Original Article

Morphological Spectrum of Bone Marrow Aspirates in Infections: A Clinico-Hematological Analysis

Divya Aggarwal, Shilpi More, Ritika Singh, Meera Sikka, Mrinalini Kotru

Department of Pathology, University College of Medical Sciences and Guru Teg Bahadur Hospital, New Delhi, India

Abstract

Context: Bone marrow examination (BME) is an invaluable tool for cases with pyrexia of unknown origin and pancytopenia. However, it is under-utilized for diagnosing infectious etiology and there is a paucity of literature regarding its role in infective pathology. **Aims:** This study aims to bring to light the role of BME in diagnosing infectious pathology. **Settings and Design:** A retrospective study was carried out on bone marrow aspirates (BMAs) sent to the hematology department over the past 4 years. Clinical details, peripheral smears and BMA were retrieved from the records and analyzed. **Subjects and Methods:** Leishman-stained peripheral smears and BMA were studied along with bone marrow biopsy wherever feasible. **Results:** A total of 52 cases were studied. The most common clinical presentation was fever, clinical finding was splenomegaly and hematological finding was anemia. Based on the morphological findings in combination with clinical history, cases were categorized into–parasitic (26.9%), viral (23.1%), tubercular (11.5%), and nonspecific infections (38.5%). Parasites such as *Leishmania donovani*, microfilaria, plasmodium falciparum, and vivax were reported in 14/52 (27%) cases. Associated BMA findings were plasmacytosis, eosinophilia, reactive lymphocytosis, or dyserythopoiesis. In 38% (20/52) cases, no specific cause of infection was found in the bone marrow. These patients showed histiocytosis, hemophagocytosis, maturation arrest in myeloid lineage, relative myeloid hyperplasia, dysmyelopoiesis, toxic granulation/vacuolation in myeloid cells, lymphocytosis, increased plasma cells or monocytosis in marrow. **Conclusions:** Increased histiocytes, hemophagocytosis, dysplastic changes, maturation arrest, relative myeloid hyperplasia or reactive plasmacytosis, lymphocytosis, and monocytosis are BMA features which must alert the pathologist towards an infectious disease process, a knowledge of these changes can help extend the scope of BME beyond hemato-lymphoid malignancies.

Keywords: Bone marrow aspirate, morphology, parasitic infections, tuberculosis, viral infections

Introduction

Bone marrow examination (BME) is a useful tool in the work-up of patients with pyrexia of unknown origin and pancytopenia.[1,2] Infections are a commonly implicated cause in both scenarios. Infections are a common cause of pancytopenia in both children and adults and these are often treatable and reversible. Some of the common infectious agents associated with acquired aplastic anemia and resultant pancytopenia include Epstein–Barr virus (EBV), Human immunodeficiency virus (HIV), Parvovirus, cytomegalovirus, and Leishmaniasis. In addition, there are umpteen number of viruses, bacteria, protozoa, and fungi which can result in bone marrow suppression and pancytopenia.[2]

Received: 25-02-2023 **Revised:** 20-03-2023
Accepted: 22-05-2023 **Published:** 06-09-2023

Access this article online

Quick Response Code:

Website: http://www.jmau.org/

DOI: 10.4103/jmau.jmau_20_23

Systemic infections result in a variety of morphologic changes in the bone marrow. Peripheral blood films and bone marrow aspirates (BMAs) are frequently examined for various parasites, but less commonly for other infectious disease processes. A systematic and detailed examination of BMAs can provide pointers toward an infectious etiology, which can help guide appropriate patient management. The constellation of findings combined with the clinical history serves as a useful tool for further categorizing an infectious disease process into-parasitic, bacterial, viral, or fungal. The aim of this study was to bring to light the role of various

Address for correspondence: Prof. Mrinalini Kotru, Department of Pathology, University College of Medical Sciences and Guru Teg Bahadur Hospital, GTB Enclave, Dilshad Garden, New Delhi - 110 095, India.
E-mail: mrinalini.kotru@gmail.com

How to cite this article: Aggarwal D, More S, Singh R, Sikka M, Kotru M. Morphological spectrum of bone marrow aspirates in infections: A clinico-hematological analysis. J Microsc Ultrastruct 2024;12:114-9.

morphological soft pointers on BMA smears for diagnosing infectious pathology.

