

## “A Clinico-Hematological Study of Pancytopenia”.

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**Abstract:** This is a clinic-hematological study, conducted in the winter months, at a tertiary care hospital, in South India, to identify the causes of pancytopenia. Out of total 1983 cases of complete hemograms, 28 cases were categorized as pancytopenias and out of these 12 cases were subjected to bone marrow examination. The remaining 16 cases of pancytopenia, were put on periodic follow up with peripheral blood smear examination, based on clinical data.

The period of study was during the winter months, with increased frequency of viral fevers. Hence, one should not be in a hurry to do a bone marrow examination, as the transient decrease in the counts, may improve, as the fever subsides and also it is important not to hesitate doing the procedure.

**Key words:** pancytopenia, bone marrow, viral fever.

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### I. Introduction

Pancytopenia is the simultaneous presence of anemia, leucopenia and thrombocytopenia that may result from various disease processes, involving the bone marrow primarily or secondarily<sup>(1)</sup>.

The complete hematological work up including a good peripheral blood smear examination, bone marrow aspiration and biopsy with clinical correlation is of utmost importance to evaluate the cause of pancytopenia and planning further investigations and treatment<sup>(2)</sup>.

We present our experience with 28 cases of pancytopenia, over a period of 4 months.

### II. Material And Methods

This is a cross sectional study, conducted in the department of Pathology, at a tertiary care hospital, in south India. A total of 28 cases of pancytopenia are analysed with clinico-hematological features.

Bone marrow aspiration smears and trephine biopsy sections, in patients, fulfilling the criteria of pancytopenia were examined. Criteria for diagnosis of pancytopenia were: Hemoglobin less than 10gm/dl, TLC less than 3500/mm<sup>3</sup> and platelet count less than 1,00,000/mm<sup>3</sup><sup>(3)</sup>. Bone marrow aspiration was performed using Salah needle either from posterior iliac crest or sternum and biopsy with Jamshidi needle from posterior iliac crest, under local anesthesia, with informed consent.

The relevant clinico-hematological parameters were recorded. The causes of pancytopenia are analysed based on clinico-hematological parameters, including peripheral blood film, bone marrow aspiration, bone marrow biopsy (in cases of dry tap), clinical features, age, gender and compared with the various studies published in literature.

The bone marrow aspiration smears were stained with Leishman's stain and the trephine biopsy core was decalcified, routinely processed, embedded in paraffin and sections stained with Hematoxylin and Eosin. Special stains like reticulin were performed wherever necessary.

### III. Results

A total of 1981 complete hemograms were done during a period of 4 winter months, in the department of Pathology, at a tertiary care hospital in south India. Out of which 28 cases fulfilled the criteria of Pancytopenia, constituting 1.4%.

In these 28 cases, only 12 cases (42.85%) cases were subjected for bone marrow examination.

The male to female ratio in cases of pancytopenia was 1:3.5.

The age of the patients ranged from 6-65 yrs. The most common age group was 2<sup>nd</sup> decade constituting 28.7% of the cases, followed by 4<sup>th</sup> decade (14.3%) and 1<sup>st</sup> and 3<sup>rd</sup> decade each of 10.7% and 4<sup>th</sup>, 5<sup>th</sup> and 6<sup>th</sup> decade constituted each 7.1%.

In 57.15%(16cases) of pancytopenia, bone marrow examination was not done, as the counts improved , when a repeat hemogram was done , after a period of 10-15 days. The case details , based on etiology will be discussed.

#### IV. Discussion

Bone marrow examination is useful in the investigation of PUO(pyrexia of unknown origin), as it leads to an etiological diagnosis in many of the cases.

