Received: 19 November 2023 | Accepted: 18 April 2024

DOI: 10.1111/ijlh.14304

CASE IMAGE

ISLH International Journal of Laboratory Hematology WILEY

Differentiation syndrome in acute promyelocytic leukemia: A leopard cannot change its spots

Giulia Schiavini | Sabine Blum | Gerasimos Tsilimidos

Service and Central Laboratory of Haematology, Department of Oncology, Lausanne University Hospital (CHUV), Lausanne, Switzerland

Correspondence
Giulia Schiavini, Service and Central Laboratory of Haematology, Department of Oncology, Lausanne University Hospital (CHUV), Rue du Bugnon 46, Lausanne CH-1011, Switzerland.
Email: giulia.schiavini@chuv.ch

KEYWORDS: acute leukemias, granulopoiesis, neutrophils

Auer rods were first observed in 1903 by John Auer at John Hopkins Hospital. Since then, these rod or needle shaped azurophilic cytoplasmic inclusions, became the hallmark of acute promyelocytic leukemia (APL). They derive from the crystallization of myeloperoxidase (MPO) granules and in acute promyelocytic leukemia they can be organized in bundles, called faggot cells. Their presence in other myeloid leukemia is correlated with more differentiated blasts.[1]

The *PML-RARA* fusion oncoprotein, found in APL leukemia, is responsible for the accumulation of promyelocytes, by blocking cell differentiation. Arsenic trioxyde (ATO) and all-trans retinoic (ATRA)

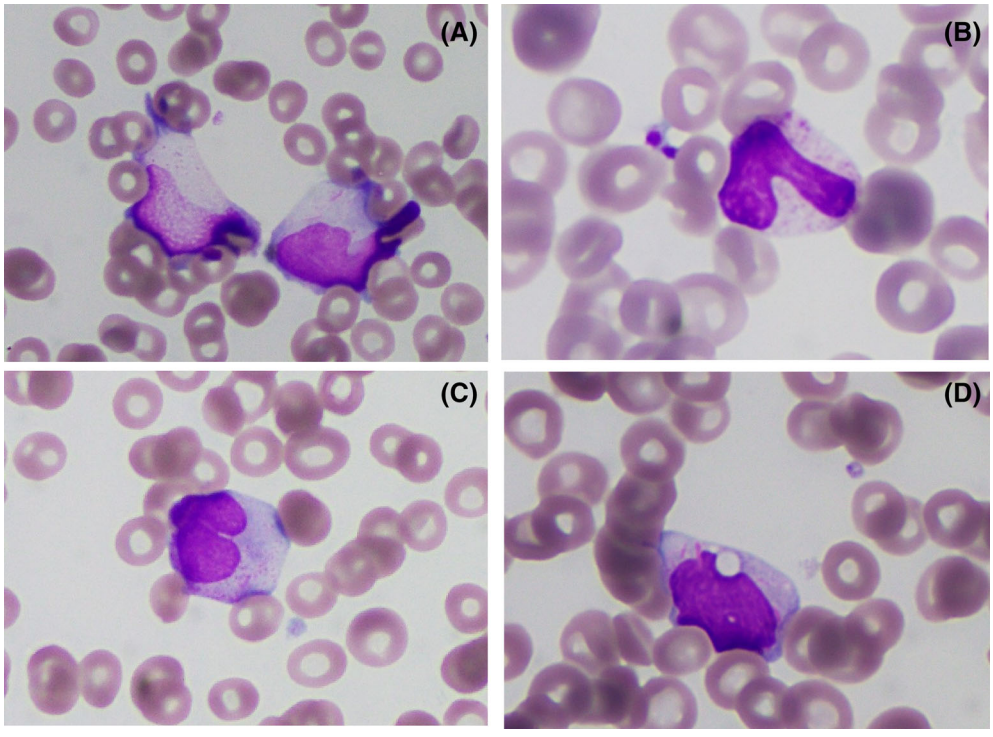

FIGURE 1 (A–D) Peripheral blood smears showed myelocytes (A–D), metamyelocyte (C) and banded neutrophils (B) with needle shaped cytoplasmic inclusions consistent with Auer rods. (Wright-Giemsa stain).

revolutionized the treatment and prognosis of APL, by triggering cell differentiation from promyelocytes to mature granulocytes.

Auer rods can also be identified in promyelocytes undergoing differentiation and can last until the latest stage of maturation, the neutrophils. This characteristic is specific of APL blasts.[2] In fact, Auer rods can be found in blasts of other AML as well as in MDS, where immature cells are targeted by chemotherapies but do not undergo differentiation. In this setting the persistence of blasts with Auer rods post treatment correlates with a poor prognostic value. Nevertheless, only in the case of differentiation syndrome in APL we might detect maturing cells promyelocyte-derived, containing Auer rods. This is not a sign of not response to treatment and does not require a deviation from the ATO-ATRA induction protocol. Clinicians and hematopathologists should keep this in mind in order not to misinterpret the images and continue with the treatment.

A 40-year-old woman, presented with pancytopenia and was diagnosed of APL. Bone marrow showed a massive infiltration of promyelocytes with Auer rods. The *PML-RARA* gene fusion confirmed the diagnosis and ATRA-ATO induction therapy was started. She developed a differentiation syndrome starting from day 12 after the beginning of ATRA and ATO, with immature cells in peripheral blood. The peripheral blood smear showed different stages of cells on differentiation, such as myelocytes (Figure 1A–D), metamyelocyte (Figure 1C), and neutrophils (Figure 1B), containing Auer rods. These immature circulating forms derive from the maturation of leukemic promyelocytes, having lost their ability to replicate, but still presenting some morphological characteristics of blasts, such as Auer rods.[3]

ACKNOWLEDGMENT

Open access funding provided by Universite de Lausanne.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

PATIENT CONSENT AGREEMENT

Informed consent has been obtained from the patient.

ORCID

Giulia Schiavini https://orcid.org/0009-0002-1537-5406
Gerasimos Tsilimidos https://orcid.org/0000-0002-0416-8420

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How to cite this article: Schiavini G, Blum S, Tsilimidos G. Differentiation syndrome in acute promyelocytic leukemia: A leopard cannot change its spots. *Int J Lab Hematol*. 2024;46(6):983-984. doi:10.1111/ijlh.14304