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Case Report

The Value of Tailored Therapy on Survival in High Risk MDS with Del5q: Report of an Unusual Case

Pasquale Niscola[1*], Carla Mazzone[1], Marco Giovannini[1], Nicolina Rita Ardu[1], Laura Cesini[1], Gianfranco Catalano[1-3], Nelida Ines Noguera[2,3], Stefano Fratoni[1], Paolo de Fabritiis[1], Esther Natalie Oliva[4]

[1]Hematology Unit and Pathology Department, S. Eugenio Hospital (ASL Roma 2), Rome, Italy

[2]Neuro Oncohematology Unit, Santa Lucia Foundation, IRCCS, Rome, Italy

[3]Department of Biomedicine and Prevention, Tor Vergata University of Rome, 00133 Rome, Italy

[4]Hematology Division, Great Metropolitan Hospital Bianchi Melacrino Morelli, Reggio, Calabria, Italy

***Corresponding author**: Pasquale Niscola, Department of Hematology, S. Eugenio Hospital, Rome, Italy

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Introduction

Interstitial deletions of chromosome 5q [del (5q)] are the most common cytogenetic abnormality in myelodysplastic syndrome (MDS), accounting for 10-15% of cases [1-3]. The most common breakpoint for (cancel: myelodysplastic syndrome; replacing for: MDS) MDS cases with isolated del (5q) is del (5) (q13q33) [4]. MDS with isolated del (5q) is associated with a relatively favourable prognosis and typical features, which include macrocytic anaemia, thrombocytosis, and the presence of hypolobated megakaryocytes [5]. When this cytogenetic finding occurs in high risk MDS or acute myeloid leukaemia, it is associated with an unfavourable outcome [1]. Treatment approaches differ according to the prognosis with an indication for lenalidomide for low risk MDS with isolated del (5q) [3, 6-8] and a common indication for azacitidine for high risk MDS [3,9], independent of karyotype. The clinical results in higher risk del (5q) MDS by lenalidomide, alone or in combination with azacitidine [10], are still limited [1,11]. In the present case, we report the sequential treatment with azacitidine followed by lenalidomide, upon clearance of bone marrow (BM) blasts that was not planned at the initial treatment stage but as the result of a tailored decision making which took into account the haematological status after six cycles of hypomethylating agent and the patient's preferences.

Case Presentation

Herein, we report on a 68-year-old woman who kept under our attention on May 2019 due to general malaise, fatigue, shortness of breath, and exertional dyspnoea. At admission, the patient presented with pallor and mild tachycardia without any other remarkable pathological findings. Her past medical history was consistent with thyroid carcinoma, treated 10 years (February 2009) later with surgery and radiotherapy, controlled arterial hypertension, and severe vertebral arthritis. A routine radiological work-up ruled out any significant abnormality. Coagulation, renal and liver function tests were normal. A complete blood count revealed a grade II neutropenia, mild thrombocytosis, and severe anaemia, for which she received transfusions with 4 packed red blood cell (pRBC) units within the first 10 days admission. Bone marrow (BM) smears and trephine biopsy revealed a norm cellular BM with multi-age dysplasia and increase megakaryocytes as well as 15% myeloid blasts. Karyotype analysis by G band staining on 20 metaphases showed a 46, XX, del (5) (q13q31), confirmed by fluorescence in situ hybridization. BM immunohistochemistry [12,13] ruled out TP53 overexpression (Figure 1). According to the