In the spectrum of bone marrow changes observed, in the present study, one case of pancytopenia in a female aged 32yrs, with PUO, the bone marrow aspiration was a dry tap. The biopsy sections showed hypocellular marrow with collections of lymphocytes and granulomas located in the interstitium. The granulomas were ill defined, with collections of epithelioid cells and foci with necrosis. Langhan's type of giant cells, were not observed. Erythropoiesis , megakaryopoiesis and granulopoiesis were suppressed(Fig 7a,b). Granulomas in marrow aspiration smears are difficult to identify probably because of the fibrosis, in and around the granulomas. Granulomas in bone marrow are an uncommon findings in western studies <sup>(5,3)</sup> but is much higher in studies from India.<sup>(7)</sup>. In the present study, morphology of the granulomas in bone marrow is similar to those seen in other organs. There are no distinguishing features in the morphology of bone marrow granulomas, to permit a definitive diagnosis of the underlying condition. <sup>(7)</sup>. Though the granulomas associated with caseous necrosis and Langhan's type giant cells would be more frequent in tuberculosis. The finding needs to be correlated with clinical , laboratory(culture, serology) and radiological data, to arrive at an etiological diagnosis. Bone marrow culture also plays a vital role, in identifying the etiology, when blood culture is negative. In one study <sup>(7)</sup>, Brucella organisms were grown, in one case. In the present study, the case of granulomas in bone marrow biopsy, on follow up, after 1month ATT (anti tuberculous treatment), showed improvement in blood cell counts. A rare case of acquired amegakaryocytic thrombocytopenia (AATP) was encountered in the present study, which was first treated as immune thrombocytopenia and later diagnosed as AATP. The patient was a female child 14yrs of age, diagnosed as ITP, 3yrs back. O/E purpuric spots were observed through out the body and there was no organomegaly. Initially , 3yrs back, the episode of thrombocytopenia occurred , after an episode of viral fever and diagnosed as ITP. Since then, the patient was on Prednisolone, on & off (for the last 3yrs). Present episode of thrombocytopenia did not show any improvement in platelet counts, even after treatment with prednisolone. A bone marrow examination was done, as the peripheral blood film showed anemia and leucopenia along with thrombocytopenia. Bone marrow aspiration smears showed hypercellular particles with erythroid hyperplasia and micronormoblastic type of erythropoiesis. Myelopoiesis showed orderly maturation. Megakaryopoiesis was markedly suppressed , with absence of megakaryocytes. Lymphocytes and plasma cells were within normal limits. There was no evidence of any deposit or leukemic process. Hence, a diagnosis of acquired amegakaryocytic thrombocytopenic purpura was made. In the management of the present case, a whole blood transfusion was given, Prednisolone was stopped and planned to be treated with Antithymocyte globulin(ATG) 15mg/kg. Several cases of amegakaryocytic thrombocytopenic purpura have been reported following prolonged administration of DES or other estrogenic hormones. Prednisolone in massive doses is moderately hematosuppressive and in some individuals prolonged administration of conventional doses(60mg/dl) may depress platelet production, ironically this depression has been observed most often in patients with ITP who were continued on prednisolone for more than 2weeks after platelet levels responded<sup>(9)</sup>. In the present study, 1 case of hypoplastic marrow was recorded in a male patients of age 63yrs , with incidence of 10.7% aplastic anemia. The incidence of aplastic anemia varies from 10-52.7% of all pancytopenia patients and is the commonest cause of pancytopenia reported from various studies through out the world<sup>(8)</sup>. Bone marrow aspiration was dry tap in 2cases and 1case smears show fatty fragments with trapped lymphocytes and plasma cells. Bone marrow trephine biopsy in all 3cases showed increased fat spaces and decreased cellularity(Fig 2a,b,c). Diagnosis of severe aplastic anemia requires that the patient have atleast two of the following: a granulocyte count below 20,000/microlit and absolute reticulocyte count $\leq 40 \times 10^9/L$ . In addition, the bone marrow biopsy must contain less than 25% <sup>(10)</sup> Mild or moderate aplastic anemia is distinguished from the severe form by the presence of mild or moderate cytopenias and more variable, but still deficient, bone marrow cellularity. These distinctions are more than sementic, they are critical for the prediction of outcome and the choice of therapy<sup>(8)</sup>. In the present study, 1 case was categorized as severe and 2cases as moderate aplastic anemias.