Subjects and Methods

A retrospective study was carried out on BMAs sent to our hematology department over the past 4 years. Fifty-two cases were found suggestive or diagnostic of an infection. The clinical details, peripheral smears, and BMAs of these cases were retrieved from records and analyzed. Bone marrow biopsy was also analyzed whenever available. The clinical parameters noted were age, sex, duration of fever, hepatomegaly, splenomegaly, lymphadenopathy, and clinical differential diagnoses. Any other relevant clinical details were noted. Patients with COVID-19 infection were not included in our study.

The Leishman stained peripheral blood films were examined for presence/absence and degree of anemia, morphology of red blood cells (RBCs), differential leucocyte count, toxic granulation/vacuolation in neutrophils, reactive or dysplastic changes in leucocytes, platelet count and presence or absence of giant platelets. Features noted on Leishman stained BMA smears were cellularity, maturation of the three lineages, features of dysplasia in one or more lineages, prominence of histiocytes, hemophagocytosis, presence/absence of parasites and plasma cells, among others.

The cases were classified into four categories after reviewing the clinical records-parasitic, bacterial/tubercular, viral, and nonspecific infections. A comparison of various parameters was done to find out pointers which were consistently related to a specific cause of infection.

Results

A total of 52 cases were analyzed, of which 14 (26.9%) cases were categorized as parasitic infections, six (11.5%) as tubercular, 12 (23.1%) cases had findings suggestive of viral etiology and 20 (38.5%) cases were placed under the category of nonspecific infections. Table 1 depicts the percentage of cases in each category.

Patients were in the age range of 1–80 years, with a male:female ratio of 1.08:1 (26 males and 24 females). The most common presenting complaint was fever, the most common clinical finding was splenomegaly and the most common hematological finding was anemia.

Among the 14 patients with parasitic infections, there were eight males and six females, in the age range of 5–70 years. Of these, there were eight cases of malaria, four cases of leishmaniasis and two cases with microfilariae.

All eight cases of malaria had a history of fever, duration ranging from 4 days to 4 months. One case had a positive result for dengue nonstructural protein 1 antigen from an outside laboratory and another had tested negative for malarial antigen. Two (25%) cases had hepatomegaly and three (37.5%) had splenomegaly. All cases had anemia with hemoglobin values in the range 4.5–9.2 g/dL, and seven out of eight (87.5%) cases had thrombocytopenia with platelet count ranging from 13,000 to 86,000/mm^3. Pancytopenia was present in three cases. A high reticulocyte count along with the presence of polychromatophils and nucleated RBCs was noticed in 50% of cases suggestive of hemolysis. The parasite was detected in peripheral smear of all cases; gametocytes of plasmodium falciparum and trophozoites of plasmodium vivax were noted [Figure 1a and b]. The differential leucocyte count revealed 2%–5% eosinophils and 2%–8% monocytes. Hemozoin pigment was noted in monocytes in two cases. BMAs were normocellular (62.5%) or hypercellular (37.5%), with myeloid: erythroid M:E ratio ranging from 0.17:1 to 1.4:1. Mild dyserythropoiesis was noted in five cases (62.5%). The parasite was visualized in bone marrow in two cases, one with plasmodium vivax and one with plasmodium falciparum. Bone marrow findings of all cases are shown in Table 2.

Leishmaniasis patients (n = 4) presented with fever ranging in duration from 10 days to 9 months, 75% (3/4) cases had mild hepatomegaly and 100% cases had massive splenomegaly (more than eight cm below costal margin). Pancytopenia was noted in three cases, and bicytopenia in the fourth case; with a normal platelet count. Haemoglobin ranged from 3.1 to 7.4 g/dL. Two cases showed absolute neutropenia and two different cases had a left shift up to myelocyte stage. The parasite was not detected on peripheral smear in any of these. BME revealed reactive plasmacytosis ranging from 4%

Table 1: Distribution of cases into different categories based on the morphological findings

Category	Number of cases (percentage of cases)
Parasitic	14 (26.9)
Malaria	8
Leishmaniasis	4
Microfilaria	2
Tubercular	6 (11.5)
Viral	12 (23.1)
Infectious mononucleosis	4
HIV	2
Nonspecific	20 (38.5)
Total	52 (100)

