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LETTER TO THE EDITOR

Multidimensional radar dot-plots, do we need it for the screening of acute promyelocytic leukemia?

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Dear Editor,

Karai and co-workers [1] described a novel flow cytometry method based on multidimensional radar dot-plots to enhance the screening of acute promyelocytic leukemia (APL). With this method, they were able to discriminate both hyper-granular and hypo-granular forms of APL from other acute myeloid leukemia (AML) subtypes.

The authors found that regardless of the mechanisms leading to the formation of PML-RARA fusion protein, aberrant promyelocytes could be recognized based on a unique pattern and position on radar dot-plots. Therefore, the results of this flow cytometric technique can support the diagnosis of APL even in cryptic cases and prompt initiation of the appropriate treatment.

APL has a favorable outcome with around 80% cure rate. Yet APL represents a medical emergency requiring instant identification, patients' hospitalization, prompt start of tailored therapy, and accurate supportive care consisting of transfusion support to maintain the fibrinogen concentration above 100–150 mg/dl, the platelet count above 30–50 × 109/L, and careful monitoring of bleeding diathesis [2]

An early death rate mostly due to severe bleeding remains a major cause of treatment failure in this highly curable disease. For this reason, current guidelines recommend initiating all-trans-retinoic acid (ATRA) therapy based exclusively on clinical suspicion without waiting for any other investigation. Simultaneously, a sample should be sent to a referent laboratory to perform genetic tests [3]. Confirmation of APL diagnosis with genetic test is mandatory for two reasons: (1)To detect the presence of the PML-RARA fusion gene and (2) to confirm the ATRA sensitivity. This because of possibility of APL cases with alternative genes fusing with *rara*. In fact, the detection of alternative fusions partners of *rara* could lead to further therapy refinement because not all the described *rara* fusion partners are responsive to ATRA/arsenic trioxide (ATO)–based therapy.

In their paper, Karai and co-workers considered several approaches for the diagnosis of APL but they ignored the immunofluorescent analysis of the PML distribution pattern using anti-PML monoclonal antibody. As described in numerous reports [4–7], the identification of a characteristic micro-speckled nuclear pattern of the PML correlates with 100% concordance with the presence of the PML-RARA fusion gene detected by reverse-transcription polymerase chain reaction and indicate responsiveness to ATRA/ATO. This technique is easy to perform, requires a peripheral blood or marrow smear, and has a turnaround time of 2 h. That is to say, it takes only 2 h to confirm not only the diagnosis of APL but also to predict ATRA sensitivity.

In summary, although multidimensional radar dot-plots is a sophisticated and elegant method to establish the diagnosis of APL, it should not be considered as the first option in the screening of APL and ATRA sensitivity.

It has to be stressed that in the presence of a strong clinical suspicion of APL and concomitant absence of a characteristic micro-speckled nuclear pattern, ATRA therapy should not be stopped until genetic tests are done. In fact, there are rare APL cases with different *rara* fusion partners that could still be responsive to ATRA treatment.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Not applicable.

References

1. Kárai B, Habók M, Reményi G, Rejtő L, Ujfalusi A, Kappelmayer J, Hevessy Z (2019) A novel flow cytometric method for enhancing acute promyelocytic leukemia screening by multidimensional dot-plots. Ann Hematol. https://doi.org/10.1007/s00277-019-03642-w.
2. Lo-Coco F, Ammatuna E, Montesinos P, Sanz MA (2008) Acute promyelocytic leukemia: recent advances in diagnosis and management. Semin Oncol 35:401–409
3. Sanz MA, Fenaux P, Tallman MS et al (2019) Management of acute promyelocytic leukemia: updated recommendations from an expert panel of the European LeukemiaNet. Blood. https://doi.org/10.1182/blood-2019-01-894980
4. Falini B, Martelli MP, Bolli N et al (1997) Immunocytochemical diagnosis of acute promyelocytic leukemia (M3) with the monoclonal antibody PG-M3 (anti-PML). Blood 90:4046–4053
5. Gomis F, Sanz J, Sempere A, Plumé G, Senent ML, Pérez ML, Cervera J, Moscardó F, Bolufer P, Barragán E, Martín G, Sanz MA (2004) Immunofluorescent analysis with the anti-PML monoclonal antibody PG-M3 for rapid and accurate genetic diagnosis of acute promyelocytic leukemia. Ann Hematol 83:687–690
6. Gupta SK, Sazawal S, Mahapatra M, Saxena R (2010) Evaluation of PG-M3 antibody in the diagnosis of acute promyelocytic leukaemia. Eur J Clin Investig 40:960–962
7. Dimov ND, Medeiros LJ, Kantarjian HM, Cortes JE, Chang KS, Bueso-Ramos CE, Ravandi F (2010) Rapid and reliable confirmation of acute promyelocytic leukemia by immunofluorescence staining with an antipromyelocytic leukemia antibody: the M. D. Anderson cancer center experience of 349 patients. Cancer. 116:369–376