In a female child of 14yrs with pancytopenia, bone marrow aspiration revealed acute leukemia. On cytochemistry, PAS block positivity and was diagnosed as ALL. The patient was referred to a specialty center for further management(Fig3a,b).

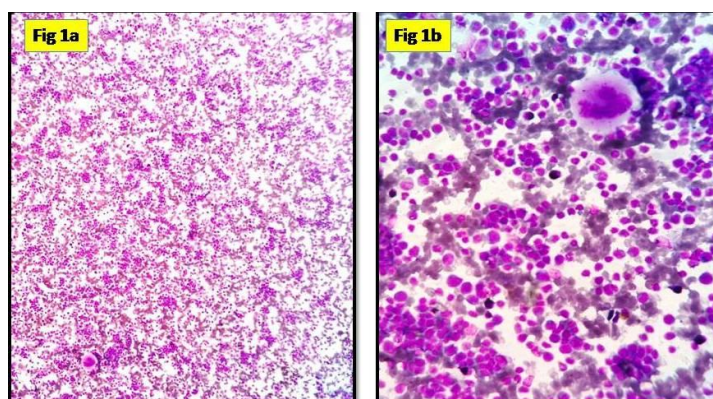
Another case, a male patient of 30yrs with pancytopenia, bone marrow aspiration and biopsy revealed lymphoma infiltrating marrow(Fig 6a,b,c). On IHC it was diagnosed as T-cell lymphoma.

We also encountered a case of primary myelofibrosis, in young male, presenting with weakness, fatigue and gross palor. Repeated transfusions did not improve the counts. Bone marrow aspiration was a dry tap. Bone

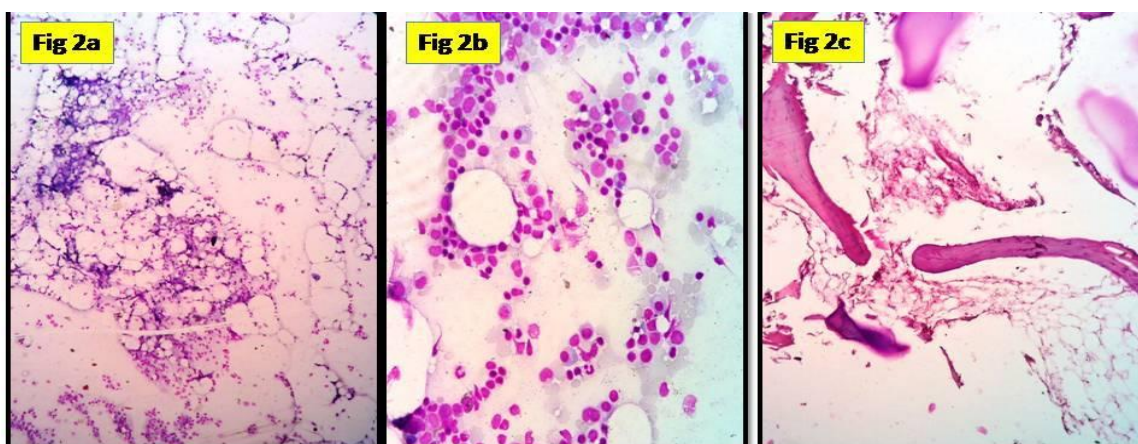
marrow trephine biopsy sections revealed Myelofibrosis of Grade III, which was more prominent with reticulin stain.(Fig 8a,b,c &d)

F 22yrs with hepatosplenomegaly with pancytopenia, bone marrow examination revealed numerous sea blue histiocytes with yellow brown pigment. Diagnosed as Niemann Pick disease(Fig9a,b).