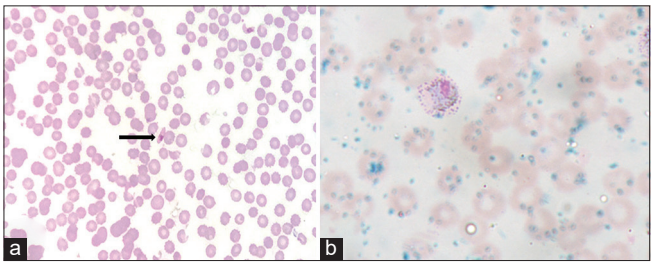

Figure 1: Peripheral smear showing (a) gametocyte of Plamodium falciparum which is highlighted by an arrow (×400); (b) trophozoite of plasmodium vivax (×1000)

Table 2: Bone marrow findings in various cases

Bone marrow findings	Number of cases
Hypercellular marrow with erythroid hyperplasia	28/52
	3 cases of malaria
	2 of tuberculosis
	1 leishmania
	9 of viral
	13 nonspecific
Dyserythropoiesis	15/52
	5 of malaria
	1 leishmania
	1 of viral
	8 nonspecific
Malarial parasite	2/52
Reactive plasmacytosis	17/52
	4 of leishmania
	4 TB
	2 HIV
	7 nonspecific
LD bodies	4/52
Microfilaria	2/52
Dysmyelopoiesis	9/52
	3 of tuberculosis
	6 nonspecific
BM granuloma	2/52
Immature megakaryocytes	4/52*
Lymphocytosis	12/52
	9 viral
	3 nonspecific
Hemophagocytosis	11/52
	2 leishmania
	2 viral
	7 nonspecific
Enlarged erythroblasts	1/52†
Dysmegakaryopoiesis	3/52*
Myeloid maturation arrest	4/52*
Histiocytosis	10/52
	3 Leishmania
	7 nonspecific

*Depicts nonspecific infectious cause, †Depicts viral infections.
HIV: Human immunodeficiency virus, LD: Leishmania donovani

to 10%, with occasional binucleate forms and the presence of both extracellular and intracellular amastigote forms of *Leishmania Donovani*, based on which the final diagnosis was made [Figure 2a and b].

There were two cases of filariasis, none presented with fever or hepatosplenomegaly. One patient had bilateral inguinal lymphadenopathy and the other gave a history of easy fatiguability and frequent blackouts for 2 months. Peripheral smear examination revealed eight percent and 43% eosinophils respectively and BMAs revealed three percent and 28% eosinophils respectively. Microfilariae were detected in the bone marrow in both the cases [Figure 3].

Of the six cases with findings suggestive or diagnostic of tuberculosis, three were diagnosed cases of pulmonary Koch's and two were suspicious for abdominal Koch's, and one presented with pyrexia of unknown origin. All six patients had a history of fever, two had cervical lymphadenopathy. None of them had organomegaly. Hemoglobin values ranging from 4.6 to 11.9 g/dL were noted with three cases showing toxic granulation and vacuolations in neutrophils, and three cases with mild dysplastic changes in neutrophils. Two cases had reactive lymphocytes on the peripheral smear. On differential leucocyte count, monocytes were in the range of 2%–10%. BMAs revealed a M:E ratio ranging from 1.6:1 to 10.8:1. Reactive plasmacytosis (3%–20%) was seen in four cases and three cases revealed a mild degree of dysmyelopoiesis. Granulomas were noted in three cases in the bone marrow biopsy and one case had necrosis only. Stain for acid-fast bacilli (AFB) was positive in the latter case, which was HIV positive [Figure 4a and b]. Occasional giant cells were also present in the fourth case. One case had granuloma on both BMA and biopsy and one case in BMA only.

Viral infection was suspected in 12 cases in the age group of 1–75 years. All these patients had a history of fever, with a duration ranging from 1 day to 2 months. Hepatosplenomegaly was noted in five cases. Hemoglobin ranged from 1.4 to 14.6 g/dL. Seven cases had thrombocytopenia, five of which had a rash on the body. Reactive lymphocytes [Figure 5a-c] were noted in seven cases, of which one had absolute lymphocytosis. Another case revealed relative lymphocytosis. A total of four cases had Downey cells suggestive of infectious mononucleosis, of which two were found to be positive for the monospot test and two patients were lost to follow-up. Two cases had HIV infection, of which one had tuberculosis. On BMAs, M:E ratio was 0.8:1–10:1. Four cases revealed a preponderance of immature megakaryocytes, one case had mild trilineage dysplasia and another had dyserythropoiesis. Lymphocytes in the BMA smear were in the range of 4%–60%. Enlarged early erythroblasts were noted in one case, however, no inclusions were found. Two cases showed hemophagocytosis. Both cases with HIV had reactive plasmacytosis with erythroid hyperplasia and megaloblastic maturation, mild gelatinous transformation was noted in one case.

