A 37-year-old man presented with abdominal distention and shortness of breathing

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Presentation of Case

Dr. Samia Rahman (MD Resident): A 37-year-old man hailing from Comilla, Bangladesh (about 100 km from the capital, Dhaka, Bangladesh) got admitted himself into our department on 18th February 2020 with the complaints of abdominal distention for 9 months and shortness of breathing for 7 months. The abdominal distension was sudden in onset, progressive in nature, but there was no history of jaundice, oliguria, any heart disease, or abdominal pain. About 7 months ago, the patient experienced shortness of breathing, which was sudden in onset, gradually progressive, and occurring in mild exertion. It was so severe that the patient was unable to perform his day to day activities. The shortness of breathing was associated with a dry cough, but there was no history of chest pain or hemoptysis. The patient complaint's low-grade irregular fever, which was not recorded, persisted throughout the total course of illness, subsided spontaneously after taking paracetamol. There was no history of joint pain, oral ulcer, photosensitivity, previous history of tuberculosis, or close contact with any tuberculosis patient. There was no history of anorexia, weight loss was not documented due to repeated accumulation of fluid. There was a history of cold intolerance and alopecia. The patient's bowel habit was altered in the form of constipation. With these complaints, he was admitted to the hospital for repeated times and fluid was found both within the pleural and peritoneal cavity. The fluid was aspirated for diagnostic and therapeutic purposes. He was put on antitubercular drugs with steroid in September based on pericardial effusion with fibrin thread. The patient took these medications without significant improvement. He was diagnosed as a case of chronic inflammatory demyelinating polyneuropathy based on of the weakness of both legs 4 years ago and took steroid on an irregular basis. He was a patient of hypothyroidism for 1.5 years and was taking thyroxine.

On general examination, he was afebrile, mildly anemic, not icteric, respiratory rate 20 breaths/min, pulse rate 80 beats/min, blood pressure 110/70 mmHg, temperature 100°F, bilateral foot drop and bilateral pedal edema present, no lymphadenopathy, and no thyromegaly. On examination of the respiratory system, features consisted of right-sided pleural effusion. On examination of the cardiovascular system,
The ascites was present by shifting dullness. The neurological examination showed bilateral foot drop, flaccid type of paralysis involving both the lower limbs, muscle power 4/5. All deep tendon jerks were absent. All modalities of sensation including the sense of vibration and position were intact. The thyroid gland was not enlarged. There was no feature of thyrotoxicosis or hypothyroidism. On laboratory investigation, hemoglobin was 14.9 g/dL, erythrocyte sedimentation rate was 30 mm after 1st hour. C-reactive protein was 22 mg/L (Table I).

The X-Ray chest (done on 16nd February 2020) showed right-sided moderate pleural effusion with adjacent pulmonary inflammation and left-sided consolidation (Figure 1A).

The CT-scan revealed right-sided large pleural effusion with passive collapse consolidation adjoining lung parenchyma and mild pulmonary edema (Figure 2).

The echocardiography showed localized moderate pericardial effusion, dilated right heart, suspected atrial septal defect, moderate tricuspid regurgitation, and severe pulmonary hypertension pulmonary artery systolic pressure (90 mmHg).

The ultrasonography of the whole abdomen revealed bilateral pleural effusion (right-sided huge and left-sided mild), mild pericardial effusion, trace ascites, bilateral increased renal cortical echogenity, and few enlarged lymph nodes in the mesenteric regions. The pleural fluid study revealed exudative and lymphocyte predominant.

From the above history, physical examination, and investigation, I would like to draw a provisional diagnosis.

### Provisional Diagnosis

Disseminated tuberculosis involving pleura, peritoneum, pericardium with primary pulmonary hypertension, hypothyroidism, chronic inflammatory demyelinating polyneuropathy

### Differential Diagnosis

**Dr. Rajashish Chakrabortty (Associate Professor):** As there is polyserositis with fever so it may a case be of lymphoma with primary pulmonary hypertension, hypothyroidism, chronic inflammatory demyelinating polyneuropathy.

**Dr. Shamim Ahmed (Associate Professor):** As there is polyserositis with pulmonary hypertension it may be a case of systemic lupus erythematosus with pulmonary hypertension, hypothyroidism, and chronic inflammatory demyelinating polyneuropathy.

