

Etiological Profile of Plasmacytosis on Bone Marrow Aspirates

Kemik İliği Aspiratlarında Saptanan Plazmasitozun Etyolojik Profili

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ABSTRACT

Objective: In recent years, during routine examination of bone marrow aspirates, an increased plasma cell percentage has been noted in a good number of cases which included both neoplastic and non-neoplastic diseases. An attempt has been made to observe the spectra of conditions with plasmacytosis in bone marrow.

Methods: The present study was conducted in the department of pathology over a period of one year. A total of 114 bone marrow aspirates that showed increased plasma cells (>3.5%) constitute the study material. A detailed relevant clinical examination followed by complete blood count, peripheral smear examination and bone marrow aspiration was done in all cases.

Results: There was slight female predominance with male to female ratio of 1:1.1. The majority of patients were in 4th decade. The plasma cell concentration ranged from 5% to 36%. As far as the etiology is concerned, 96 cases (84.2%) were non-neoplastic and 18 cases (15.7%) had neoplastic etiology.

Conclusion: Bone marrow plasmacytosis can present as diagnostic dilemma and some time can be challenging to differentiate reactive from neoplastic condition as there is an overlap both in counts and morphology. Each case with plasmacytosis especially in the overlap range requires complete clinical evaluation, individualized investigations and more specific tests like immunoelectrophoresis and bone marrow biopsy with immunohistochemistry to arrive at a final diagnosis for patient management.

Key words: Reactive plasmacytosis, bone marrow, multiple myeloma, megaloblastic anaemia

ÖZET

Amaç: Son yıllarda rutin kemik iliği aspiratı incelemelerinde saptanan neoplastik ve non-neoplastik hastalıklarda giderek artan oranlarda plazma hücrelerine rastlanmaktadır. Bu çalışmada kemik iliği aspiratında plazmasitoz saptanan durumların bir spektrumu çıkarılmaya çalışılmıştır.

Yöntemler: Sunulan çalışma bir yıllık süre içinde Patoloji Bölümünde gerçekleştirildi. Çalışma materyalini artmış oranda plazma hücresi (>%3,5) gösteren toplam 114 kemik iliği aspiratı oluşturmaktadır. Tüm olgularda ayrıntılı bir klinik muayene ve takiben tam kan sayımı, periferik yayma ve kemik iliği aspirasyonu yapıldı.

Bulgular: Erkek / Kadın oranı açısından hafif bir kadın üstünlüğü görüldü (1 / 1,1). Vakaların çoğu 40'lı yaşlarda idi. Plazma hücre yoğunluğu %5-36 arasında değişmekte idi. Etyoloji açısından 96 (%84,2) olguda non-neoplastik, 18 (%15,8) olguda ise neoplastik bir etyoloji saptandı.

Sonuç: Kemik iliği plazmasitozu tanısız bir karmaşaya yol açarak, özellikle sayı ve morfolojik görünümünde çakışma olan reaktif patolojilerin neoplastik durumlardan ayırt edilmesini bazen zorlaştırabilir. Özellikle çakışma aralıklarındakiler başta olmak üzere, plazmasitozlu her hastada bireyselleştirilmiş araştırmalar ve immünelektroforez ve immunhistokimya ile boyanmış kemik iliği aspiratı incelemesi ile sonuç tanısı konabilir ve hasta yönetimi gerçekleştirilebilir.

Anahtar kelimeler: Reaktif plazmasitoz, kemik iliği, multipl miyelom, megaloblastik anemi

INTRODUCTION

Bone marrow plasmacytosis occurs in association with variety of conditions both non-neoplastic such as infections, immune disorders, various type of

anemias as well as neoplastic conditions including primary and secondary malignancies. In most neoplastic conditions, plasma cell constitutes ~10-20% of all nucleated cells but may reach up to 50%

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[1,2,3]. It is important to differentiate reactive plasmacytosis in non-neoplastic conditions from the malignant ones. High marrow plasma cell count can present a diagnostic dilemma. An attempt has been made to observe the spectra of conditions with plasmacytosis in bone marrow.

METHODS

The present study was conducted in Department of Pathology, Pt.B.D. Sharma PGIMS, Rohtak from July 2013 to June 2014. A total of 114 bone marrow aspirates that showed increased plasma cells constitute the study material. More than 3.5% was selected as the arbitrary limit above which the plasma cells were considered abnormal [4]. A detailed relevant clinical examination was done. Complete blood count was performed using an automated five part hematology analyzer (Mindray BC 5800) and peripheral smears were examined in all cases. All the bone marrow aspirate smears were stained with Leishman's stain and differential counts were done on 500 cells. Special staining for Sudan Black B, Periodic acid Schiff and Perl's stain on the smears done wherever indicated. Bone marrow biopsy was done for evaluation of bone marrow in cases with insufficient cells, dry tap or hypoplastic bone marrow. Further investigations including estimation of serum gamma globulins on Serum Protein Electrophoresis was performed to rule out or establish monoclonality.