A nonspecific infectious etiology [Figure 6a-f] was suggested in 20 cases, in the age group of 10–80 years. A history of fever for a period ranging from 2 days to 1 year was present in all but five cases. Seven cases had hepatosplenomegaly and four cases had isolated splenomegaly. Hemoglobin values noted were in the range of 3.1–11.8 g/dL. Pancytopenia was seen in seven cases, one case had bicytopenia (leukopenia and thrombocytopenia), four cases had isolated thrombocytopenia, two cases had mild leukocytosis while two cases had isolated leucopenia. Mild rouleaux formation was noted in five cases, and five cases had nucleated RBCs with dyserythropoiesis in four of them. On differential leucocyte count, neutrophils were in the range 10%–93%, lymphocytes 5%–90%, eosinophils 1%–22%, and monocytes 1%–26%. There was a left shift in the granulocytic series in four cases; four cases showed

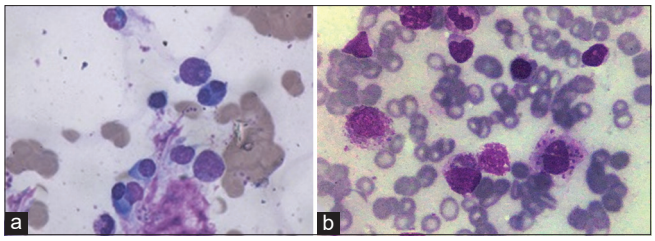

Figure 2: Bone marrow aspirate smear showing (a) reactive plasmacytosis (×400) and (b) intracellular amastigote form of *Leishmania donovani* (×1000) with a double dot appearance within the macrophage

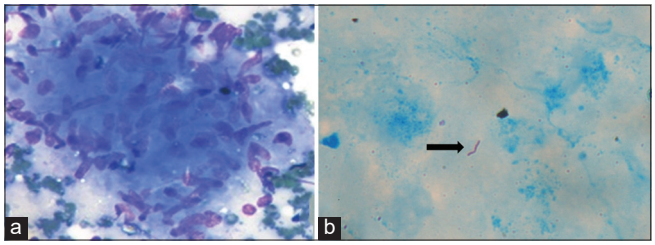

Figure 4: Bone marrow aspirate smear showing (a) epithelioid cell granuloma (×400); (b) Ziehl–Neelsen staining showing acid fast positivity (black arrow) in one of the cases confirming tubercular etiology (×1000)

toxic granulation in neutrophils, reactive lymphocytes were noted in four cases, reactive monocytes in three cases, and myeloid dysplasia in five cases. BMAs had M:E ratio ranging from 0.5 to 6.6:1. Dysplasia was noted in the erythroid lineage in eight cases, in the myeloid lineage in six cases and in the megakaryocytes in three cases. An increase in plasma cell percentage (4%–12%) was noted in seven cases with reactive changes like binucleation. There was relative myeloid hyperplasia in two cases, maturation arrest in myeloid lineage in four cases, toxic granulation in myeloid precursors in three cases, and lymphocytosis in three cases. Histiocytes were prominent in seven cases, all of which showed hemophagocytosis.

Discussion

BME is an invaluable diagnostic tool in the work-up of patients with pyrexia of unknown origin and pancytopenia.[1,2] The detection of features suggestive or diagnostic of an infectious disease process can provide support to the clinician's working diagnosis or help in appropriate and timely patient management, respectively. Our study was designed to provide comprehensive knowledge of morphologic features on peripheral smears and BMA smears which should make a pathologist suspicious of an infectious etiology.