**Dr. Rawnak Jahan (MD Resident):** The patient presented with the history of polyserositis, alopecia, cold intolerance, and constipation. It is rare but

| Investigation        | Findings  | Reference |
|----------------------|-----------|-----------|
| Hemoglobin (g/dL)    | 14.9      | 15 ± 2    |
| Erythrocyte          | 30        | 0-10      |
| Complete blood count |           |           |
| WBC count (x10⁹/L)   | 7         | 7 ± 3     |
| Platelet count       | 325       | 150-400   |
| Serum creatinine     | 1.1       | 0.6-1.3   |
| C-reactive protein   | 22.1      | <5        |
| Serum albumin (g/L)  | 32        | 35-50     |
| Total protein (g/L)  | 72        | 64-83     |
| SGPT (U/L)           | 10        | <50 (male)|
| SCOT (U/L)           | 41        | <50 (male)|

**Plural fluid**

- Appearance: Yellow
- Total RBC count (/mm³): 850
- Total WBC count (/mm³): 500
- Neutrophil (%): 5
- Lymphocyte (%): 85
- AFB staining: Not detected
- Gram staining: Bacteria not found
- Adenosine deaminase (U/L): 9.3
- Glucose (mg/dL): 108.9
- Protein (g/dL): 4.0
- Malignant cells: None
- Plasma BNP (pg/mL): 39
- TSH (mIU/L): 9.3
- Anti-TPO (IU/mL): 7.2
- Anti-thyroglobulin (IU/mL): 10.4
- HbsAg: Negative
- Anti-HCV: Negative
- HIV: Negative
- ANA: Positive
- Anti-ds-DNA: Positive
- C3 (g/L): 1.3
- C4 (g/L): 0.24 g/L
- Anti-cardiolipin Ab IgG: Negative
- Anti-cardiolipin Ab IgM: Negative
- Lupus anticoagulant: Positive
- Anti-B-2 glycoprotein-1 Ab IgG: Positive
- Anti-B-2 glycoprotein-1 Ab IgM: Positive

**ENA Profiles (Nucleosome, Histone, SmD1, RNP, SS-A, SS-B, Sc170, CENP-B, Jo-1, Po60, PNCA, CACA, PM-Sd, Mi-2, Ku, AMA-M2) were negative**
hypothyroidism may be present with polyserositis.

**Disseminated tuberculosis**

*Dr. Rahman:* Polyserositis is defined as the general inflammation of serous membranes associated with simultaneous effusions in various cavities.\(^1\)

Tuberculosis is a chronic infectious disease caused by *Mycobacterium tuberculosis*, mainly affect the lungs but can involve any organ.

Disseminated tuberculosis is defined as having two or more noncontiguous sites resulting from lymphohematogenous dissemination of the *M. tuberculosis*. The extrapulmonary involvement only one-fifth of all tuberculosis cases and there may be no histological and radiological features of the pulmonary infection. So, the diagnosis difficult as clinical manifestations are nonspecific and it can mimic several other disorders.\(^2\)

Pericardial involvement in tuberculosis may present as acute pericarditis, chronic pericardial effusion, cardiac tamponade, or pericardial constriction. It is insidious onset and may present with fever and vague precordial pain, dyspnea, or cardiomegaly on a chest radiograph. The direct extension of infection from adjacent mediastinal lymph nodes or through lymphohematogenous route is the main pathogenesis of pericardial involvement. If acute effusive tuberculosis pericarditis remains untreated, the mortality rate approaches to 85%.\(^2\)

Disseminated tuberculosis may present with tuberculous ascites. The clinical presentation of tuberculous ascites is non-specific and can mimic many other infectious diseases. So, the diagnosis is often delayed. This delay in the diagnosis and treatment of tuberculous ascites are considered as major factors for high mortality in tuberculosis. The pathogenesis of peritoneal tuberculosis is usually secondary to the hematogenous spread of tubercles from a pulmonary focus.\(^3\) The tuberculous peritonitis initiates as a sub-acute disease and its symptoms progress for several weeks to months. The common presentations are abdominal pain and are frequently associated with abdominal distension. The pain usually non-localized and vague, mainly occurs due to the tuberculous inflammation of the peritoneum and mesentery. Less often, it may be present as intermittent sub-acute intestinal obstruction due to matted bowel loops caused by adhesions of the mesentery and omentum.\(^4\)

Among extrapulmonary tuberculosis, tuberculous pleural effusion is the more common cause. It occurs due to *M. tuberculosis* infection of the pleura. That results in intense chronic accumulation of fluid and inflammatory cells within the pleural space. Usually, presentations of the tuberculous pleural effusion are fever, cough, and pleuritic chest pain.\(^5\)

In our case, the points favor to tuberculosis are polyserositis, fever and on echocardiography, fibrin thread was found. The patient is on antitubercular drugs, but no response. So, it may be a case of drug resistant tuberculosis.

