

# Localized Tuberculosis and Myelofibrosis with Myeloid Metaplasia : An Extremely Unusual Presentation

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Myelofibrosis with myeloid metaplasia (MMM) is usually considered primary agnogenic, however, it may be secondary to various diseases, The association of tuberculosis with MMM is exceedingly rare, however, the pathogenetic relationship between the two is difficult to define. We present a case report showing simultaneous presentation of localized active tuberculosis and MMM The literature on the subject is also reviewed with special emphasis on pathogenic relationship between the two.

## Case Report

A 28 year old thin build man presented with generalized Weakness, weight loss and progressively increasing pallor since one and a half years. Two weeks before attending the medicine clinic, he developed low grade fever and also noticed a nodular swelling on left side of the neck, On examination, he was found to have severe anaemia, hepatosplenomegaly and enlarged scalene lymph node on left side of the neck. Laboratory work up revealed Hb 3.0 gm/dl, a leukoerythroblastic picture with many teardrop shaped red cells. The bone marrow aspiration was difficult and yielded a dry tap. Subsequent bone trephine biopsy revealed a cellular marrow with large number of mature and immature megakaryocytes and markedly increased marrow fibrosis which was confirmed by reticulin stain (Figure 1).

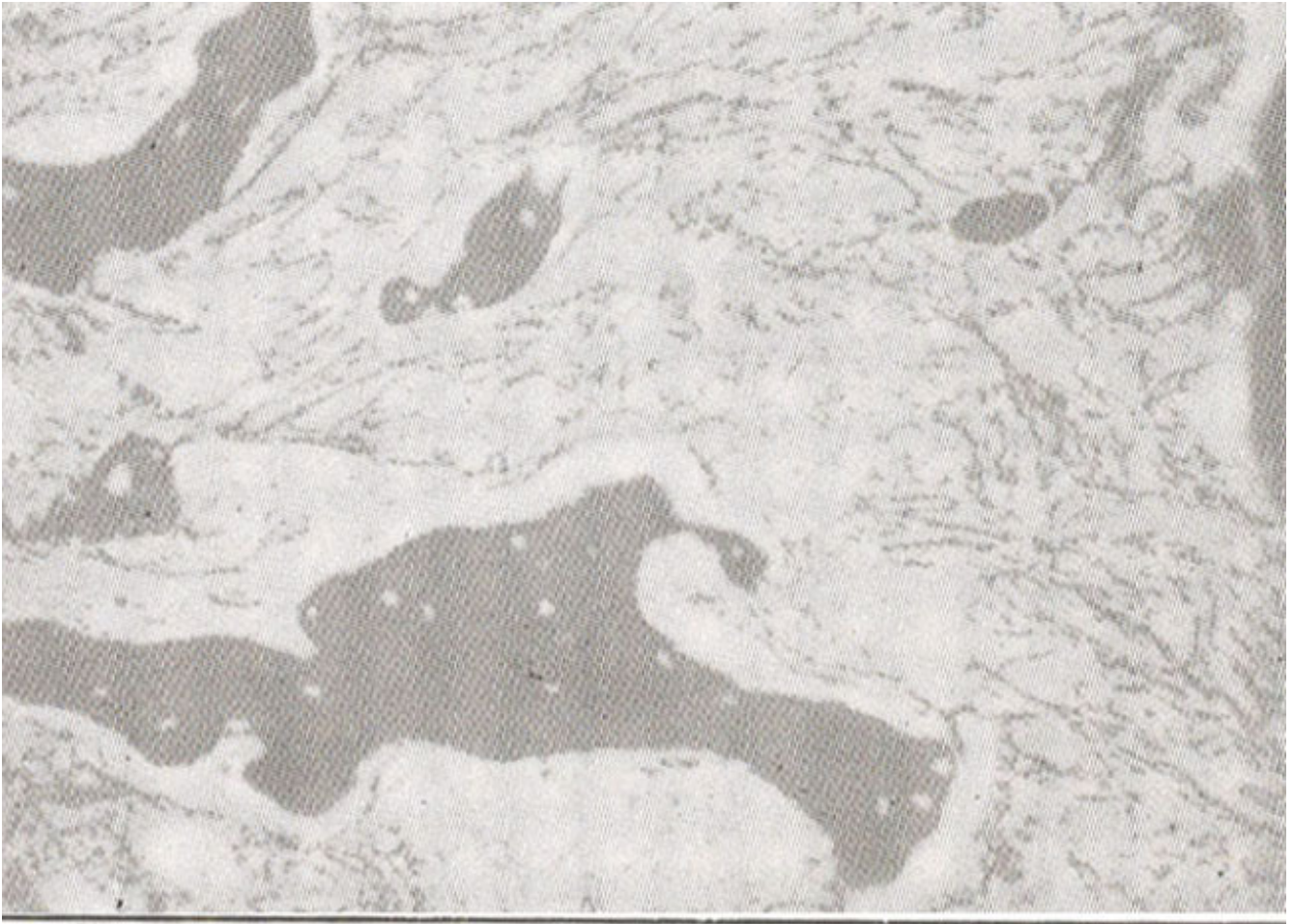


Figure 1. Bone marrow biopsy. Reticulin stain showing increased fibrosis.

