar crackles and 2+ bilateral lower limb pitting edema and no resolution of tricuspid valve vegetations, the patient was evaluated by cardiothoracic surgery for possible utilization of AngioVac drainage cannula (Angiodynamics, USA). The plan was discussed at length with the patient and family and consultants and the patient's family was made aware of the patient's condition.



Figure 1: Initial chest X-ray with bilateral infiltrates initial diagnosis of community-acquired pneumonia was made.



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Figure 2: EKG showing prolongation of PR interval (537ms).





**Figure 3:** Transthoracic echocardiography showing: Large tricuspid valve vegetation (yellow arrow) sized 3.62 x 1.6 cm in the A) 4 chamber view, and also seen in the B) substernal view. C) Color doppler shows severe tricuspid valve regurgitations.





**Figure 4:** Followup chest X-ray showing progressive worsening with bilateral hazy and consolidative patchy opacities, right greater than left, with moderate right and trace to small left-sided pleural effusions, noted.



**Figure 5:** Lung perfusion scan was performed showing heterogenous activity bilaterally throughout the lungs with multifocal mismatched segmental perfusion defects (i.e., High probability for multifocal bilateral pulmonary emboli).



**Figure 6:** CT chest demonstrating enlarged pulmonary trunk with a pulmonary embolus visualized in the left posterior basal artery, multiple peripheral pulmonary nodules, cavities, and wedge-shaped consolidations and a feeding vessel sign or "a fruit on the branch sign "(a distinct vessel leading directly to a nodule or mass) indicative of septic pulmonary emboli was also demonstrated (blue arrow). Bilateral consolidations, right greater than left, with mild to moderate pleural effusion on right.





**Figure 7** (Movie File 1 and 2): Follow up Transthoracic echocardiography showing : Large tricuspid valve vegetation (yellow arrow) sized 2.5 x 1.9 cm in the A) 4 chamber view, and also seen in the B) Color doppler shows severe tricuspid valve regurgitations and C).



**Figure 8:** Representation of labs during hospital course (days in hospital displayed). A) Complete Blood count highlighting WBC, Platelets, Hemoglobin and Hematocrit, B) Kidney function highlighting serum creatinine, Blood Urea Nitrogen, and Glomerular filtration rate.

#### DISCUSSION

We herein present a case of a 33-year-old woman with Intravenous Drug Use (IVDU) presenting with a lifethreatening complication of acute Infective Endocarditis (IE) involving the TV cusps and multiple septic emboli. Right sided IE can present with persistent fever, positive blood culture and bacteremia, multiple septic emboli indifferent organs, and right heart failure from increased pulmonary pressure, severe tricuspid valve regurgitation, or obstruction of pulmonary circulation through multiple pulmonary emboli.<sup>[6]</sup> Our patient presented with majority of presentation listed above including multiple septic pulmonary emboli seen in the CT images, possible pulmonary infarctions, pleural effusion, and right sided heart failure due to involvement of TV with large (3.62 x 1.6 cm ) mobile vegetation surrounding all three valve leaflets and also prolapsing in the right atrium, causing a severe tricuspid valve regurgitation. While Transesophageal Echocardiography (TEE)<sup>[7]</sup> is more sensitive to detect vegetations than Transthoracic Echocardiography (TTE), in our case the TV vegetation was proven to be best detected by TTE examination technique. Microorganisms implicated in the IVDA right sided IE is usually Methicillin Resistant Staphylococcus Aureus (MRSA), pseudomonas aeruginosa, and other gram-negative organisms, fungi, streptococci, and enterococci.<sup>[8]</sup> A US population-based data analysis showed a continuing uptrend with a twelve-fold increase in IVDU IE hospitalizations.<sup>[9]</sup> While uncomplicated tricuspid



valve IE can be medically treated successfully in majority of IVDU, those with bacteremia persisting more than 7 days despite antimicrobial therapy; large persisting TV vegetations (>20mm); right heart failure secondary to severe TV regurgitation; recurrent pulmonary septic emboli with or without right sided heart failure; and right heart failure due to severe TV regurgitations not responding to diuretic therapy expectably will have poor antibiotic penetrations as we presented in this case, and hence intervention (surgical or percutaneous ) would be the optimal management option.<sup>[4,6]</sup> A therapeutic challenge remains in IE cases where surgical risk is high, and in that regard, patients with high operative risk, novel approaches with minimal invasive percutaneous aspiration system to debulk tricuspid valve vegetations has emerged to facilitate reducing the bacterial load (through debulking) and hence allowing for antimicrobial therapeutic effect to be achieved. Percutaneous aspiration techniques of tricuspid valve vegetations with AngioVac (AngioDynamics, USA) have shown successful procedural outcomes and low complication rates. In a single center experience study<sup>[10]</sup> by George et al 2017, evaluating 33 patients (of whom 73% were IVDU) with large tricuspid valve vegetations (mean size of  $2.1 \pm 0.7$  cm) and high operative surgical risk due to multiple co-morbidities, who underwent a bail out percutaneous tricuspid valve vegetation removal and showing 61% reduction of the vegetation size post procedure, clearing bacteremia, stabilizing the patients with high hospital survival index of 90.9%.

In summary, our case illustrated a case of complicated right sided IE in IVDU and highlighted management challenges and bail out options in IVDU patients with multiple comorbidities. It also emphasizes the importance of a coordinated multidisciplinary<sup>[11]</sup> management between different specialties from cardiology, infectious disease, and cardiothoracic surgery to address all these challenges related to IE in this group of IVDU.

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