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# A Case Report of Tuberculosis Related Bicytopenia in a 12-Year Girl

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**ABSTRACT**
The great variability in the clinical presentation of TB poses a diagnostic and therapeutic challenge for physicians. In addition, TB infection can seriously affect the hematopoietic system during its course, with involvement of both myeloid and lymphoid cell lines and plasma components. In this case report, we reported a rare case of tuberculosis related bicytopenia in a 12-year girl at a tertiary hospital. Bone marrow examination is an extremely important and effective way of diagnosing and evaluating hematologic and metastatic neoplasm as well as non-hematological disorders responsible for cytopenia. The etiological spectrum of cytopenias in children is varied from infections including dengue fever and enteric fever to serious illnesses including acute leukemia. A thorough history and clinical examination are vital to reach a tentative diagnosis and for planning further investigations. Tuberculosis should be included in the etiological investigation of cytopenias in childhood, especially in endemic countries. Investigations should include bone marrow evaluation.

## INTRODUCTION

Tuberculosis is a major health problem in the developing world. Although pulmonary tuberculosis is promptly diagnosed and treated, diagnosis of extra pulmonary tuberculosis is often delayed because of its nonspecific presentation[1]. Extra pulmonary tuberculosis can present with various hematological manifestations, including pancytopenia[2,3]. The great variability in the clinical presentation of TB poses a diagnostic and therapeutic challenge for physicians. In addition, TB infection can seriously affect the hematopoietic system during its course, with involvement of both myeloid and lymphoid cell lines and plasma components[4]. Tuberculosis may rarely present with pancytopenia and the recovery of peripheral blood counts with antituberculosis therapy is taken to indicate that there is no underlying hematological disease. Several factors are considered to cause pancytopenia in disseminated or extrapulmonary tuberculosis including hypersplenism, histiocytic hyperplasia, maturation arrest, or infiltration of the bone marrow by caseating or noncaseating granulomas causing reversible or irreversible fibrosis[1]. These hematological changes may act as a marker for the diagnosis, prognosis and response to therapy[4]. In this case report, we reported a rare case of tuberculosis related bicytopenia in a 12 year girl at a tertiary hospital.

**Case Report:** A 12 years old girl, was admitted from casualty, presenting complaints were fever with chills for 2 weeks, c/o vomiting on eating, c/o giddiness with 1 episode of syncope. c/o generalized weakness, c/o polymorphic rashes all over the body, c/o bleeding per vaginum. Patient had history of chicken pox infection a month ago. On clinical examination, patient was conscious and oriented, comfortably seated in bed. Afebrile, heart rate was 76 beats per minute, SPO2-98% on room air. Blood pressure was 110/70 mm Hg, on systemic examination, no abnormality detected in cardiovascular and respiratory system. Per abdomen was soft and non-tender. Investigations showed bicytopenia (hb-4.5mg/dl, platelet count-11000) hypokalemia (K+-2.2meq/dl). USG pelvis suggestive of large mass of size 9x5x7 cm in the pelvis anterior to the uterus with a small cystic and large solid component suggesting of ovarian mass. Multiple enlarged retroperitoneal lymph nodes in the upper abdomen are present, largest being 4cm. Left ovary visualized and appears normal. uterus with mild blood within endometrial cavity, mild free fluid in the pelvis. CT neck, chest abdomen+ pelvis with iv contrast was done. CT was suggestive of cavitary lesion in upper lobe of right lung with multiple necrotic lymph nodes in neck, retromediastenum, retroperitoneal regions and ovarian cystic mass. PET CT was done further to rule out malignancy, which suggested likely tubercular pathology. Metabolically active large area of parenchymal consolidation with necrosis and cavitation in the upper lobe of the right lung with adjoining bronchocentric nodularity and few small discrete nodules in bilateral lungs with multiple necrotic right supra clavicular, mediastinal and retroperitoneal lymphadenopathy as described above are secondary to infective etiology likely Koch's. Biopsy from Right Supraclavicular Lymph Node was suggestive of Tuberculous lymphadenitis. Zones of caseation and many Langhans giant cells seen. Acid fast bacilli not detected on Ziehl Nelson stain. There is no malignancy. Supraclavicular lymph node biopsy was positive for gene xpert and histopathology confirmed tubercular etiology. Cytogenetic study (GTG-banding) following unstimulated culture revealed 46,XX chromosome complement. No abnormality was detected. On Bone marrow trephine biopsy, M:E ratio was approximately 1:4. Erythropoiesis is normoblastic and megaloblastic in nature. Granulopoiesis follows sequential maturation. Megakaryocytes are increased in number and loosely clustered, however, they are otherwise morphologically unremarkable. CD 117 has highlighted approximately 15-20% marrow progenitor cells, majority of which are megaloblastic erythroid cells. Immunohistochemistry for CD 34 has revealed marrow progenitors within normal limits. The marrow has been screened for CD 20 and CD 3. There is an expected population of interstitial "T" lymphocytes and scattered 'B' lymphocytes. There is no evidence of lymphoma. The marrow is remarkable for megaloblastic dyserythropoiesis. Patient was given PCV transfusion Patient was started on 1st line Anti-tubercular therapy (rifampicin, isoniazid, ethambutol, pyrazinamide), after sensitivity confirmation by XDR gene xpert. Patient platelet count didn't improve despite RDP transfusions, so injection methyl prednisolone pulse therapy was given (30 mg/kg) for 5 days. Intravenous immunoglobulin was given further (10gms) as platelet count didn't improve, Patient was given injection rituximab 500 mg. 1 pint SDP was further given and tab Prednisolone started 60mg/day. Patient improved gradually clinically and labs showed improvement in platelet counts. Patient was shifted out of ICU, as platelet count: reached 1 lakh. tab Prednisolone was given in tapering doses with ATT. Opinion was taken from gynecology, i/v/o ovarian mass, advised repeat USG after 6 weeks, for suspected tuberculosis related/hemorrhagic cyst, nature and prognosis explained to patient and relatives. Patient was discharged with follow up advises.