RESULTS

A total of 830 bone marrow aspirations were received during the study period for various haematological disorders. Out of them, 114 cases (13.7%) showed increase plasma cells. There were 53 (46.4%) males and 61 (53.5%) females. The patients had age ranging from 4 months to 85years, maximum number of patients (n=52) was more than 40 years.

The chief presenting complaints were fever, weakness, body ache, bone pain, abdominal pain, melena and bleeding. Hepatosplenomegaly and lymphadenopathy were found in 39 cases (34.2%) and 17 cases (14.9%) respectively. The associated peripheral blood findings in descending order were anemia 59 cases (51.7% cases), pancytopenia 47 cases (41.2%), thrombocytopenia 14 cases (12.2%) and leukocytosis 5 cases (4.3%).

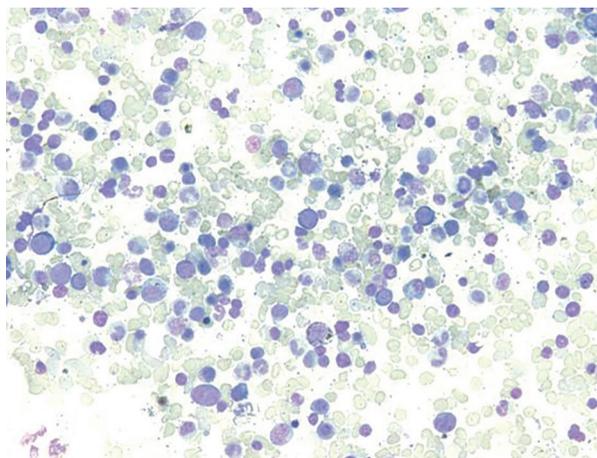


Figure 1. Bone marrow Aspirate showed megaloblastic erythroid hyperplasia with plasmacytosis (Leishman stain \times 100X)

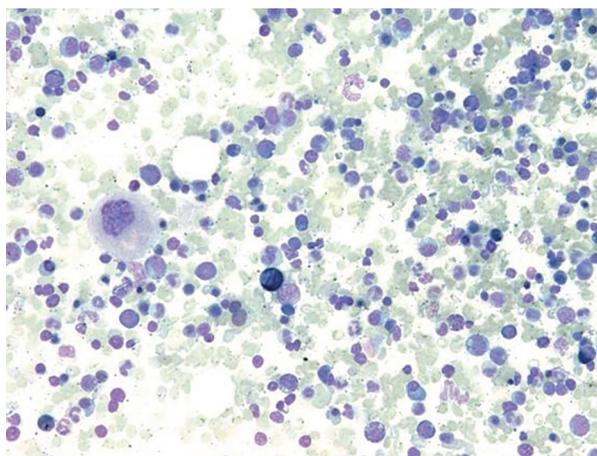


Figure 2. Bone marrow Aspirate showed nonspecific myeloid reaction with plasmacytosis (Leishman stain \times 100X)

The plasma cell concentration ranged from 5% to 36%. The cases were arranged according to the plasma cell percentage, 88 cases (77.1%) had 5-9%, 16 cases (14.0%) had 10- 20% and 10 cases (8.7%) had > 20% plasma cells respectively. As far as the etiology is concerned, 96 cases (84.2%) were non-neoplastic and 18 cases (15.7%) had neoplastic etiology [Table 1] [Figure1, Figure 2, Figure 3, Figure 4].

Other significant findings on the bone marrow aspirates revealing plasmacytosis were lymphocytosis 47 cases (41.2%), prominence of reticulum cells 26 cases (22.8%) and increased eosinophilic precursors in 9 cases (7.8%).

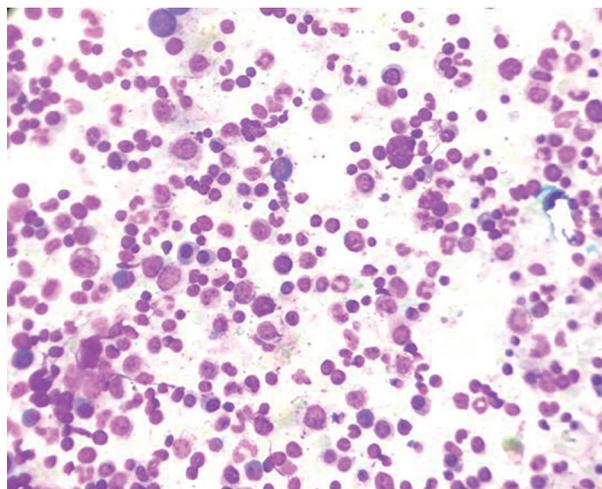


Figure 3. Bone marrow Aspirate showed normoblastic erythroid hyperplasia with plasmacytosis (Leishman stain x 100X)

