Received: 31 October 2023 | Revised: 21 November 2023 | Accepted: 27 November 2023

DOI: 10.1002/jha2.834

eJHaem

British Society for Haematology

HAEMATOLOGY IMAGES

# Erythroblastic islands: A fertile ground for CD47 expression in myelodysplastic syndrome and acute erythroid leukaemia

**Sophie Le Grand**[1] | **Christian Récher**[1] | **Alban Canali**[2] | **Véronique De Mas**[2] | **Jean-Baptiste Rieu**[2]

[1]Department of Haematology, University Hospital of Toulouse, Cancer University Institute of Toulouse, Oncopole, Toulouse, France

[2]Laboratory of Haematology, University Hospital of Toulouse, Cancer University Institute of Toulouse, Oncopole, Toulouse, France

**Correspondence**
Jean-Baptiste Rieu, Laboratoire d'Hématologie, Centre Hospitalier Universitaire de Toulouse, Institut Universitaire du Cancer—Oncopole, 1 Avenue Irène Joliot-Curie, 31100 Toulouse, France.
Email: rieu.jeanbaptiste@iuct-oncopole.fr

An 80-year-old man presented with myelodysplastic syndrome with excess blasts (MDS-EB) and complex monosomal karyotype (without del(17p)). Bone marrow examination (images, May–Grünwald–Giemsa, 100× objective) showed 5% myeloblasts, erythroid lineage predominance (87%) with 8% proerythroblasts, marked dyserythropoiesis (Figure 1, upper left image) and presence of numerous erythroblastic islands (Figure 1, lower left image). Due to worsening cytopenias after five cycles of 5-azacitidine, a new bone marrow aspirate was performed, revealing increased erythroblastic lineage (85% marrow cellularity) with 75% atypical immature erythroblasts (Figure 1, upper centre image), occasionally forming erythroblastic islands around macrophages (Figure 1, lower centre image), diagnosing acute erythroid leukaemia (AEL). Flow cytometric immunophenotyping confirmed expression of erythroid markers (CD235a, CD36 and CD71) in atypical immature erythroblasts (Figure 1, upper right image, in green), with no CD34 and myeloid markers (Myeloperoxydase (MPO), CD13, CD33 and CD117). Additionally, it revealed 3% myeloblasts expressing CD34 and all myeloid markers, but no erythroid markers (Figure 1, upper right image, in red). It also showed increased CD47 expression in atypical immature erythroblasts compared to other bone marrow cells, including myeloblasts (Figure 1, lower right image). Next-generation sequencing detected two *TP53* mutations (variant allele frequency (VAF) 43% and 44%). Considering the patient's age and comorbidities, supportive care has been implemented. Retrospective molecular testing confirmed the presence of the same two *TP53* mutations (VAF 47% and 47%) at the time of MDS diagnosis.

CD47 is a macrophage immune checkpoint, which is upregulated in MDS and acute myeloid leukaemia associated with a poor prognosis. Additionally, it has been shown that increased CD47 expression enhances intercellular mitochondria transfer between immature erythroblasts and macrophages within erythroblastic islands, promoting highly proliferative erythroid populations in physiologic erythropoiesis [1]. Although it has not been demonstrated yet, a comparable mechanism may occur in neoplastic erythroblastic islands. As illustrated in this case, MDS and AEL are recognised as part of a disease continuum and increased CD47 expression has been observed in both myeloblasts and erythroblasts [2]. Therefore, anti-CD47 immunotherapy should be a therapeutic option to consider in cases of AEL and MDS with increased dysplastic erythroid lineage. Above all, this case underscores the importance of gathering all relevant information at diagnosis to make treatment decisions considering the availability of novel therapeutic approaches.

## AUTHOR CONTRIBUTIONS

Sophie Le Grand, Jean-Baptiste Rieu, Christian Récher, Alban Canali and Véronique De Mas wrote the paper. Jean-Baptiste Rieu took the pictures. Jean-Baptiste Rieu performed the bone marrow examinations and flow cytometric immunophenotyping. Alban Canali per-