While the burden of childhood TB in India is not known, regional data from the World Health Organization (WHO) indicate that sputum microscopy smear-positive TB in children (<14 years old) accounts for 0.6%-3.6% of all reported cases.5 However, because the majority of children are sputum

microscopy smear negative, these data underestimate the true burden of childhood TB. It is estimated that childhood TB constitutes 10-20% of all TB in high burden countries[6], accounting for 8-20% of TB-related deaths[7,8]. A wide spectrum of hematological abnormalities such as anaemia, leucocytosis, monocytosis, lymphopenia, leukopenia, thrombocytopenia, thrombocytosis, leukemoid reaction and pancytopenia have been described previously in mycobacterial infection[9]. These occur via non-immunologic mechanisms secondary to granulomatous infiltration of the bone marrow, hemophagocytic syndrome, hypersplenism, malabsorption, nutritional deficiency, or as a side-effect of anti-tubercular therapy[9]. Acquired causes of pancytopenia can be nutritional deficiencies, idiopathic or secondary to exposure to radiation, drugs and chemicals (chemotherapy, chloramphenicol, sulfa drugs, anti epileptics, gold etc.), viral infections (cytomegalovirus, Epstein-Barr virus, hepatitis B or C, HIV etc.), auto-immune, paroxysmal nocturnal hemoglobinuria and marrow replacement disorders (leukemia, myelodysplasia, myelofibrosis)[10]. Megaloblastic anemia and infections such as enteric fever, malaria, kala-azar and bacterial infections are the common causes of pancytopenia in developing countries[11]. The clinical presentation of children with bicytopenia or pancytopenia can be fever or pallor. Clinically, anemia leads to fatigue, breathlessness and cardiac symptoms. Thrombocytopenia leads to bruising and mucosal bleeding and leucopenia leads to increased susceptibility to infection. The clinical profiles of these patients are however variable depending on the underlying etiology[2]. Bone marrow examination is an extremely important and effective way of diagnosing and evaluating hematologic and metastatic neoplasm as well as non-hematological disorders responsible for cytopenia. Bone marrow examination involves the study of bone marrow aspirates, imprint smears and trephine biopsy. These three procedures are complementary to each other and superiority of one method over the other depends on the specific disease process[12]. The bone marrow findings may vary depending on the causative factors, from normocellular with non-specific changes to hyper cellular being overshadowed by malignant cells. Decrease in production of homeopathic cells can occur as a result of infections, drugs, toxins, or malignant cells infiltration leading to hypocellular bone marrow whereas normocellular or hyper cellular marrow can be found in conditions of ineffective hematopoietic, maturation arrest of lines and peripheral sequestration of blood cells including megaloblastic anemia and hypersplenism. Kashongwe[13] described a case of a 42 years man presenting bleeding and pancytopenia., bacteriological pulmonary TB was established by genotypic rapid test and treatment following the WHO guidelines on drug-sensitive TB treatment. Patient recovered entirely with the WHO recommended regimen associated with general and local treatment of the bleeding. They emphasized the importance of always suspecting tuberculosis in a tuberculosis -endemic area, even when the clinical manifestations are atypical, like pancytopenia and also of properly investigating the differential diagnosis. Even though prognosis seems to be less good, actual treatment regimen is still effective. The haematological abnormalities are common in patients with tuberculosis (TB). However, autoimmune bicytopenia is extremely rare in childhood TB. M. Khemiri[14] reported a case of 11-year-old girl presented with 4-week history of fever and cough associated to weight loss. The diagnosis of active pulmonary TB was achieved based on radiological and microbiological findings. Simultaneously, laboratory investigations revealed autoimmune haemolytic anaemia associated to immune thrombocytopenia. These hematological disorders were successfully treated with anti-tubercular drugs only. Tuberculosis should be included in the etiological investigation of autoimmune ''cytopenias'' in childhood, especially in endemic countries, since they may respond to anti tubercular drugs. Tuberculosis remains a diagnostic challenge because the presentations are nonspecific. Delay in diagnosis owing to lack of specific clinical features is the main reason for the poor prognosis in disseminated tuberculosis. Wang[15] described that simultaneous culture and histopathological examination of bone marrow in diagnosing disseminated tuberculosis is more sensitive than just performing a mycobacteria blood culture.

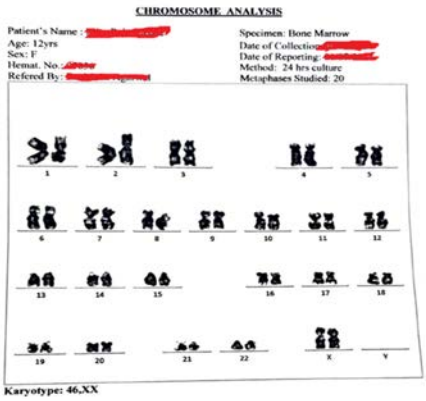


Fig. 1: Chromosome Analysis

## CONCLUSION

The etiological spectrum of cytopenia in children is varied from infections including dengue fever and enteric fever to serious illnesses including acute leukemia. A thorough history and clinical examination are vital to reach a tentative diagnosis and for planning further investigations. Tuberculosis should be included in the etiological investigation of cytopenia in

childhood, especially in endemic countries. Investigations should include bone marrow evaluation.

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