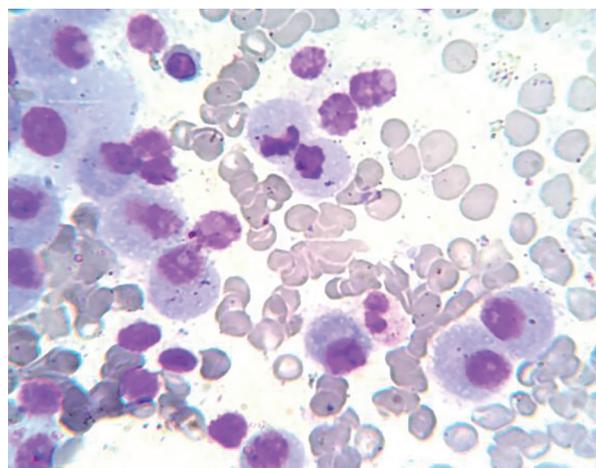


Figure 4. Bone marrow Aspirate showed plasmacytosis (Leishman stain x 1000X)

Table 1. Clinical presentation and bone marrow findings in patients with plasmacytosis

Non neoplastic	Clinical and/or bone marrow diagnosis	n	%
Anemia (n=77)	Nutritional deficiency anemia	40	35.0
	Hemolytic anemia	17	14.9
	Hypoplastic marrow	20	17.5
Thrombocytopenia (n=6)	Megakaryocytic	5	4.3
	Amegakaryocytic	1	0.8
Infections (n=4)	Non-specific myeloid reaction	13	11.4
	Acute Leukemia	4	3.5
Primary neoplastic (n=6) Leukemia	Chronic Myeloid Leukemia	1	0.8
	Chronic Lymphoproliferative disorder	1	0.8
	Multiple Myeloma	10	8.7
Plasma cell dyscrasias (n=11)	Waldenstrom Macroglobinemia	1	0.8
	Metastasis	1	0.8
Secondary (n=1)			

DISCUSSION

In recent years, during routine examination of bone marrow aspirates, an increased plasma cell percentage has been noted in a good number of cases, which included both neoplastic and non-neoplastic diseases.

Reactive plasmacytosis is polyclonal characterized by a diffuse distribution of mature plasma cells in the bone marrow. Morphological features suggesting a reactive nature of plasma cells, although not specific, are mature forms of plasma cells, perivascular location of plasma cells and plasmacytic satellitosis [5,6].

The mechanism of polyclonal proliferation of plasma cells is probably multifactorial and is considered as a defense response mechanism to the underlying disease processes. Some types of infection and abnormal immune reactions also lead to marked proliferation of plasma cells [2]. Increased release of paracrine growth factors such as cytokines, IL-6 or IL-10 are known to stimulate plasma cell generation, may also contribute to this process [5,6,7].

Reactive conditions such as chronic infection, autoimmune diseases, hypersensitivity states, megaloblastic anemia, hemolytic anemia, diabetes mellitus, cirrhosis, drug related agranulocytosis streptokinase treatment, angio-immunoblastic lymphade-

nopathy and multicentric Castleman's disease are associated with bone marrow plasmacytosis [1,2,3].

Neoplastic processes are diagnosed based on morphological findings, protein electrophoresis and bone marrow immunohistological examination. In myelomatosis, the marrow is most often hypocellular that is reduced hematopoietic elements, and the plasma cells mainly abnormal, shifted to the left, focal in distribution, associated with reticulum cells, and usually more numerous than 20% [8].

In our study, we have tried to represent the data related to degree of plasmacytosis in various conditions. Less than 10% plasmacytosis has been chiefly found in various types of anemia, 10- 30% plasma cells were found infections and hypoplastic marrows. In reactive conditions, the percentage range was 5%- 24%. However, in cases of plasma cell dyscrasias the range varied from 20- 40%. In non-neoplastic conditions plasma cells were chiefly mature however, in plasma cell dyscrasias range of mature and immature plasma cells was found. The marrows in plasmacytic response were usually normocellular for age, and the plasma cells were mainly mature, uniformly distributed, often related to reticulum cells, and rarely more numerous than 20% of the total count. In our study, maximum cases (84.2%) with plasmacytosis had a benign etiology.

The mechanism of the significance of bone marrow plasmacytosis has not been addressed. Bone marrow plasmacytosis can present as diagnostic dilemma and some time can be challenging to differentiate reactive from neoplastic condition as there is an overlap both in counts and morphology. Each case with plasmacytosis especially in the overlap range requires complete clinical evaluation,

individualized investigations and more specific tests like immunoelectrophoresis and bone marrow biopsy with immunohistochemistry to arrive at a final diagnosis for patient management.

Declaration of Conflicting Interests: The authors declare that they have no conflict of interest.

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