Monoclonal Gammopathy Responsive to Decitabine Given for Acute Myeloid Leukemia in a Frail Patient

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The concomitant occurrence of acute myeloid leukemia (AML) and plasma cell dyscrasias has been sporadically reported [1–4]. This association may represent an incidental finding rather than a disorder of a common pluripotent stem cell. Although the pathogenesis of these coexisting disorders is unclear, a pathogenetic involvement of the inflammatory cytokine, interleukin (IL)-6, and the tumor suppressor p53 (TP53) has been suggested [5]. In addition, aberrant DNA methylation, which causes the inactivation of the promoter and consequently the inhibition of tumor-suppressive gene transcription (gene silencing), is a well-known and common event in AML [6] as well as in malignant plasma cell disorders [7–9], including monoclonal gammopathy of undetermined significance (MGUS) [7]. In particular, methylation changes in some upregulated genes were found in up to 17% of samples from MGUS patients [7]. Significant increasing apoptosis of malignant plasma cells exposed in vitro to epigenetic agents, such as azacitidine [9–10] and decitabine [11], has been demonstrated. In addition, simultaneous clinical responses to azacitidine in cases of MGUS concomitant with chronic myelomonocytic leukemia [12] as well as of AML coexisting with multiple myeloma [5] have

recently been reported. However, although it is not unexpected, the clinical antileukemic effect of decitabine in patients with coexisting AML and plasma cell disorder has not been observed in clinical practice so far. Herein, we report the case of an older AML patient with MGUS, diagnosed at the initial diagnostic work-up after admission due to symptomatic pancytopenia.

The patient was a 74-year-old man who presented with an oligoblastic myelodysplastic syndrome-related AML. At disease onset (November 2016), his bone marrow evaluation showed 23% myoblasts and 10% infiltrating malignant plasma cells associated with a serum IgG-kappa paraprotein (about 15 g/L), although the occurrence of overt multiple myeloma or amyloidosis was ruled out by the appropriate examinations. Therefore, the simultaneous occurrence of AML and MGUS was diagnosed. Given the patient's age and the burden of comorbidities, he was unsuitable for standard AML remission induction chemotherapy. Thus, according to regulatory prescription and institutional practice, he was started on decitabine (20 mg/m² for 5 days every 4 weeks) given with life-prolonging and palliative intent. Hypomethylating therapy with decitabine allowed for the achievement of complete AML remission that was

firstly demonstrated and subsequently confirmed after 4 and 12 treatment courses, respectively. Meanwhile, a progressive disappearance of the monoclonal peak from the electrophoretic pattern was observed, although the paraprotein was still only minimally detectable on immunoelectrophoresis until 12 months after the initiation of decitabine therapy. In addition, plasma cells were not found on bone marrow smears or the trephine biopsy specimen. This pattern of response has so far been stably maintained by regular epigenetic therapy (10 cycles of decitabine), which the patient continues to receive without remarkable side effects. Therefore, the 2 disorders, AML and MGUS, which were both concomitantly progressive before treatment, were responsive to decitabine. The complete remission of AML and, at the same time, the disappearance of paraproteins from the electrophoresis was achieved. While some evidence of epigenetic mechanisms exerted in vitro in malignant plasma cells by decitabine have been reported [11], no evidence regarding the clinical activity of this agent in the setting of plasma cell dyscrasia has been published to date.

In conclusion, we have provided an incidental observation of anecdotal value that is in line with our previous report on

chronic myelomonocytic leukemia patients [12], in which we observed the disappearance of MGUS under epigenetic therapy with azacitidine. Therefore, both azacitidine and decitabine, which are hypomethylating agents available in clinical practice, demonstrate novel and highly rel-

evant antimyeloma effects. Our findings suggest the need for further evaluation of the potential role of epigenetic therapy, either alone or ideally in combination with other antimyeloma compounds, in the treatment of patients with plasma cell neoplasms.

Disclosure Statement

The authors have no conflicts of interest to disclose.

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