

Large Pink Inclusions in Multiple Myeloma Cells

This article was published in the following Scient Open Access Journal:

Journal of Blood Disorders, Symptoms & Treatments

Received July 28, 2017; Accepted August 05, 2017; Published August 11, 2017

Juan Zhang¹, Mingyong Li^{1*}, Xianyong Jiang² and Yuan He¹

¹Clinical Laboratory of Sichuan Academy of Medical Science & Sichuan Provincial People's Hospital, Chengdu, Sichuan, China

²Haematology Bone Marrow Inspection laboratory of Peking Union Medical College Hospital, Beijing, China

Abstract

Objective: Several intracytoplasmic morphological changes in the plasma cells of multiple myeloma have been described previously, especially the Auer rod-like inclusions, but large pink inclusions have not been reported yet. In this paper, we intend to report a rare case of inclusions in multiple myeloma.

Methods: Bone marrow aspiration from the right superior iliac spine was examined twice. Cells were stained with "Wright-Giemsa" method and also analyzed by flow cytometry, immunohistochemical staining and fluorescence in situ hybridization (FISH). Bone scan demonstrated bilateral ribs, thoracic vertebrae, with multiple low density shadows, which was confirmed subsequently as a lytic lesion on CT scanning. Complete blood count, serum chemistry and coagulation tests were also examined.

Results: Bone marrow aspirate from the right superior iliac spine at the time of myeloma diagnosis showed about 58.5% of all nucleated cells being plasma cells, of which many had large pink intracytoplasmic inclusions. Repeat bone marrow biopsy later showed persistence of these morphological findings. All of Flow cytometry, immunohistochemistry and FISH examination support the diagnosis of multiple myeloma.

Conclusion: This is the first time to report a multiple myeloma case with such giant pink inclusions. It is a rare and unique case. Due to its rarity, it remains unknown whether this morphological finding confers any prognostic implication.

Keywords: Multiple Myeloma (MM); Intracytoplasmic inclusion; M protein; Auer rod-like inclusions

Introduction

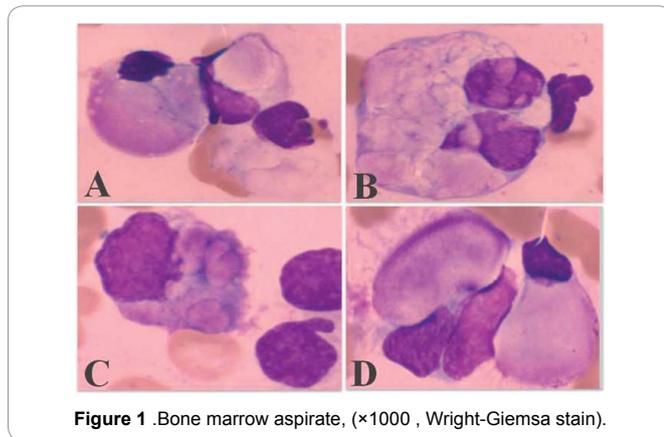
Cytoplasmic crystalline inclusion bodies in plasma cells have been repeatedly reported, mainly concentrated in the Auer rod-like inclusions. Additionally, spindle shaped, prismatic crystal, coarse azurophilic granules and so on have also been reported. Along with more MM patients were diagnosed, much more intracellular cytoplasmic inclusion bodies have been gradually reported, but the nature and prognosis of the inclusions are still not clear.

Case report

A 65-year-old woman presented with fatigue, dizziness, edema and weight loss. Bone scan demonstrated bilateral ribs, thoracic vertebrae, with multiple low density shadows, which was confirmed subsequently as a lytic lesion on CT scanning. Immunohistochemical results showed that CD38 (+), CD138 (+), CD15 (scattered+), CD20(+), CD79a(+), PC(+). The results of flow cytometry were consistent with those of immunohistochemistry. Fluorescence in situ hybridization (FISH) displayed IGH41 %(+), TP53(-). A complete blood count showed severe anemia. Haemoglobin was 67 g/L, white cell count $4.17 \times 10^9/L$, neutrophils $1.95 \times 10^9/L$, platelets $48 \times 10^9/L$. Alb 28g/L, Ca 1.96mmol/L, Glu 6.9mmol/L, K 4.2mmol/L, ALT 14U/L, Cr 56 $\mu\text{mol/L}$ with normal serum phosphate and bicarbonate levels and anion gap. Coagulation tests results: PT 15.1s, INR 1.32, APTT 22.1s, D-Dimer 9.22mg/L FEU, AT-III 66% (reference range 83-128). BNP 1149ng/L, NT-pro BNP 3242pg/ml. Serum protein electrophoresis (SPE): M protein 44.50g/L, IgG 41.96g/L, immunofixation electrophoresis (IFE): IgG κ Strongly positive. IgA 0.21g/L, IgM 0.27g/L, β_2 -MG 2.620mg/L, κ 707.5mg/dl, λ 6.23mg/dl, κ/λ 131.5. The patient was finally diagnosed with multiple myeloma, IgG κ type, Durie-Salmon IIIA stage, ISS II stage.