3 cases showed features of megaloblastic anemia(Fig1a,b & Fig4a,b). Out of the remaining 16cases, 2cases , showed dimorphic picture of RBC, a repeat hemogram 2-3weeks after B12, FA and Iron replacement therapy showed improvement in counts. The rest of the 14cases, where fever was the main presenting symptom and PS showed transformed lymphocytes(Fig5a,b), repeat hemogram done after 15-20days interval, showed improvement in the counts.



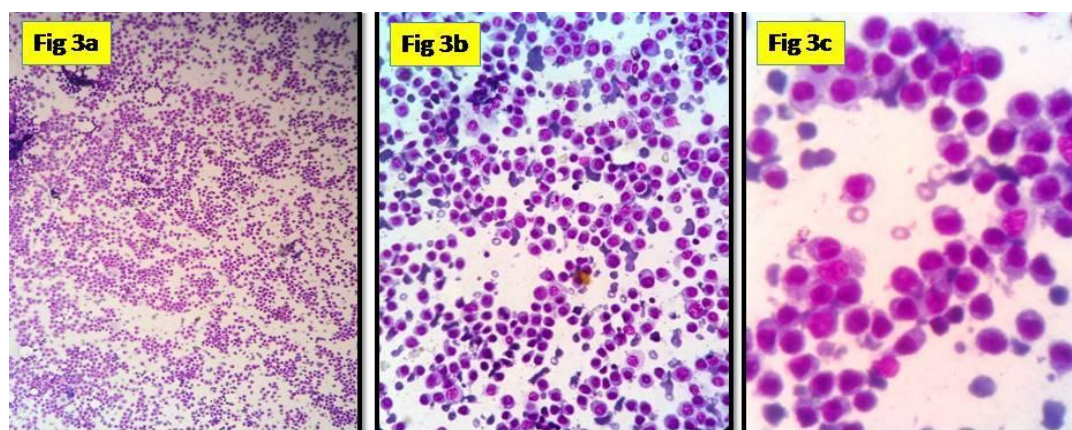
**Fig 1:** Bone marrow aspiration smear: Giemsa stain: X 10 times-Increased cellularity, Erythroid hyperplasia, b) X 40



**Fig 2a :** X10: Bone marrow aspiration: Giemsa stain: decreased cellularity

**Fig 2b:** X40:Relative increase of plasma cells & lymphocytes.

**Fig 2c:** Bone marrow trephine biopsy: Hypoplastic marrow.



**Fig 3a, 3b, 3c:** X10, X40, X100: Giemsa stain: Lymphoma infiltrating Marrow.

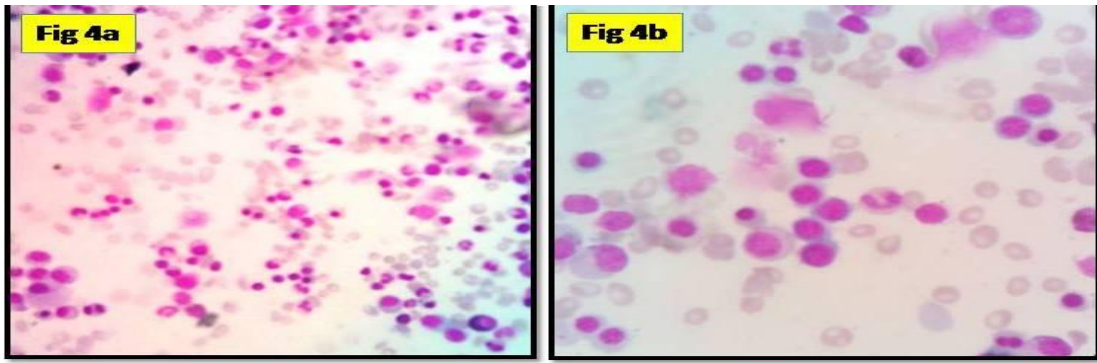


Fig 4a & 4b: Bone marrow aspiration: Giemsa stain. Erythroid hyperplasia- Megaloblastic anemia.

