**ABSTRACT**

**INTRODUCTION:** Syphilis is caused by spirochete Treponema pallidum. A common mode of transmission is via sexual contact and mainly targeting high-risk populations such as those with Human Immunodeficiency Virus and men who have sex with men (MSM). It has a wide range of presentations based on the four main overlapping clinical stages. Due to the lack of vaccines to prevent syphilis, prompt diagnosis and management of infected persons are warranted to reduce disease burden and its clinical effects.

**CASE PRESENTATION:** We present an unorthodox case of pancytopenia in a 55-year-old male patient who developed chronic progressive weakness, generalized body aches, and intermittent fever. His blood tests revealed pancytopenia and bone marrow biopsy revealed caseous necrosis. Since the patient had a positive history of MSM, syphilis serology was sent, which turned out to be positive. The patient responded to intravenous benzylpenicillin and oral doxycycline.

**CONCLUSION:** Of note, not every pancytopenia in the elderly is due to malignancy, bone marrow aplasia or acute viral / parasitic insult; other uncommon causes also exist. Syphilis should be kept among the differentials of pancytopenia when more common causes have been excluded. A good sexual history is pertinent to reaching the correct diagnosis in such cases.

**KEY WORDS:** Syphilis (MeSH); Sexually Transmitted Infections (STI) (MeSH); Pancytopenia (MeSH); Treponema pallidum (MeSH); Sexually Transmitted Diseases (MeSH); Bone Marrow (MeSH).


**INTRODUCTION**

A spirochete bacterium Treponema subspecies pallidum is the causative agent of systemic disease syphilis. It can be acquired or congenital. Acquired syphilis is primarily transmitted via sexual contact, and risk is further augmented in high-risk sexual behaviors, such as men who have sex with men (MSM) and Human Immunodeficiency Virus. Transmission via sexual route usually occurs within 1-2 years of infection. In contrast, the transmission for congenital syphilis takes place from infected mother to fetus. Acquired syphilis encompasses early and late syphilis, which further includes primary, secondary, and early latent syphilis as well as late latent and tertiary syphilis (e.g., cardiovascular, neurosyphilis, and gummatous), respectively. Gummatous syphilis causes destructive lesions and most commonly affects the skin and bony tissues. Due to the lack of vaccine availability against syphilis, timely diagnosis and management are essential to decrease disease burden and its clinical effects in affected individuals.

Here we present a rare case of pancytopenia in an elderly man who ultimately turned out to be presenting from syphilis involving the bone marrow. To the best of our knowledge this is the first case report of its type in Pakistan. A similar study has been published in Annals of Internal Medicine describing acquired syphilis leading to bone marrow and liver involvement.

**CASE REPORT**

A 55-year-old man with significant past history of having been treated successfully for Hepatitis C Virus (HCV) infection with direct-acting antivirals (DAAs) 3-year back, presented to medical outpatient department (OPD) for third consecutive time with progressive weakness, on and off generalized body aches for the last 1 year and palpitations for past 3 months. He took Diagesic-P (acetaminophen 500 mg /thioridazine 3 mg/caffeine anhydrous 70 mg) but provided only temporary relief. He had difficulty keeping up his routine activities. Additionally, he stated un-documented low-grade intermittent fever. Febrile episodes mostly occurred at nights with no associated sweats. He also had a history of undocumented weight loss. Moreover, he reported a 3-month history of palpitations related to mild to moderate exertion but relieved with rest. He denied any travel or use of recreational drugs, sleep and appetite changes, and bladder or bowel habits abnormalities. His two consecutive polymerase chain reaction (PCR) tests for HCV RNA were negative, and there was no history of cardiac disease. His medical history was otherwise unremarkable. Patient was a civil engineer by profession, and his significant exposure was to silica at work sites. Patient's family history was significant for pulmonary tuberculosis (TB) in his brother, for which he was successfully treated 5 years back, ischemic heart disease in his father, and diabetes mellitus (DM) in his mother.

