Journal of Bangladesh College of Physicians and Surgeons
Vol. 43, No. 1, January 2025

Polyarteritis Nodosa with Tubercular Pericardial Effusion: A Rare Coexistence of Childhood Vasculitis and Infectious Disease

T FERDOSH[a], MM ISLAM[b], MK TALUKDER[c], MI ISLAM[d]

Abstract:

Polyarteritis nodosa (PAN) is a systemic vasculitis that affects medium-sized arteries, resulting in inflammation and damage to multiple organs. PAN may develop following bacterial or viral infections representing a post-infectious autoimmune response. Tuberculosis (TB) can affect any organ of the body and it is one of the most important causes of pericardial effusion in developing countries. This case report presents a young girl with a rare co-occurrence of PAN and tubercular pericardial effusion having a history of fever, polyarthritis, weight loss, digital gangrene, and respiratory distress. On examination, the patient had signs of heart failure, pericardial effusion, and diminished peripheral pulsation in both anterior and posterior tibial arteries and arteria dorsalis pedis. The patient improved dramatically after receiving combined immunosuppressive and anti-tubercular therapy. This case was a unique coexisting situation where the patient presented with unusual presentations and also demonstrated the complex interplay between autoimmune and infectious diseases which needs a comprehensive diagnostic and treatment approach.

Key words: Polyarteritis nodosa, Tuberculosis, Tubercular pericardial effusion, Adenosine deaminase assay, Anti-tubercular therapy

(J Bangladesh Coll Phys Surg 2025; 43: 85-88)
DOI: https://doi.org/10.3329/jbcps.v43i1.78784

Introduction:

Polyarteritis nodosa (PAN) is a necrotizing inflammation of medium or small-sized arteries which affects almost any organ/organ system, though pulmonary involvement is uncommon.[1] The clinical features for the systemic PAN at presentation are as follows: fever (87%), myalgia (83%), skin (88%), renal (19%), severe gastrointestinal (GI) (10%), and neurological involvement (10%).[2] Involvement of the gastrointestinal tract, kidneys, heart, and central nervous system is associated with higher mortality.[1] Cardiac involvement in PAN includes myocarditis and coronary arteritis, that subsequently leads to heart failure and myocardial ischemia. Pericarditis and arrhythmias have also been reported.[3] PAN can be idiopathic, or it can be associated with an infectious etiology such as hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), parvovirus B19, cytomegalovirus, Epstein-Barr virus, streptococcal infections, etc.[4] PAN has also been reported in association with tuberculosis (TB).[5] TB is a common cause of pericardial effusion.[6] This report presents a case where a rare co-occurrence of PAN and tubercular pericardial effusion was observed. The simultaneous presence of immune-mediated and infectious diseases in a single patient needs meticulous laboratory workup and effective treatment to reduce mortality and morbidity.

Case report:

S, a 12-year-old immunized girl presented with history of high-grade intermittent fever associated with generalized bodyaches and polyarthritis affecting the large joints of both upper and lower limbs for one month. She also had progressive blackening of the left little fingertip and severe pain for 20 days. On query, the mother gave a history of anorexia and 6 kg weight loss in the last month. There was no history of photosensitivity, oral ulceration, Raynaud's phenomenon, cough, chest pain, abdominal pain, neurological or bowel-bladder involvement, and contact with a known TB patient. She was initially treated at a nearby government medical college hospital for this illness, with inj. methylprednisolone, injectable antibiotics along with other supportive management. But while getting treatment, she developed respiratory distress and

a. Dr. Taslima Ferdosh, Resident (Phase B), BSMMU, Department of Paediatrics, BSMMU, Shahbag, Dhaka, Bangladesh
b. Dr. Mohammed Mahbubul Islam, Associated Professor of Paediatric Rheumatology, Department of Paediatrics, BSMMU, Dhaka, Bangladesh
c. Professor Manik Kumar Talukder, Professor of Paediatric Rheumatology, Department of Paediatrics, BSMMU, Dhaka, Bangladesh
d. Professor Mohammad Imnul Islam, Professor, Department of Paediatrics, BSMMU, Dhaka, Bangladesh

Address of Correspondence: Dr. Taslima Ferdosh, Resident (Phase B), BSMMU, Department of Paediatrics, BSMMU, Shahbag, Dhaka, Bangladesh. Mobile: 01676509706, E-mail: taslima1992mir@gmail.com