Peripheral smear and BME have a key role in the diagnosis of parasitic infections, among which parasites such as malaria, babesia, trypanosoma, and microfilaria are usually detected in peripheral smears while leishmania is usually seen in BMAs. In our study, 100% of malaria demonstrated parasites in peripheral smear and 25% of cases revealed parasite in the bone marrow as well. Thrombocytopenia was found in

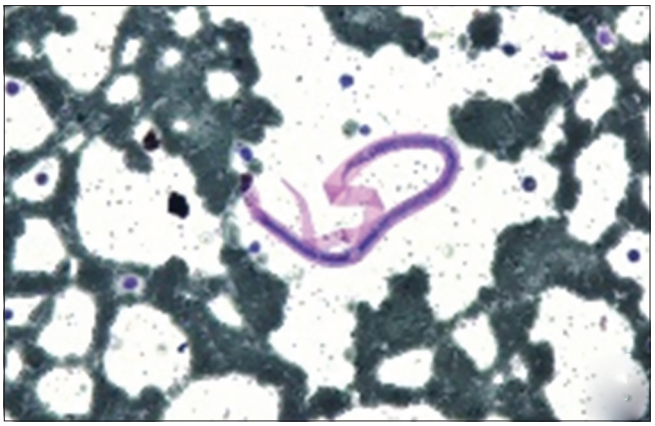

Figure 3: Bone marrow aspirate smear showing microfilaria, a sheathed structure with presence of numerous nuclei (×400)

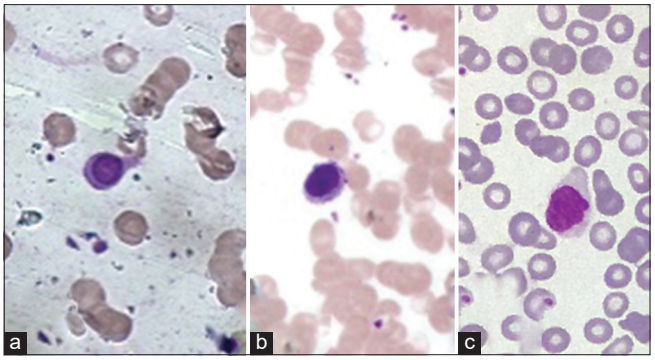

Figure 5: Peripheral smear (×400) showing (a-c) reactive lymphocytes in cases with viral infections with a large granular lymphocyte in (b) and Downey cell; (c) in a case of infectious mononucleosis

87.5% of cases which is similar to the reported figure of 60%–80% in other studies.[3,4] Possible causes are enhanced splenic sequestration, peripheral destruction, decreased platelet survival, or reduced platelet production.[5] Other potential associations were mild eosinophilia, mild monocytosis, hemozoin pigment in monocytes, and haemolytic anemia. Reported nonspecific associations with malaria include hemolytic anemia, monocytopenia or monocytosis, and pancytopenia.[6] However, it must be kept in mind that none of these is a specific indicator of the disease, but a combination of such findings in the appropriate clinical context should initiate a diligent search for the organism and if required, repeat blood films stained at an appropriate pH.

Leishmaniasis accounted for a total of four cases. A history of residence in or travel to endemic places, such as Bihar, Uttar Pradesh, Jharkhand, and West Bengal can usually be elicited in cases of leishmaniasis and should be especially sought in cases of fever with massive splenomegaly. In all four of our cases, a history of residence or travel to one of the endemic areas was present. BME is helpful for diagnosing leishmaniasis, with a reported diagnostic sensitivity of 55%–97%.[7] Reactive plasmacytosis and/or prominent histiocytes with hemophagocytosis are suggestive findings, and demonstration