Initial evaluation revealed gross pallor and mild edema feet. A few healed skin lesions were noted on the lateral aspect of the foot near lateral malleolus. Rest of the physical examination was insignificant. Patient's baseline workup was done, and he was started on treated for Iron Deficiency Anemia (IDA). Patient improved but revisited after third months with anemia and same vague symptoms. Physical exam revealed blood pressure of 140/80 mmHg, regular pulse rate (PR) of 70/minute with normal volume and
character, respiratory rate (RR) of 18/minute, and oxygen saturation (SpO2) of 95% while breathing ambient air. The remainder of systems review was unremarkable. The differential diagnoses (DDs) based on his history were IDA, pancytopenia secondary to hypersplenism from HCV, miliary TB involving bone marrow, multiple myeloma (MM), aplastic anemia, and myelodysplastic syndrome (MDS). The patient's initial blood tests revealed a low hemoglobin of 5.6g/dl, white cell count of 3,000/cmm and platelet count of 80,000/cmm. The red cell morphology was hypochromic and microcytic with anisocytosis.

Erythrocyte sedimentation rate was 70mm/1’ hour. Liver function tests, renal function tests, serum albumin and serum calcium were within normal limits. Hepatitis serology was positive with negative PCR; viral screening for hepatitis B and HIV was negative. Furthermore, electrocardiogram, echocardiography, chest X-ray, urine R/E, ultrasound (US) abdomen & pelvis, peripheral smear, serum ferritin, serum vitamin B12, thyroid function tests, HbA c, Mantoux test, X-ray skull, serum calcium, and SPEP. For aplastic anemia, normal range is (0.7–1.5 g/dl). MM was classified into four overlapping clinical presentations and duration, syphilis is mainly a clinical diagnosis and is confirmed by serologic tests, such as VDRL, rapid plasma reagin, TPHA, fluorescent treponemal antibody immobilization (FTA-ABS), T pallidum fluid analysis was indicated as per guidelines; however, patient declined despite detailed counseling. He was started on intravenous penicillin during hospital stay as per protocol and was discharged home on oral doxycycline for 4 weeks in addition to symptomatic management. On follow up the patient had improved clinically, and his blood counts also showed improvement.

**DISCUSSION**

Syphilis is a common health concern. It is more prevalent in developing countries. Based on the vast array of presentations and duration, syphilis is classified into four overlapping clinical stages. Primary syphilis is characterized by painless superficial clean based ulcers (chancre) and painless regional lymphadenopathy (LAD). Secondary syphilis has systematic presentation ranging from skin rash involving palms and soles, fever, LAD, mucous patches, arthritis, prostatitis, alopecia, condylomata lata (wart-like lesions), and hepatospleno-megaly (HSM). Latent syphilis is characterized by the absence of clinically apparent disease with positive serology and is further divided into early and late latent syphilis based on = 1 year and > 1-year duration. Tertiary syphilis involves almost every organ in the body but mainly classified into; 1) Gummatous (gummas) involving the skin, soft tissue, bone, and visceral organs. We can postulate that the caseous necrosis on bone marrow of our patient might have very well been the syphilitic gummas causing pancytopenia. 2) Cardiovascular syphilis characterized by valvular disease and aortic aneurysm. 3) Neurosyphilis manifesting as meningitis, stroke, cranial nerve (CN) palsies, tabes dorsalis, and myelitis. T pallidum is too slim and thin to be seen by light microscope, but it can be visualized by dark microscopy.

Syphilis is more prevalent in developing countries. Syphilis is mainly a clinical diagnosis and is confirmed by serologic tests, such as VDRL, rapid plasma reagin, TPHA, fluorescent treponemal antibody immobilization (FTA-ABS), enzyme immunoassay, etc. It is among the four curable STIs caused by bacteria. According to Cohen et al; the mainstay treatment for syphilis is penicillin G.

**CONCLUSION**

It can, therefore, be concluded that any patient with viral hepatitis and pancytopenia should not be treated on the lines of hypersplenism only. Other causes need to be ruled out and collateral history is of utmost importance in reaching the correct diagnosis. Similarly, only tuberculosis should not be considered when caseous granulomas are seen in a biopsy specimen. If we had not considered alternate diagnosis, the patient would have been exposed unnecessarily to anti-tuberculous treatment and its potential hepatotoxic side effects on the background of viral hepatitis.

**REFERENCES**

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AUTHOR’S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

AB & KZE: Management of the case, drafting the manuscript, critical review, approval of the final version to be published

SOH: Identification, diagnosis and management of the case, approval of the final version to be published

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

Authors declared no conflict of interest

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DATA SHARING STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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KMUJ web address: www.kmuj.kmu.edu.pk
Email address: kmuj@kmuj.edu.pk