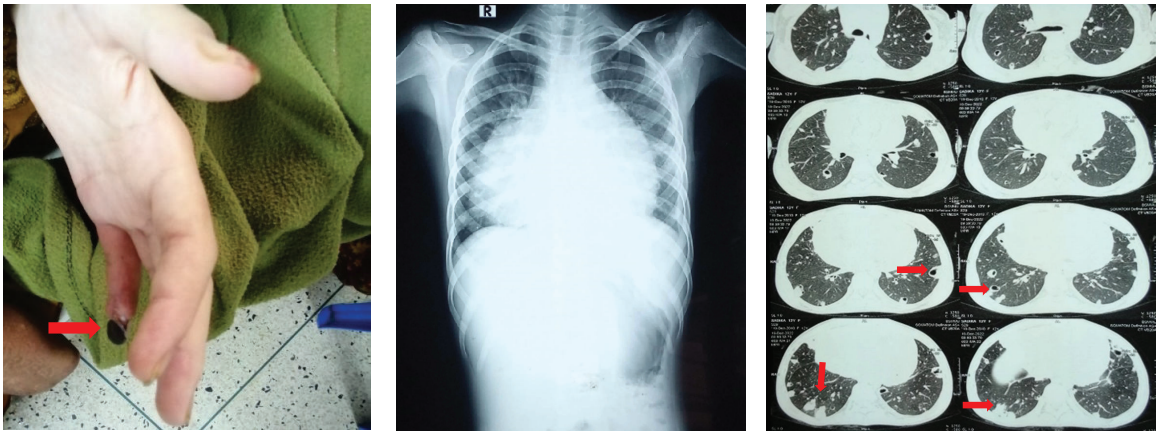
Received: 14 Sept., 2024 **Accepted:** 18 Dec., 2024

was referred to our hospital. On examination, S was dyspnoeic, moderately pale, and had normal temperature with tachycardia (136 beats/min), tachypnoea (36/min), and blood pressure was 90/60 mmHg, bedside urine for albumin was nil and BCG mark was present. Her JVP was raised, the tip of left little finger was found gangrenous (Fig-1), and all peripheral pulses were present but diminished in both (anterior and posterior) tibial arteries and arteria dorsalis pedis. She was moderately underweight (-2.6 SD) and signs of arthritis were present in both knees, ankles, and left shoulder joints. Her apex beat was impalpable, heart sounds were muffled and she had vesicular breath sound with crackles at the bases. She also had tender hepatomegaly and ascites. Considering PAN with heart failure due to cardiac tamponade as the most probable diagnosis, we urgently did chest x-ray and echocardiography along with other investigations and arrange for pericardiocentesis.

Her laboratory investigations showed low hemoglobin (8.6 gm/dl) with raised ESR (85 mm in 1st hour), raised CRP (48 mg/L) with neutrophilic leukocytosis and thrombocytosis. She had gene x-pert for TB from both sputum and stool that were not detected, Mantoux test (MT) was 0 mm, and LDH was high (467 U/L). Her anti-nuclear antibodies (ANA-IF method), anti-ds DNA and anti-neutrophil cytoplasmic antibodies (ANCA) were undetectable and compliments (C_3, C_4) were within normal limits. Chest x-ray showed globular enlargement of cardiac shadow (Fig.- 1b), and massive pericardial effusion was observed in the echocardiographic analysis (Vivid S70N echo device, General Electric Medical System Company, Milwaukee, WI, USA). Multiple nodular lesions with and without cavitation were found all over the lung field along with pericardial effusion was found in contrast enhanced -computerized tomography (CECT) of the chest (Fig-1c). By duplex ultrasound study of upper and lower limbs revealed features of vasculitis (arterial wall thickening, luminal narrowing with irregularities) and severe reduction of blood flow in posterior tibial, anterior tibial, and dorsalis pedis arteries of both lower limbs and digital arteries of left small finger, moderate reduction of blood flow in left ulnar artery. The pericardial fluid study showed chocolate color, hazy fluid with leucocyte count - 7,400/cmm with neutrophil predominant, raised protein (3.9g/dl), low sugar (49 mg/dl), high (183.39U/L) adenosine deaminase (ADA). In addition, both the gram stain and acid-fast stain were negative. No growth was found in the culture sensitivity, and cytospin did not show malignant cells in the pericardial fluid.

Due to our patient had received immunosuppressive drugs (such as IV methylprednisolone, followed by oral prednisolone and mycophenolate mofetil), we decided not to perform an interferon-gamma release assay (IGRA). Additionally, the patient did not show any improvement after treatment with antibiotics, immunosuppressive therapy, and repeated paracentesis. Therefore, we initiated a therapeutic trial with anti-tubercular drugs, taking into account the high protein and ADA levels found in the analysis of the pericardial fluid.

Significant improvement was observed after administering anti-tubercular therapy (ATT). So finally we diagnosed this girl with TB pericardial effusion with PAN. She was treated with immunosuppressive therapy (methylprednisolone and mycophenolate mofetil) for PAN and ATT for pericardial effusion. She was on regular follow-up and gaining weight, and her constitutional symptoms had improved suggesting a good clinical response.