**Lymphoma**

*Dr. Chakrabortty:* Serous effusion is one of the rare and uncommon presentations of lymphoma. The involvement of peritoneal and pericardial cavities is rare in the case of lymphoma. Non-Hodgkin's lymphoma and Hodgkin's disease are associated with pleural effusion in 20-30% of cases. Serous fluids are more common in T-cell neoplasms, mainly the lymphoblastic lymphomas. Impaired lymphatic drainage and thoracic duct obstruction are the main etiology for the development of pleural effusion in Hodgkin's disease. In non-Hodgkin's lymphoma, direct pleural infiltration predominantly causes pleural effusion. Immunocytochemistry, morphometry, flow cytometry, and cytogenetics/molecular genetics (PCR, *in situ* hybridization, and Southern blotting) tests are used in the diagnosis of lymphoma. It has been performed on effusion specimens. Serous effusions are uncommon presen-

![Figure 2: CT-scan chest showing right-sided pleural effusion](image-url)
tations of lymphomas without the involvement of thoracic and extrathoracic sites. The primary effusion lymphomas presented with no detectable solid tumor mass but exclusive or dominant involvement of serous cavities. The etiology of primary effusion lymphomas is mainly due to the release of vascular endothelial growth factor/vascular permeability factor that leads to vascular leakage and obstructive or infiltrative tumor mass. The presence of pleural effusion during the presentation is associated with extremely poor prognosis. It may indicate a relapse of the disease after chemotherapy. When there are lymphomatous pleural effusions with and without mediastinal mass associated with respiratory distress, thoracocentesis for the diagnostic and therapeutic purpose is the treatment of choice.

**Systemic Lupus Erythematosus**

*Dr. Ahmed:* Systemic lupus erythematosus is a chronic autoimmune inflammatory connective tissue disease of unknown etiology. It involves multiple systems. Autoimmune diseases predominantly affect women of childbearing age, rarely involve men but they can involve men usually before the age of 50 years and associated acute inflammation. The male-female ratio is 1:9. The symptoms are equivalent to those of both men and women. It only presented with skin rash, extreme fatigue, and joint pain. But the disease in men has a more complex clinical course. In males, renal, central nervous system and vascular diseases are more affected than women. The frequency of pleuritis and/or pericarditis is about 50% during the disease progression.

Throughout the disease course, skin involvement occurs in 80% of cases. The rash is frequently photosensitive, but not always. Acute onset of an erythematous rash located on the cheeks is called a butterfly rash. Other acute skin lesions are erythematous-macular, popular, or maculopapular and bullous lesions, mainly to sun-exposed areas. Symmetrical arthritis involves a small joint of the hands, wrists, and knees.

The active systemic lupus erythematosus may be presented with large volume effusions, but it’s rare. If it occurs, it is mainly associated with complications of chronic lupus disease, such as nephrotic syndrome, constrictive pericarditis, and heart failure. The pathogenesis of serositis is fluid and protein leaks due to increased permeability of the microvascular circulation as a result of inflammation of the pleural and peritoneal microvessels.

In this case, the patient is male and presented with serositis. There is also pulmonary hypertension. So, one of our differential diagnoses is systemic lupus erythematosus, though it is very rare in males.

**Hypothyroidism**

*Dr. Jahan:* Hypothyroidism is rarely presented with ascites, pericardial effusion, or pleural effusion. The incidence of ascites is <4% whereas pericardial effusion is 3 to 6% in recent studies. The pleural effusion is uncommon, may be small, and produces no or minimal clinical sign. The diagnosis is difficult and delayed due to the rarity of this condition. Multiple effusions involving body cavities and tissue edema due to hypothyroidism are extremely rare.

