

Auer rod-like inclusions and hemophagocytosis in neoplastic cells of multiple myeloma

Abstract

Objective: Several intracytoplasmic morphological changes in the plasma cells of multiple myeloma have been described previously. However, Auer rod-like inclusions and hemophagocytosis are rarely found in these types of cells. In this paper, we intend to report a rare case of multiple myeloma.

Methods: Bone marrow aspiration from the right superior iliac spine was examined twice. Cells were stained with May-Grünwald-Giemsa method. Bone scan demonstrated a focal lesion in the left iliac crest, which was confirmed subsequently as a lytic lesion on CT scanning. By flow cytometry, plasma cells expressed CD38, CD138, and CD56, CD184 and were negative for CD10, CD19, CD20, CD22, CD27 and CyclinD1, with extensive strong Kappa light chain immunostaining. A complete blood count and serum chemistry were also examined.

Results: It was of note that bone marrow aspirate from the right superior iliac spine at the time of myeloma diagnosis showed about 15% of cells being plasma cells, many of which had Auer rod-like, needle-shaped or spindle-shaped intracytoplasmic inclusions in neoplastic plasma cells and phagocytosed erythroid progenitors and mature red blood cells in the aspirate. A smaller proportion of these inclusions were mixed with both needle-shaped and spindle-shaped intracytoplasmic inclusions. Unlike Auer rods in myeloid cells, these Auer rod-like inclusions were longer. Repeat bone marrow biopsy later showed persistence of these morphological findings and prominent hemophagocytosis.

Conclusions: To the best of our knowledge, this is the first time to report a multiple myeloma case with both needle-shaped or/and spindle-shaped intracytoplasmic Auer rod-like inclusions and hemophagocytosis phenomenon simultaneously. This is a rare and unique case. Due to its rarity, it remains unknown whether this morphological finding and hemophagocytosis phenomenon confers any prognostic implication for patients with plasma cell dyscrasias.

Case

A 61-year-old man presented with fatigue, edema and weight loss. Bone scan demonstrated a focal lesion in the left iliac crest, which was confirmed subsequently as a lytic lesion on CT scanning. A complete blood count showed severe anemia. Hemoglobin was 72g/L, white cell count $4.17 \times 10^9/L$, neutrophils $1.95 \times 10^9/L$, platelets $48 \times 10^9/L$. Serum creatinine was $328 \mu\text{mol}/L$; adjusted serum calcium was $2.04 \text{ mmol}/L$ with normal serum phosphate and bicarbonate levels and anion gap. The LDH level of the patient was $208 \text{ U}/L$, with reference range of $0-250 \text{ U}/L$. Serum protein electrophoresis demonstrated IgG of $6.4 \text{ g}/L$, IgA $1.32 \text{ g}/L$, IgM $1.04 \text{ g}/L$. Urinary $\beta 2$ -microglobulin protein measured $32 \text{ mg}/L$. Serum free κ light chains were $702 \text{ mg}/dL$ ($598-1329$) and λ light chains $309 \text{ mg}/dL$ ($298-665$).

Bone marrow aspirate from the right superior iliac spine at the time of myeloma diagnosis showed about 15% of cells being plasma cells (Figure 1). Approximately 7% of the neoplastic plasma cells had Auer rod-like, needle-shaped or spindle-shaped intracytoplasmic inclusions (panels A-D) and phagocytosed erythroid progenitors (red arrows) and mature red blood cells (blue arrows) in the aspirate (panels A-C). A smaller proportion (about 2%) of these inclusions was mixed with both needle-shaped and spindle-shaped intracytoplasmic inclusions (panels D). Unlike Auer rods in myeloid cells, these Auer rod-like inclusions were longer. Repeat bone marrow biopsy later showed persistence of these morphological findings and prominent

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hemophagocytosis. By flow cytometry, plasma cells expressed CD38, CD138, CD56 and CD184, and were negative for CD10, CD19, CD20, CD22, CD27 and CyclinD1, with extensive strong Kappa light chain immunostaining. Finally, the patient was diagnosed as IgG κ MM, Salmon-Durie B stage and ISS stage.