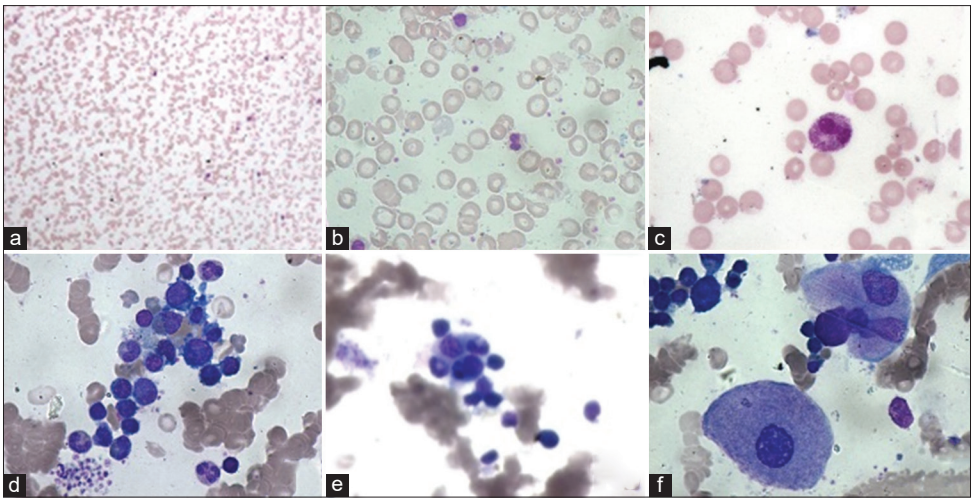

Figure 6: Soft pointers for infections: Peripheral smear showing (a) rouleaux formation (×40), (b) dysplastic neutrophil and dysplastic erythroblasts in the form of nucleated RBCs (×400), (c) toxic granules in a neutrophil (×400); Bone marrow aspirate smears showing (d) dyseryhtropoiesis (×400), (e) hemophagocytosis (×1000), (f) histiocyte with dyspoietic megakaryocyte (×1000). RBC: Red blood cell

of intracellular or extracellular parasites is diagnostic. All four of our cases of leishmaniasis were associated with reactive plasmacytosis and histiocytosis and hemophagocytosis was also noted in three and two cases respectively.

Besides Leishmaniasis, marrow plasmacytosis can be seen in various bacterial infections, viral infections (such as EBV and HIV), hypersensitivity, dysimmune diseases (such as Castleman disease and Immune thrombocytopenia), malignant diseases even without marrow involvement such as Hodgkin's Lymphoma, non-Hodgkin's Lymphoma, Chronic myeloid leukemia, and various other conditions as well such as iron deficiency anemia, megaloblastic anemia, and cirrhosis.[8] Erythroid hyperplasia, mild dyserythropoiesis, and dysmyelopoiesis have also been reported in association with leishmaniasis.[6] In our study, one of the case was associated with erythroid hyperplasia and dyserythropoiesis. Increased eosinophils and eosinophilic precursors are seen in 15%–27% of cases.[9,10] We, however, did not find any increase in eosinophils in any of our cases.

Filariasis affects over 120 million people worldwide.[11] Peripheral blood eosinophilia may serve as a nonspecific screening method in endemic areas.[12] In our study, out of two cases of filariasis, one case had mild eosinophilia with markedly raised erythrocyte sedimentation rate and the other case had marked eosinophilia in blood film and increased eosinophils and eosinophil precursors on BMAs. Microfilaria can be demonstrated in both peripheral smears and bone marrow.

Tuberculosis is a common cause of pyrexia of unknown origin in the Indian subcontinent. In a study by Gupta *et al*., 45% of cases of pyrexia of unknown origin were diagnosed as tuberculosis on BME.[1] Peripheral blood films' findings are suggestive of an infectious etiology in our study included toxic granulation in neutrophils, myeloid dysplasia and/or reactive lymphocytes. Other nonspecific features on bone marrow were relative myeloid hyperplasia, reactive plasmacytosis, and dysmyelopoiesis. Granuloma, giant cells, necrosis and/or demonstration of AFB are important morphological features for suggesting or confirming a diagnosis of tuberculosis. AFB was positive in only one case which was associated with HIV infection. This is in accordance with other studies where AFB has been demonstrated in 25% of the bone marrow biopsies only.[13]

Thrombocytopenia, relative lymphocytosis, and the presence of reactive lymphocytes are pointers to a viral etiology. Marrow lymphocytosis with the presence of atypical lymphocytes as seen on peripheral smear can also be seen. Hemophagocytosis and erythroid hyperplasia with giant erythroblasts and multinucleated erythroblasts along with the presence of viral inclusions are some of the marrow findings in viral infections.[8,14] A total of 12 cases had features suggestive of viral etiology in our study of which four were found to be associated with EBV (infectious mononucleosis) and two with HIV. Thrombocytopenia and relative lymphocytosis with reactive lymphocytes was the most common finding. Suggestive BMA findings in our study were the presence of immature megakaryocytes, dysplasia in one or more lineage, hemophagocytosis, and enlarged early erythroblasts.

We did not find any case with a fungal infection, the propensity of which is reported to be around seven percent in one of the studies.[15] Most of our cases were immunocompetent and fungal infection could not be detected in any case despite detailed morphological assessment and special stains.