The mechanism of multiple effusions in hypothyroidism is a) it occurs as a part of generalized polyserositis; b) increased plasma proteins leak due to abnormal capillary permeability and the compensatory mechanism that increases lymph flow and protein return rate are failed; c) alteration in albumin metabolism causes exudative polyserositis; d) mucopolysaccharides and protein accumulated in pericardial space; e) hyaluronic acid deposition in the skin which causes edema; and f) ascites and pleural effusion are as a result of a cardiac tamponade that produces right-sided or congestive heart failure. The complete absorption of effusions was done by thyroid replacement therapy.

*Dr. Samia:* To reach the diagnosis and exclude the differential diagnosis, further investigations were done. In lymphoma, there will be lymphadenopathy, organomegaly, high adenosine deaminase level in pleural fluid. But in this case, adenosine deaminase was low. So, lymphoma is excluded. In hypothyroidism, polyserositis is unusual. To cause polyserositis, serum thyroid stimulating hormone level will be significantly high. But in this case, it is only 9 mIU/L. So, hypothyroidism is excluded. As the previous echocardiography revealed localized moderate pericardial effusion, fibrin thread, dilated right heart, suspected atrial septal defect, moderate tricuspid regurgitation and severe pulmonary hypertension (pulmonary artery systolic pressure - 90 mmHg), normal left ventricular systolic function (left ventricular ejection fraction - 65%). For further evaluation, echocardiography was done.

*Dr. Chowdhury Meshkat Ahmed (Professor, Cardiology):* There is no pericardial effusion, fibrin thread, or a feature of constrictive pericarditis. Pulmonary hypertension was present (pulmonary artery systolic pressure- 76 mmHg). To exclude the atrial septal defect, transeosophageal echocardiography was done. It revealed no feature of mark right atrial pressure. The interatrial septum was intact and there was no feature of the atrial septal defect (Figure 3).

At that moment, the pleural fluid study report reveals an exudative, lymphocyte-predominant, and low adenosine deaminase level. So, the diag-
nosis of disseminated tuberculosis is excluded. Then ANA and anti-Ds DNA were done which were positive. Subsequently, lupus anticoagulant, anti-B-2 glycoprotein-1 Ab IgG, anti-B-2 glycoprotein-1 Ab IgM, were done which were also positive. The X-Ray chest (29th February 2020) revealed elevated right hemidiaphragm (Figure 1B). There was no pleural effusion. Both lung fields were clear.

Finally, we got the clue that it is a rare case of male systemic lupus erythematosus, presented with polyserositis, with anti-phospholipid syndrome with shrinking lung syndrome. Then we discharge the patient with hydroxychloroquine, steroid, and vaccination. The patient was advised to follow-up after 1 month.

Dr. Ahmed’s Diagnosis
Systemic lupus erythematosus with anti-phospholipid syndrome with shrinking lung syndrome with pulmonary hypertension

Discussion

Dr. Ahmed: Systemic lupus erythematosus involves multiple systems, nine times more common in women than men. The prevalence of the disease is approximately 130/100,000 in the United States, with African Americans, Hispanics and Asians more frequently affected than non-Hispanic whites.

The common clinical features are fever, erythematous rash, macular, popular, or maculopapular and bullous lesions, mainly to sun-exposed areas, anemia, oral ulcers, polyarthralgia, non-erosive arthritis, symmetrical arthritis that involves small joint of the hands, wrists and knees, polyserositis, thrombocytopenia, renal, neurologic, pulmonary and cardiac abnormalities. The pulmonary manifestations occur in 4-5% of cases, among them half of the patients presented with lung involvement throughout the disease course. It is more common in men than in women. It involves airways, vessels, parenchyma, pleura, and respiratory muscles. Pleuropulmonary involvement may be primary or secondary (as a complication), may be acute or chronic.