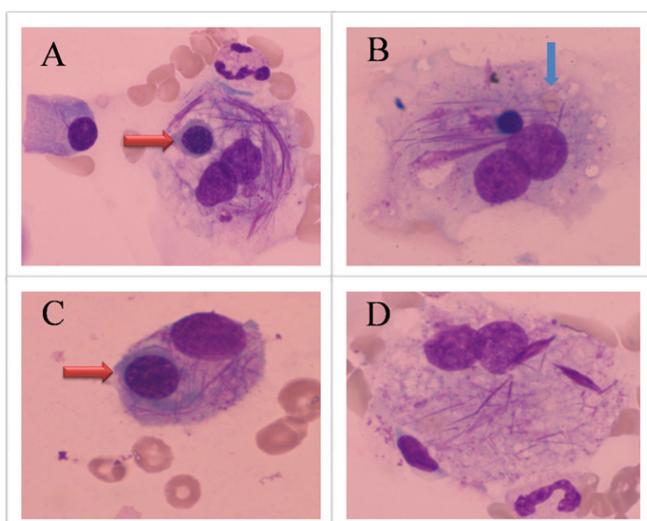


Figure 1 Bone marrow aspirate, ($\times 1000$, may-Grünwald-Giemsa stain).

The first description of such inclusions in myeloma is commonly attributed to Steinmann who described it in a case of a 51-year-old woman with a parasternal tumor.¹ Although there were prior reports of intracytoplasmic crystalline inclusions in myeloma, Steinmann was able to prove for the first time that these findings do not originate from depositions of immunoglobulins.¹ Following that report, a further handful of cases have been described.²⁻¹⁶ Pulling together the cases reviewed by Hutter et al.² and all other reports since then up to now and including our case, it appears that nearly all displayed κ light chain restriction (24 of 26 cases, 92%); only two cases of λ light chain restriction has been described.^{5,6} In terms of frequency of the involved immunoglobulin class, one-half of cases were associated with an IgG monoclonal paraprotein (14 of 28 cases, 50%), followed by eight cases (28%) with isolated serum-free light chains or Bence-Jones proteinuria without the involvement of intact immunoglobulins, four of IgA (14%) and one case each of an IgM and combined IgG-IgM paraproteinemia. These inclusion bodies were initially thought to be depositions of excessive immunoglobulins, but have been more recently confirmed to be of lysosomal origin, given their strong a-N-esterase activity and negativity with antibodies against immunoglobulin or light chain.^{2,11,12} According to the results, we hypothesize that the inclusion bodies may be the fusionated lysosomal granules. However, since this morphological pattern of presentation of multiple myeloma is very rare, its prognostic significance is currently largely unknown.

Hemophagocytosis in multiple myeloma has been reported in literature mostly by histocytes or rarely by plasma cells. Hemophagocytosis by neoplastic plasma cells has rarely been described.^{12,17} Jeanette Ramos et al.¹⁷ reported a case with infiltrating of atypical plasma cells comprising of 20% nucleated cells, diagnostic of plasma cell myeloma, many plasma cells contained phagocytosed red blood cells, erythroid progenitors and platelets in the aspirate and biopsy. By flow cytometry, plasma cells expressed CD38, CD138, and CD56 and were negative for CD45, CD19, CD20, CD27, and CD81. Our case is similar to the reported case, while it not only has hemophagocytosis phenomenon, but also has needle-shaped or/and spindle-shaped intracytoplasmic Auer rod-like inclusions simultaneously. On the basis of the few reported cases,^{12,17} hemophagocytosis does not appear to be associated with any recurrent myeloma-associated genetic abnormality, nor is it associated with any particular immunophenotypic characteristics. While cytopenias have been reported in some cases, it is uncertain whether they are a direct result of the hemophagocytic activity of the neoplastic plasma cells.

To the best of our knowledge, this is the first time to report a multiple myeloma case with both needle-shaped or/and spindle-shaped intracytoplasmic Auer rod-like inclusions and hemophagocytosis phenomenon simultaneously. This is a rare and unique case. Due to its rarity, it remains unknown whether this morphological finding and hemophagocytosis phenomenon confers any prognostic implication for patients with plasma cell dyscrasias. Unfortunately, the patient of our case died quickly and was only one week since the final diagnosis. Additionally, there is no known cytogenetic association as most reports have not provided results of karyotyping, nor is it associated with any particular immunophenotypic characteristics. Only with the

description of more cases in the future can we then be able to draw some conclusions in this regard.

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Conflict of interest

The author declares no conflict of interest.

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