Various soft pointers of an infectious etiology can be picked up on peripheral smear and BMAs which should result in a search for a specific cause. Even if a specific cause cannot be determined, the clinician should be informed of the possibility of an infectious etiology, so as to guide further testing and

management. Rouleaux formation, evidence of mild hemolysis, left shift in neutrophils, reactive lymphocytes, reactive monocytes, and erythroid or myeloid dysplasia (in the form of dyspoietic nucleated RBCs or pseudo pledger huet neutrophils, ringed neutrophils in myeloid series) on peripheral blood films are a few suggestive features. Bone marrow findings of relative myeloid hyperplasia, myeloid maturation arrest, toxic granulation, dysplasia in any of the hematopoietic lineages, reactive plasmacytosis, prominence of histiocytes and/or hemophagocytosis can be important pointers indicating an infective etiology.[8,16]

A high index of suspicion, detailed clinical history and examination, careful peripheral blood film and BMA smear examination, and a correlation of all findings are required to make a diagnosis of infection.

Conclusions

A careful and detailed examination of peripheral blood films and BMA smears must be performed in light of the clinical picture in each case. It is of important to make note of subtle findings, which in isolation or combination can alert the pathologist of an infectious etiology. A diligent search for parasites, granulomas, or viral inclusions should be done in suggestive cases. The suspicion of a nonspecific infection must also be reported to the clinician, as it can help in guiding patient management and in providing a direction to further testing in cases such as pyrexia of unknown origin and pancytopenia. A knowledge of these changes and careful examination of each smear can help extend the scope of marrow examination beyond hematolymphoid malignancies.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Gupta R, Setia N, Arora P, Singh S, Singh T. Hematological profile in pyrexia of unknown origin: Role of bone marrow trephine biopsy vis-à-vis aspiration. Hematology 2008;13:307-12.
2. Weinzierl EP, Arber DA. The differential diagnosis and bone marrow evaluation of new-onset pancytopenia. Am J Clin Pathol 2013;139:9-29.
3. Mueller I, Galinski MR, Baird JK, Carlton JM, Kochar DK, Alonso PL, *et al.* Key gaps in the knowledge of *Plasmodium vivax*, a neglected human malaria parasite. Lancet Infect Dis 2009;9:555-66.
4. Srichaikul T. Hemostatic alterations in malaria. Southeast Asian J Trop Med Public Health 1993;24 Suppl 1:86-91.
5. Angchaisuksiri P. Coagulopathy in malaria. Thromb Res 2014;133:5-9.
6. Miller CE, Bain BJ. The utility of blood and bone marrow films and trephine biopsy sections in the diagnosis of parasitic infections. Mediterr J Hematol Infect Dis 2015;7:e2015039.
7. Srivastava P, Dayama A, Mehrotra S, Sundar S. Diagnosis of visceral leishmaniasis. Trans R Soc Trop Med Hyg 2011;105:1-6.
8. Diebold J, Molina T, Camilleri-Broët S, Le Tourneau A, Audouin J. Bone marrow manifestations of infections and systemic diseases observed in bone marrow trephine biopsy review. Histopathology 2000;37:199-211.
9. Chandra H, Chandra S, Kaushik RM. Visceral leishmaniasis with associated common, uncommon, and atypical morphological features on bone marrow aspirate cytology in nonendemic region. J Trop Med 2013;2013:861032.
10. Daneshbod Y, Dehghani SJ, Daneshbod K. Bone marrow aspiration findings in Kala-Azar. Acta Cytol 2010;54:12-24.
11. Kaushal S, Iyer VK, Mathur SR. Morphological variations in microfilaria of *Wuchereria bancrofti* in cytology smears: A morphometric study of 32 cases. Acta Cytol 2012;56:431-8.
12. Musso D, Vialette V. Predictive value of the eosinophil counts in the biological diagnosis of lymphatic filariasis in French Polynesia. Med Mal Infect 2012;42:585-90.
13. Basu D, Saravana R, Purushotham B, Ghotekar LH. Granulomas in bone marrow – A study of fourteen cases. Indian J Pathol Microbiol 2005;48:13-6.
14. Jha A, Adhikari RC, Sarda R. Bone marrow evaluation in patients with fever of unknown origin. J Pathol Nepal 2012;2:231-40.
15. Kumar V, Bhatia A, Madaan GB, Marwah S, Nigam AS. Role of bone marrow examination in the evaluation of infections: Clinico-hematological analysis in a tertiary care Centre. Turk Patoloji Derg 2020;36:17-22.
16. Beffermann N, Pilcante J, Sarmiento M. Acquired hemophagocytic syndrome related to parainfluenza virus infection: Case report. J Med Case Rep 2015;9:78.