World Health Organization classification of myeloid neoplasms at that time [14], the diagnosis was MDS with excess blasts-2 (EB-2). Based on haematological and laboratory findings and according to the revised international prognostic scoring system (R-IPSS) for MDS [15], the patient was diagnosed with high-risk MDS (R-IPSS score 5.5). According to standard clinical practice [3,9], in February 2020, the patient received azacitidine 75 mg/m2 for 7 days including 2-day break (AZA 5-2-2) every 28 days for six cycles without any clinical complications but maintaining a remarkable dependence on pRBC transfusions. A comprehensive haematological re-evaluation demonstrated the disappearance of blast from BM, which showed a marked trilinear dysplasia with erythroid hypoplasia and increased micromegacaryocytes as well as the persistence of del (5q) cytogenetic abnormality. The blood crasis showed a persistent transfusion-dependent anaemia in absence of neutropenia as well as thrombocytosis. Even in the absence of any benefit on the anaemia, these findings indicated a clinical response to hypomethylating treatment that was proposed to be continued. However, given the persistence of the transfusion burden, the patient's fatigue and discouragement, as well as the distance from the haematological centre, she refused to continue on treatment and requested any other options for home care. So that, after a discussing the options with the patient and her family and the provision of an informed written consent, from March 2020 the patient is regularly receiving therapy with lenalidomide (10 mg/day for 21 days every 28 days) without any adverse events. After two weeks on treatment, she achieved a near normal haemoglobin level of 13.5 g/dl. After three months of lenalidomide treatment, a cytogenetic analysis showed a normal karyotype. The cytogenetic complete remission (CR) stably persisted until the present report. Indeed a comprehensive revaluation performed in January 2023 confirmed the lastly maintained CR after 34 months the start of lenalidomide therapy.

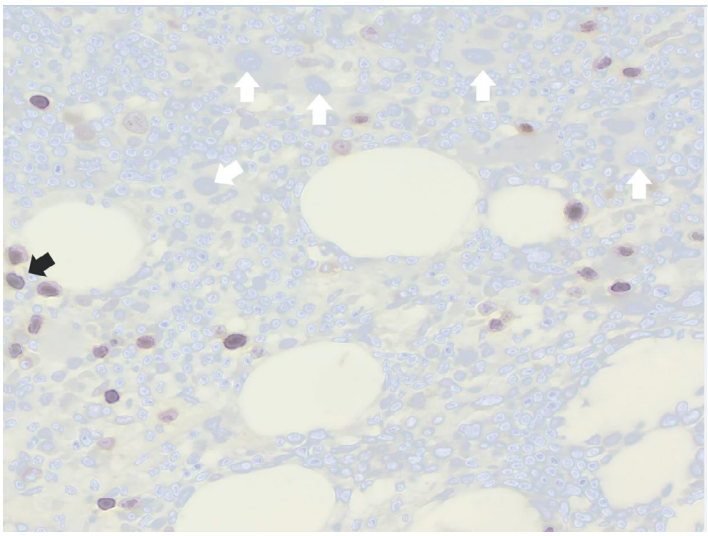

Figure 1: Low-risk del (5q) MDS: bone marrow is hyper cellular with numerous small sized megakaryocytes with round monolobated nuclei (white arrows). Around 5% of bone marrow cells show a strong p53 staining (black arrow).

Discussion and Conclusions

In conclusion, we report on a high-risk MDS patient harbouring a del (5q) abnormality, which confers a poor prognosis on the outcome of this neoplasm. In addition, our patient presented a negative TP53-mutational status, evaluated by immunohistochemically TP53 expression only [12,13]. The hypomethylating agent, azacitidine, represents the treatment of choice to treat high risk MDS, independent of karyotype, allowing for an overall response rate of 56%, including a 5.6% CR as well as a marrow CR rate of 11.1% [1,3,9]. Moreover, hypomethylating therapy may represent a reasonable option for low risk MDS with

del (5q) after the failure of first line therapy, such as lenalidomide [11]. The response to azacitidine reverted the patient's MDS to a prior MDS with isolated del (5q) allowing lenalidomide treatment to be effective in achieving a long-lasting CR. (complete remission: to be delated). Indeed, our patient is well and active 40 months after the primary MDS diagnosis, continuing to receive oral lenalidomide, compatible with her complete functional autonomy and quality of life. Although our case is anectodical and represents only an incidental observation, it may suggest that the sequential use of azacitidine followed by lenalidomide in del (5q) MDS patients responding, at least partially, to hypomethylating therapy may be a suitable option, which may deserve future controlled studies in large cohort of patient precisely stratified.

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

Compliance with Ethical Standards: Not applicable (the article does not contain any findings and/or images that make the patient recognizable; however, she has expressed informed consent to this report). No animals were involved in this research. The article was not founded.

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