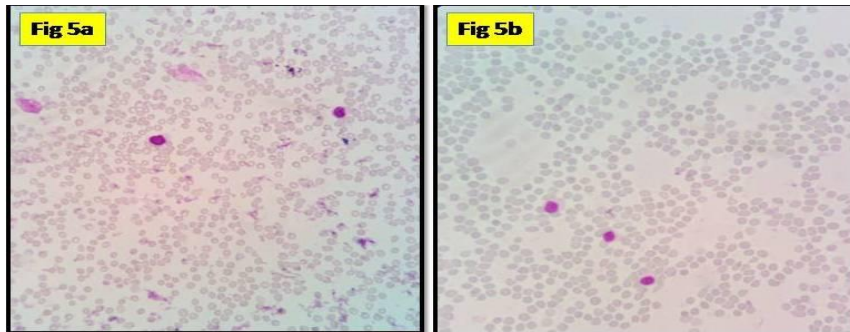


Fig 5a & 5b: Peripheral blood smear picture: Pancytopenia, with transformed lymphocytes.

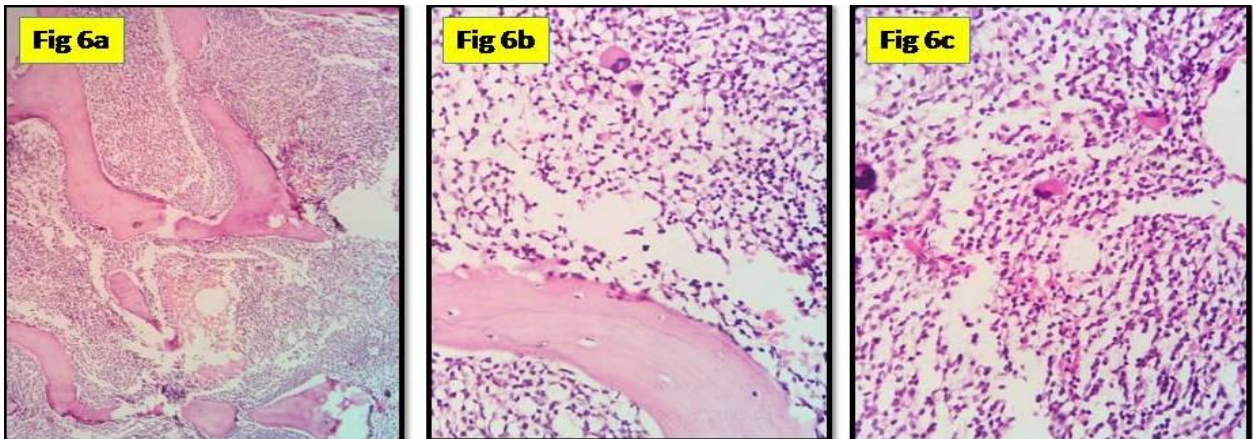


Fig 6a, 6b, 6c: x10, x40, x40: Bone marrow trephine biopsy: Hypercellular marrow .