Fine needle aspiration of scalene lymph node was carried out which showed few atypical cells with hyperchromatic nuclei and epithelioid cells in a lymphocytic background. The possibility of Hodgkin's disease was questioned with recommendation of histological evaluation. The excisional biopsy of lymph node revealed extramedullary hematopoiesis and caseating granulomas compatible with tuberculosis (Figure 2).

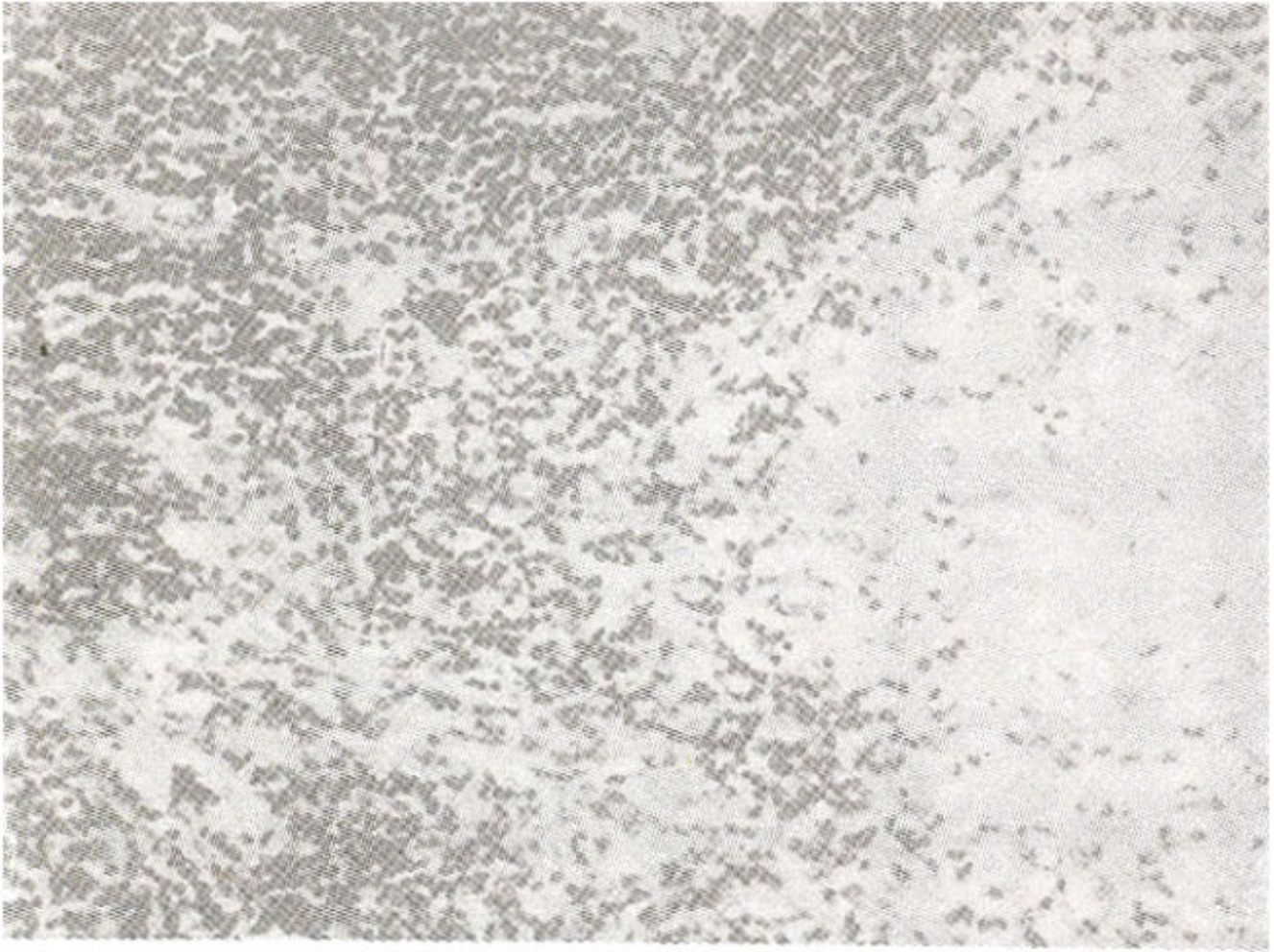


Figure 2. Scalene lymph node biopsy, showing caseating epithelioid granuloma on right side and extramedullary hematopoietic cells intermixed with lymphocytes on left side (H & E stain x100).

AFB stain was negative. No evidence of pulmonary or military tuberculosis was found.