(a) (b) (c)

Figure 1: *(a) Blackening of the tip of left little finger (arrow), (b)- CXR P/A view- globular enlargement of cardiac shadow, (c)- CECT of the chest- multiple nodular lesions with and without cavitation (arrow) present in all over lung fields along with pericardial effusion.*

Discussion:

PAN is a systemic necrotizing vasculitis that affects medium-sized arteries, causing inflammation, ischemia and necrosis of the affected organ.[1] In our patient gangrenous change was found in the left little fingertip, accompanied by diminished peripheral pulsation; which is similar to the findings of a 4-year-old girl who presented with fever, polyarthralgia, palpable nodules in legs, and progressive ischemia of the second to fifth right fingers and the second right toe along with diminished peripheral pulsation.[7]

Cardiac involvement in polyarteritis nodosa is uncommon. Documentation of large pediatric series of polyarteritis nodosa is limited. Eleftheriou et al conducted a study in Great Ormond Street for Children NHS Foundation Trust in London, found only 3 children with cardiac involvement among 69 PAN patients.[2] Cardiac manifestations in polyarteritis nodosa include pericarditis, myocardial infarction, coronary arteritis, arrhythmia, systolic dysfunction, electrocardiographic (ECG) abnormalities, congestive heart failure and valvular regurgitation.[3] Pericardial effusion is a rare cardiac involvement of PAN, only few case report was found regarding such coexistence.[8–12] In a Colombian case report, they mentioned an 8-year-old schoolboy having hemodynamic compromise secondary to pericardial effusion and severe systolic dysfunction. Later, cardiac catheterization revealed multiple aneurysmal dilatations of coronary, mesenteric, and renal arteries, diagnosed as polyarteritis nodosa, and successfully treated with corticosteroids and cyclophosphamide therapy along with pericardiocentesis.[12] Hu et al reported another case of a 74-year-old white woman with diffuse myalgias, low-grade fever, and pericardial effusion, and the diagnosis was confirmed at autopsy in a pericardiectomy specimen.[9]

Though pericarditis and pericardial effusion can occur in PAN, TB is the most common etiology of pericardial effusion in our subcontinent.[6] It is often difficult to establish a definite diagnosis in tuberculosis in this clinical findings and laboratory workup. Moreover, literature showed that IGRA may be false negative after getting immunosuppressive therapy.[13] Belard et al also found that oral prednisolone (dose e" 10 mg) severely suppressed QuantiFERON Gold test performance in their study.[14] The measurement of ADA activity is a useful diagnostic tool for identifying tubercular pericardial effusion (TB-PE), with a commonly accepted cut-off level of 40 U/L.[15] Moreover, there is no evidence of elevated ADA in case of pericardial effusion due to PAN. It is possible that the patient had PAN, which led to the development of pericarditis and subsequently a tubercular infection. Alternatively, the patient could have had tubercular pericardial effusion, which led to the development of PAN due to a post-infectious autoimmune response.[5,16]

The association of PAN and TB-PE is rare and the symptoms of both conditions can overlap, and the presence of one may mask the symptoms of the other. Only few cases reported previously showing an association of polyarteritis nodosa with tuberculosis in adults but no such case reports were found in children.[5,15,17] A Korean case report described a 46-year-old man who, while getting the anti-tubercular drug for pulmonary tuberculosis developed visual disturbance, peripheral neuropathy, and sudden abdominal pain, later his investigations confirmed the diagnosis of polyarteritis nodosa by sural nerve biopsy and renal arteriography.[5]

Treatment for PAN usually involves immunosuppressive therapy, such as corticosteroids or other immunomodulatory agents.[1] For TB-PE, treatment involves using anti-tuberculosis drugs in combination with steroids and supportive measures like pericardiocentesis.[18] In this particular case, the patient received both immunosuppressive therapies like methylprednisolone and mycophenolate mofetil for PAN, and anti-tuberculosis drugs for TB-PE. The use of steroids given for PAN can also help prevent constrictive pericarditis that may occur following TB-PE.[18] With this treatment, the patient's symptoms gradually improved.

In conclusion, the coexistence of PAN and TB-PE is a rare and challenging condition to diagnose and treat as well. Early detection and prompt treatment are essential to prevent complications and improve outcomes. Clinicians should remain vigilant for such presentations of both conditions and be prepared to consider a broad range of treatment options to achieve optimal outcomes. A multidisciplinary team approach involving rheumatologists, infectious disease specialists, and cardiologists may be necessary to provide comprehensive care for these patients.

Conflict-of-interest: None

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