A bone marrow aspiration revealed plasma cells constituted 58.5% of nucleated cells. The Figure 1 shows plasma cells demonstrating varied size, and the cytoplasm is filled with large or giant pink variable-shaped intracytoplasmic inclusion bodies, which

*Corresponding Author: Mingyong Li, Clinical Laboratory of Sichuan Academy of Medical Science & Sichuan Provincial People's Hospital, Chengdu, China, Postcode: 610072, Fax: +86 028-87394056, Tel: +86 028-87394644, Email: limingyong0115@163.com



push the nucleus to one side (panels A-D). Repeat bone marrow biopsy later showed persistence of these morphological findings.

Discussion

A few cases of multiple myeloma with intracytoplasmic inclusions are described in literature, of which most are described as Auer rod-like inclusions, other forms include needle-like, coarse, azurophilic granules, prismatic, spindle shaped, spherical, cylindrical shape and so on [1]. The varied crystalline intracytoplasmic inclusions can also be seen in other types of hematologic disorders, such as chronic lymphocytic leukemia, lymphoplasmacytic lymphoma, mucosa-associated lymphoid tissue lymphomas and acute myeloid leukemia [2], but still now, no reports have described large pink inclusions in any type of cells.

Since the first description of inclusions in myeloma by Steinmann in a case of a 51-year-old woman with a parasternal tumor [3], cytoplasmic crystalline inclusion bodies in neoplastic or mature plasma cells have been described. Steinmann was also the first time to prove that these inclusions do not originate from depositions of immunoglobulins but have been more recently confirmed to be of lysosomal origin (fusionated lysosomal granules), given their strong a-N-esterase activity and negativity with antibodies against immunoglobulin or light chain. Following that report, many more cases have been described [1,2,4-9]. Pooling together the cases reviewed by Hutter [1] and other

reports since then up to now, including our cases, it appears that this phenomenon is rare and is always associated with a IgG k-type paraprotein, only one case of λ light chain restriction [4-12]. Although plasma cell myeloma with these inclusion bodies has been considered to be a morphologic variant and has intrigued investigators, the prognostic value of this morphologic variant is currently unclear [9-12]. Additionally, there is still no known cytogenetic association nor any particular immunophenotypic characteristic relationship.

To the best of our knowledge, this is the first time to report a multiple myeloma case with such giant-variable shaped pink intracytoplasmic inclusions. Only with the description of more cases in the future can we then be able to draw some conclusions in this regard.

References

1. Hütter G, Nowak D, Blau IW, Thiel E. Auer rod-like intracytoplasmic inclusions in multiple myeloma. A case report and review of the literature. *Int J Lab Hematol*. 2009;31(2):236-240.
2. Gupta A, Gupta M, Handoo A, Vaid A. Crystalline inclusions in plasma cells. *Indian J Pathol Microbiol*. 2011;54:836-837.
3. Steinmann B. Über azurophile stabchenformige Einschlüsse in den Zellen eines multiplen myeloms. *Dtsch Arch Klin Med*. 1940;185: S49-S61.
4. Metzgeroth G, Back W, Maywald O, et al. Auer rod-like inclusions in multiple myeloma. *Ann Hematol*. 2003;82(1):57-60.
5. Ali N, Moiz B. Azurophilic inclusions in plasma cells. *Singapore Med J*. 2009;50(3):e114-15.
6. Frotscher B, Salignac S, Lecompte T. Multiple myeloma with unusual inclusions. *Br J Haematol*. 2008;144:1.
7. Kulbacki EL, Wang E. IgG- λ plasma cell myeloma with cytoplasmic azurophilic inclusion bodies. *Am J Hematol*. 2010;85(7):516-517.
8. Parmentier S, Radke J. Pseudo-Auer rods in a patient with newly diagnosed IgG myeloma. *Blood*. 2012;119(3):650.
9. Noujaim JC, D'Angelo G. Auer rod-like inclusions in kappa light chain myeloma. *Blood*. 2013;122(17):2932.
10. Abdulsalam AH, Bain BJ. Auer-rod like inclusions in multiple myeloma. *Am J Hematol*. Published Online First: 17 Dec 2013.
11. Oh SH, Park CJ. Auer rod-like crystal inclusions in plasma cells of multiple myeloma. *Korean J Hematol*. 2010;45(4):222.
12. Ramos J, Lorscheid R. Hemophagocytosis by neoplastic plasma cells in multiple myeloma. *Blood*. 2014;123(11):1634.