The common cardiac manifestation of systemic lupus erythematosus is pericarditis. The pericardial effusion occurs in 40% of cases. But the initial presentation of systemic lupus erythematosus with pericarditis, pericardial effusion, and subsequent heart failure are uncommon. Acute pericarditis presented with precordial or substernal pleuritic chest pain which changed by positional variation (relieved by sitting upright). The patient may present with dyspnea, fever, tachycardia, and decreased or muffled heart sounds. The examination may reveal pericardial rub, but it may be absent. Electrocardiogram classically reveals diffusely elevated ST segments with peaked T-waves. Intramuscular triamcinolone injection or oral methylprednisolone is the treatment of choice in mild pericarditis. Severe pericarditis or pericardial tamponade treated with an intravenous bolus of methylprednisolone (initial dose usually 1 g for three days). Pericardiocentesis is used for cardiac tamponade with or without hemodynamic instability. Intravenous immunoglobulin, methotrexate, azathioprine, and mycophenolate mofetil have been described for recurrent pericarditis secondary to systemic lupus erythematosus.

Anti-phospholipid syndrome is an autoimmune disease characterized by arterial and/or venous thrombosis and/or recurrent pregnancy loss, in the presence of antiphospholipid antibodies (anticardiolipin antibody, lupus anticoagulant). Anti-phospholipid syndrome mainly causes acquired venous thrombosis but both arterial and venous thrombosis may occur. Deep vein thrombosis in lower extremities with or without pulmonary thromboembolism is the most common. Anti-phospholipid syndrome may be primary or secondary. Secondary anti-phospholipid syndrome associated with autoimmune disease, mainly systemic lupus erythematosus.

Shrinking lung syndrome is a rare and uncommon presentation of systemic lupus erythematosus. It may also occur in patients with other connective tissue diseases, like primary Sjögren syndrome, scleroderma, rheumatoid arthritis, and undifferentiated connective tissue disorder. It is presented with progressive dyspnea, usually accompanied by pleuritic chest pain. The chest X-ray reveals elevated unilateral or bilateral hemidiaphragm, lung volume reduction with no parenchymal abnormalities. Pulmonary function tests reveal a restrictive ventilatory defect, Forced vital capacity ranged from 21 to 80% of the predicted capacity.
The classical triad of systemic lupus erythematosus are dyspnea, raised diaphragm, and a restrictive pulmonary defect. The clinical examination reveals no parenchymal lung disease and normal chest X-Ray (other than raised hemidiaphragm and reduced lung volumes). In adults, approximately 28–40% of neuropsychiatric lupus manifestations develop before or around the time of the diagnosis of systemic lupus erythematosus. Estimates of the prevalence of neuropsychiatric lupus have ranged from 14% to over 80% in adults. In which total spectrum of headache (39–61%), seizures (8–18%), cerebrovascular disease (2–8%), psychosis (3–5%), cranial neuropathy (1.5–2.1%), and movement disorder (1%). It affects both the central and the peripheral nervous system. Peripher neuropathy is a known but uncommon manifestation of systemic lupus erythematosus. Chronic inflammatory demyelinating polyneuropathy is the main feature in systemic lupus erythematosus which is rare. It has sub-acute onset, affects mainly motor and affects proximal and distal muscles, reflecting segmental demyelinating.

Based on the criteria of systemic lupus erythematous of European League Against Rheumatism and the American College of Rheumatology, the total were 17 (positive-ANA, anti-DsDNA, fever-2, non-scarring alopecia-2, pleural or pericardial effusion-5, anti-dsDNA-6, lupus anti-coagulant, anti-beta-2-microglobulin-2).

Dr. Abir (MD Resident): How you will differentiate between the lymphoma and systemic lupus erythematosus by fluid study?

Dr. Samia (MD Resident): In both cases, fluid will be exudative, lymphocyte-predominant, but in lymphoma adenosine deaminase will be high. In systemic lupus erythematosus, it will be low.

Dr. Rayhan (MD Resident): What is the treatment of shrinking lung syndrome?

Dr. Samia (MD Resident): Corticosteroid is the treatment of choice. Beta-agonist, theophylline, immuno-suppressive therapy may be given, those are resistant to steroid.

Dr. Asik (MD Resident): What is the prognosis of shrinking lung syndrome?

Dr. Samia (MD Resident): Long-term prognosis is good. The great majority of the patient had significant clinical improvement and mild to moderate improvement on pulmonary function with treatment. The mortality rate is very low.

Dr. Rawnak (MD Resident): What will be the treatment of pulmonary hypertension in this case?

Dr. Samia (MD Resident): As it is a case of primary pulmonary hypertension, we prescribed him ambriasant (5 mg) at night, and tadalafil (10 mg) at morning with diuretics.

Conflict of Interest

Authors declare no conflict of interest

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