The patient was started on antituberculous therapy and within days the fever subsided with marked clinical improvement. A hematological assessment made after 3 months revealed haemoglobin level of 6.0 gm/dl and a weight gain of 2.2 kg. After completion of the therapy, the patient was well with a haemoglobin level of 10.2 gm/dl.

### Discussion

Myclosclerosis with myeloid metaplasia is grouped under the heading of myeloproliferative disorders and is characterized by splenomegaly, presence of immature granulocytes and erythroblasts together with distorted and tear drop shaped red cells in the peripheral blood and marrow fibrosis. It is usually considered agnogenic and many synonyms have been applied to this disease including agnogenic myeloid metaplasia, chronic primary myelofibrosis, chronic fibrogenic megakaryocytic leukemia<sup>1</sup> and megakaryocytic myelosis<sup>2</sup>. The neoplastic character of the disease has been established by demonstrating the clonal replication of the erythrocytic, granulocytic and megakaryocytic lineages. The fibroblastic proliferation on the other hand is not clonal and is reactive rather than neoplastic<sup>3</sup>. The

enhanced collagen content of marrow is the result of release of fibroblastic growth factors especially platelet derived growth factor (PDGF), transforming growth factor B (TGF-B), tumour necrosis factor alpha (TNF-alpha) and interleukin 1, released from megakaryocytes and other marrow cells. The reactive nature of the fibroblastic proliferation is determined by isoenzyme studies or chromosomal karyotyping<sup>4</sup>.

A number of cases of MMIM may follow secondary to various diseases including polycythemia vera, essential thrombocythemia, leukaemia and metastatic carcinoma. Exposure to benzene and ionizing radiation has also been described in genesis of MMIM. Another less well recognized condition with MMIM is tuberculosis. The tuberculosis in these cases either presents as isolated pulmonary disease or as localized caseous or granulomatous disease of blood forming organs including spleen, lymph nodes and liver. In some cases, the disease presents as miliary tuberculosis<sup>5</sup>. The pathogenetic relationship between tuberculosis and MMIM is complex and difficult to define. Various explanations for the co-existence of tuberculosis and MMIM have been described. The findings may be a mere coincidence, or the blood disorder or its treatment may lead to an increased susceptibility to tuberculosis. Few studies favour the tuberculous infection as a cause of MMIM<sup>6,7</sup>.

Tuberculosis is very common in this part of the world and localized as well as miliary tuberculosis is frequently seen in clinical practice. MMIM is an uncommon hematological disorder and most of the cases are either agnogenic or secondary to polycythemia vera and leukaemia. In our case, the remarkable hematological improvement achieved within three months of anti-tuberculous treatment points towards the possible causative role in myelofibrosis. This case report also points to the important fact that despite a high incidence of tuberculosis in our country the myelofibrosis in association with tuberculosis infection has not been cited in local literature. It could be due to limited medical facilities, improper follow-up of the patients or lack of awareness of the possibility of tuberculous infection in cases of myelofibrosis. Thus, it seems that the incidence of MMIM may be much higher in our population and a painstaking search should be made to find out tuberculous infection in a case of myelofibrosis or vice versa. The importance of tuberculosis in the myeloproliferative disease cannot be under-estimated both from the point of view of management of the patient, as well as an understanding of the nature of blood disorder.

## Acknowledgement

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## References

1. Wittels, B. The myeloproliferative disease In: Wittels, B., Bennington, J.L eds. Surgical pathology of bone marrow- core biopsy diagnosis. 1st edition, Philadelphia, W.B. Saunders, 1985, pp. 30-40.
2. Ward, H.P. and Block, N.H. The natural history of agnogenic myeloid metaplasia (AMM) and a critical evaluation of its relationship with the myeloproliferative syndrome. *Medicine*, 1971;50:357-420.
3. Jacobson, R.J., Salo, A. and Fialkow, P.J. Agnogenic myeloid metaplasia: A clonal proliferation of hematopoietic stem cells with secondary myelofibrosis. *Blood*, 1978;51:189-194.
4. Greenberg, B.R., Woo, L., Veomett, I.C. et al Cytogenetics of bone marrow fibroblastic cells in idiopathic chronic myeloid fibrosis *Br J. Haematol* 1957;66:487-490.
5. Pero-silva, A., Garcia-Saavedra, V. and Llorente-Cabera, A. (Thrombotic myeloproliferative syndromes and tuberculosis. Apropos of 3 cases *Med Clin. (Bare)*. 1990;94:582-584.
6. Tassies, D., Cervantes, F., Nicolas, J.M. et al Tuberculosis in chronic myeloproliferative syndromes: Its incidence and principle characteristics in series of 562 patients. *Nied Clin. (Bare)*, 1991:321-323.



7. Andre J., Schwartz. R., Damcshek, W. et al Tuberculosis and myelosclerosis with myeloid metaplasia: Report of three cases JAMA, 1961,178:1169-1 174.