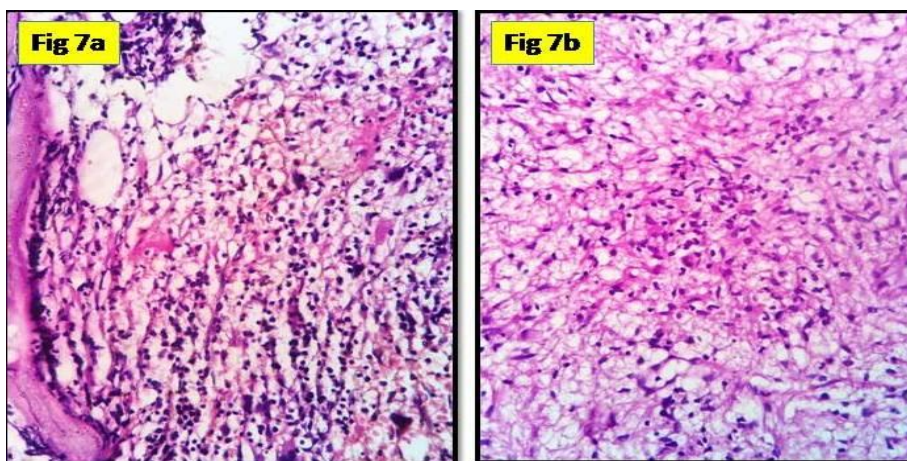
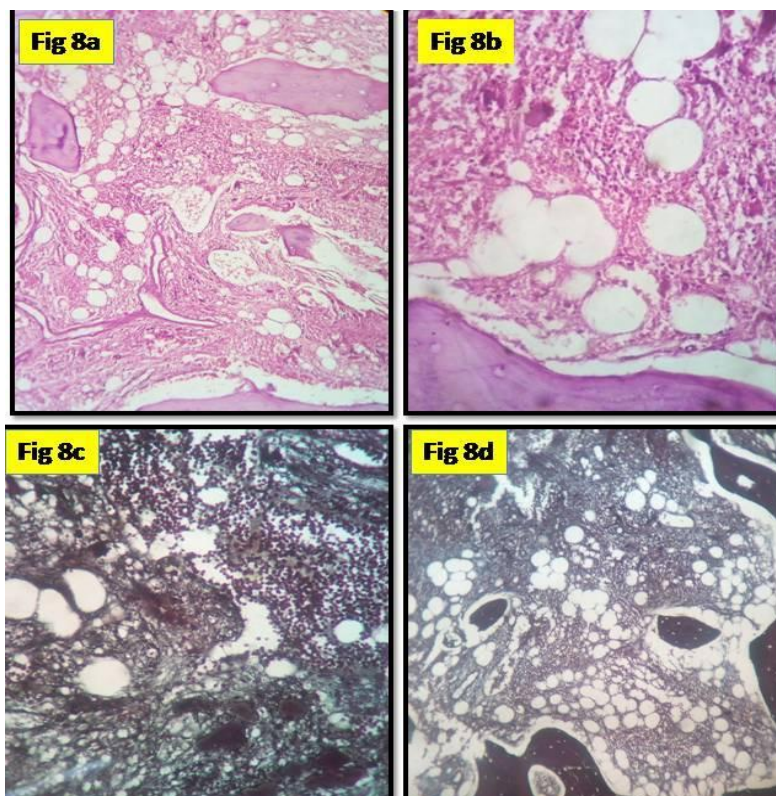
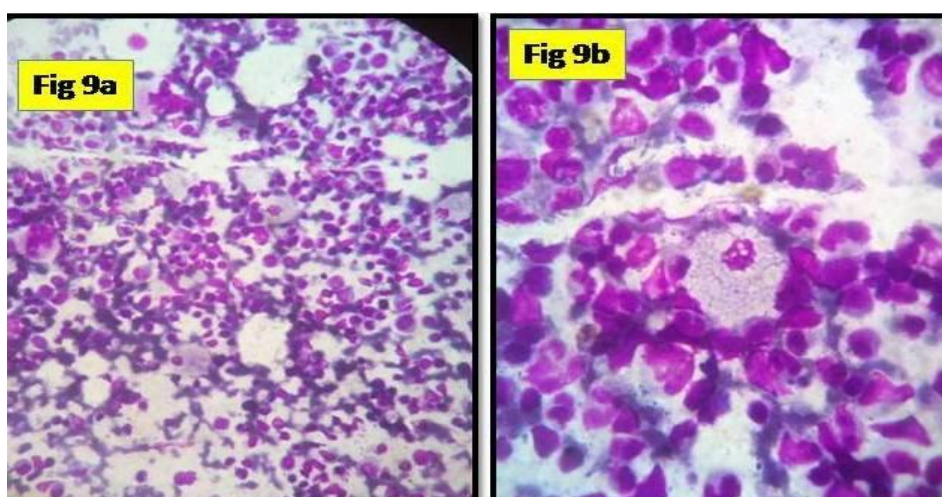


Fig 7a & 7b: Bone marrow trephine biopsy: x10 & x40: Granulomatous inflammation: Tuberculosis.