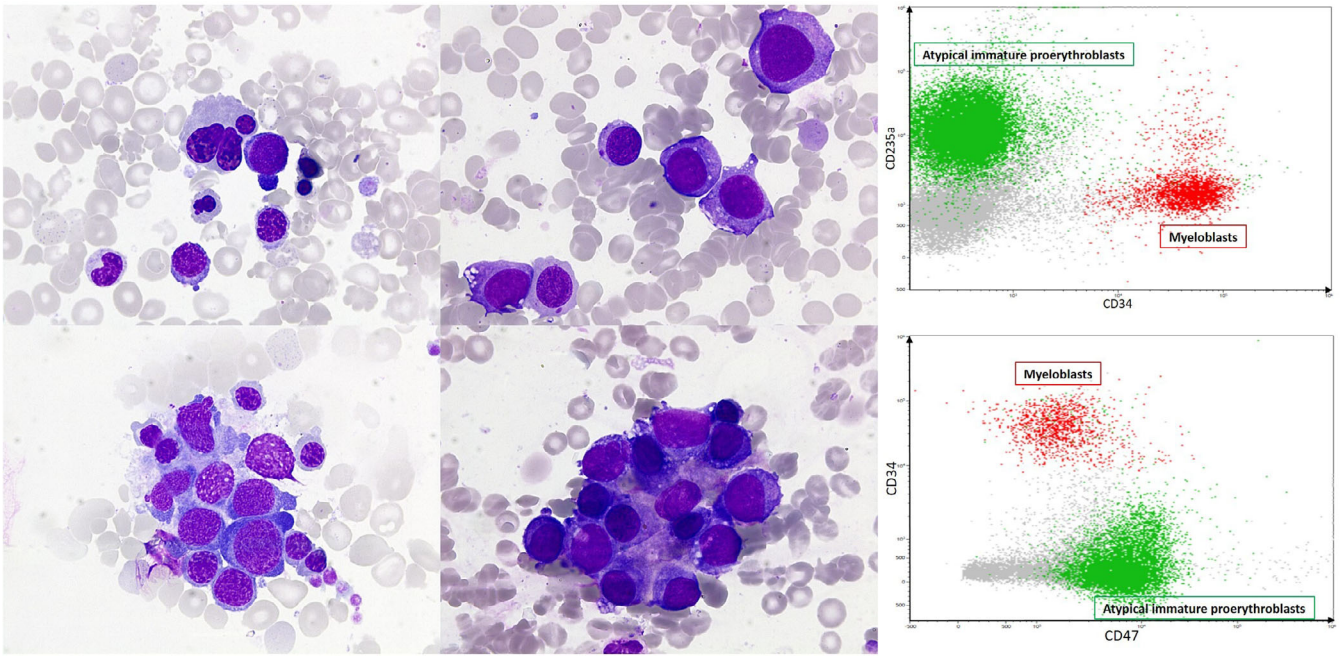


**FIGURE 1** Left images: Bone marrow examination at the time of myelodysplastic syndrome (MDS) diagnosis, May–Grünwald–Giemsa, 100× objective. Marked dyserythropoiesis with gigantism, nuclear budding and multinuclearity (upper left image). Erythroblastic island consisting of proerythroblasts and early to late erythroblasts surrounding a central macrophage (lower left image). Centre images: Bone marrow examination at the time of acute erythoid leukaemia (AEL) diagnosis, May–Grünwald–Giemsa, 100× objective. Atypical immature proerythroblasts (upper centre image). Erythroblastic island consisting of atypical immature proerythroblasts surrounding a central macrophage (lower centre image). Right images: Flow cytometric immunophenotyping in bone marrow sample showing CD34– CD235a+ atypical immature proerythroblasts (upper right image, in green) and CD34+ CD235a– myeloblasts (upper right image, in red) with an increased CD47 expression in atypical immature proerythroblasts (lower right image, in green).

formed cytogenetic studies. Véronique De Mas performed molecular studies. Christian Récher and Sophie Le Grand performed clinical examination and follow-up of the patient.

## CONFLICT OF INTEREST STATEMENT

The authors declare they have no conflicts of interest.

## FUNDING INFORMATION

Centre Hospitalier Universitaire de Toulouse.

## DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analysed in this study.

## ETHICS STATEMENT

This manuscript respect ethics policy of CHU Toulouse for treatment of human research participants.

## PATIENT CONSENT STATEMENT

The authors did not obtain written informed consent from the patient but the patient did not object to his data being used for research purposes (as required by ethic policy of CHU Toulouse). Written permission for reproduction from the copyright owners will be provided if the submission is accepted.

## CLINICAL TRIAL REGISTRATION

The authors have confirmed clinical trial registration is not needed for this submission.

## ORCID

*Christian Récher* https://orcid.org/0000-0002-3332-4525
*Alban Canali* https://orcid.org/0000-0002-1609-3307
*Jean-Baptiste Rieu* https://orcid.org/0000-0002-0950-979X

## REFERENCES

1. Yang C, Yokomori R, Chua LH, Tan SH, Tan DQ, Miharada K, et al. Mitochondria transfer mediates stress erythropoiesis by altering the bioenergetic profiles of early erythroblasts through CD47. J Exp Med. 2022;219(12):e20220685. https://doi.org/10.1084/jem.20220685
2. Maag AH, Swanton H, Kull M, Vegi NM, Feuring M. Immunophenotypical profiling of myeloid neoplasms with erythroid predominance using mass cytometry (CyTOF). Cytometry A. 2023;103(7):551–62. https://doi.org/10.1002/cyto.a.24716

**How to cite this article:** Le Grand S, Récher C, Canali A, De Mas V, Rieu J-B. Erythroblastic islands: A fertile ground for CD47 expression in myelodysplastic syndrome and acute erythroid leukaemia. eJHaem. 2024;5:278–79. https://doi.org/10.1002/jha2.834