**Fig 8a & 8b:** H&E Bone marrow trephine biopsy.X10 & X40 Myelofibrosis.  
**Fig 8c & 8d:** Reticulin stain: Bone marrow trephine biopsy. X10 & X40 Myelofibrosis.



**Fig 9a & 9b:** Bone marrow aspiration: Giemsa stain: Storage disease: Nieman-pick's disease.

## V. Summary

In the present study, the commonest cause of pancytopenia was episode of viral fever constituting 14cases(50%) where the blood cell counts improved after the fever subsided and when the transformed lymphocytes diasappeared from the peripheral blood.

Two cases(7.1%) showed improvement in counts after B12/FA replacement therapy. The commonest bone marrow changes were cases(10.7%) of megaloblastic anemia and 3cases(10.7%) of hypoplastic marrow, followed by 1case each(3.5%) of amegakaryocytic thrombocytopenic purpura, acute leukemia(ALL), lymphoma infiltrating marrow(T cell lymphoma), storage disorder(Niemann pick disease), Myelofibrosis, 1case of tuberculous granulomas , in case of PUO, which showed improvement with antituberculous therapy.

## **VI. Conclusion**

Though bone marrow examination is an absolute indication in cases of pancytopenia, it is important to wait for atleast 2-3weeks, do a repeat hemogram, especially in cases of viral fever where the counts usually improve after fever subsides. Also when dimorphic RBC are observed in the peripheral blood , a replacement therapy with B12/FA/iron should be given and if the same picture persists, a bone marrow examination should be done to look for other pathology like MDS etc.

In cases of PUO bone marrow examination is a very useful investigation. In cases diagnosed as ITP, when the patient does not show improvement in counts, a repeat bone marrow examination should be done, as very rarely; acquired amegakaryocytic thrombocytopenia may be the cause.

## **References**

- [1]. Williams WJ, BentkrE, Erskv AJ. Hematology-third edition, Singapore, McGraw Hill Book company 1986; 161-84.
- [2]. Khodek K, Morwans, Buxi G, Yadav RB, Chaturvedi NK. Bone marrow examination in case of pancytopenia. J Indian Academy of Clin Med. 2001; 2:55-59
- [3]. Tilak N, Jain R. Pancytopenia-A clinical and hematological analysis of 77 cases. Indian J Pathol Microbiol 1999; 42(4): 399-404.
- [4]. Bodem CR, Hamory BH, Taylor HM, Kleopfer L. Granulomatous bone marrow disease. A review of the literature and clinicopathologic analysis of 58cases. Medicine(Blatmore). 1983 Nov;62(6):372-83.
- [5]. PEASE GL. Granulomatous lesions in bone marrow. Blood, 1956 Aug; 11(8):720-34.
- [6]. Vilalta-Castel E, Valdes-Sanchez MD, Guerra-Vales JM, Teno-Esteban C, Garzon A, Lopez JI et al. Significance of granulomas in bone marrow: a study of 40cases. Eur J Haematol. 1988 Jul; 41(1):12-6.
- [7]. SampathKumar-Kandala Jeevan, RoshniPaul-Tara, Shantiveer Uooin, Megha Uppin. Bone marrow granulomas: A retrospective study of 47 cases(A single center experience).
- [8]. Keis u M and Ost A. Diagnosis in patients with severe pancytopenia suspected of having aplastic anemia. Eur J Hematol 45:11-14, 1990.
- [9]. Text book of Blood: Andl(133, 134)Wintrobe's