INTERFERENCE OF DAPSONE IN HBA\textsubscript{1c} MONITORING OF A DIABETIC PATIENT WITH POLYCHONDritis

J. SERRATRICE (1), B. GRANEL (1), L. SWIADER (1), P. DISDIER (1), C. DE ROUX-SERRATRICE (1), D. RACCAH (2), P. J. WEILLER (1)

We report the case of a 80-year-old man treated with Dapsone (4,4'-diaminodiphenyl sulfone) for relapsing polychondritis. During the follow-up, diabetes mellitus appeared. Fasting glycemia remained high, but surprisingly HbA\textsubscript{1c} remained in the normal range. This unusual phenomenon is discussed.

CASE REPORT

A 80-year-old man was regularly surveyed in our service since 1987 for a relapsing polychondritis and treated with Dapsone, 100 mg per day, with a good outcome on chondritis. During the follow-up, a prostate carcinoma was diagnosed in 1990 and treated with surgery and brachytherapy. An \textit{in situ} bladder carcinoma was treated in 1997 with BCG therapy. Both carcinomas were regularly surveyed and remained controlled: PSA was \(< 0.5 \text{ ng/mL (N < 4)}, periodic bladder cytologies showed no malignant cells.

Biological survey showed a normal red blood cell count with a mild hemolysis [bilirubin = 35 mMol/L (0 < N < 17), LDH = 350 U/\text{L} (150 < N < 320) and reticulocytosis 155 \times 10^9/{\text{L}}] due to a chronic Dapsone-induced methemoglobinemia which was evaluated around 2%.

In 1999, fasting glycemia was controlled several times around 1.3 g/L (7.4 m\text{Mol/L}) checked on 100 U/\text{mL and 30U/mL} lithium heparinate test-tubes. Fasting insulinemia was normal at 6 m\text{Mol/L (4 < N < 6)} and HbA\textsubscript{1c} was in the normal range: 4.2% (N < 6.5%). Proteinuria was about 0.23 g/24 h and albuminuria around 58 mg/24 h (microalbuminuria). Diet was proposed and compliance was good during two years.

At the last visit in January 2002, he complained of polydypsia, polyuria and weight loss. Fasting glycemia was 1.7 g/L (9.5 m\text{Mol/L}). Several fasting glycemia were controlled per 24 hours. At 7 AM fasting glycemia was 1.93 g/L (10.7 m\text{Mol/L}). At 10 AM 2.07 g/L (11.5 m\text{Mol/L}). At 15 PM fasting glycemia was 2.52 g/L (14 m\text{Mol/L}). At 18 PM fasting glycemia was 2.07 g/L (11.5 m\text{Mol/L}). Glycated hemoglobin (HbA\textsubscript{1c}) was still normal: 4%. Insulinemia and plasma level of peptide C were also normal. Faced with such features, antidiabetic treatment with acarbose (Gluco\textsubscript{t}) was begun with a good outcome on clinical symptoms and glycemia. Since then, evaluation of long-standing glycemic control was based on fructosamine concentration and remained correct.

DISCUSSION

In our case, Dapsone (4,4'-diaminodiphenyl sulfone), an anti mycobacterium leprae and immunomodulatory agent was used to control a relapsing polychondritis with a good outcome on inflammation in an 80-year-old patient. Treatment tolerance was acceptable with a low level of dapsone-induced methemoglobinemia and hemolysis. During the follow-up, diabetes mellitus appeared. Fasting glycemia was controlled several times with different methods and remained high, since surprisingly HbA\textsubscript{1c} remained in the normal range.

Methemoglobin is hemoglobin in which the iron has been oxidized (\(\alpha\text{2}^{3+} \beta\text{2}^{3+}\)). This oxidized hemoglobin is no longer capable of reversibly binding oxygen and may be induced by dapsone treatment.
Four minor fractions of HbA called HbA_{1a1}, HbA_{1a2}, HbA_{1b}, HbA_{1c} have been separated by Allen, using red cell hemolysat chromatography [1]. HbA_{1c} may represent 5% of the total hemoglobin. These hemoglobins are progressively produced in circulating red blood cells during their 120 days life span. HbA_{1a1} and HbA_{1a2} respectively contain fructose 1-6 bisphosphate and glucose-6 phosphate fixed on N-terminal valin of beta chain. HbA_{1c} contains glucose fixed in the same way. This fixation between reductive function in 1 of glucose and the NH2 of valin requires Amadori rearrangement [1]. It is non-enzymatic and irreversible. Glucose level increases with red blood cell aging and is proportional to glucose concentration. In diabetes mellitus, HbA_{1c} may rise until 15% and evaluation of this glycated hemoglobin is used to evaluate long-standing glycemic control as recom-\text{mended by Diabetes Consensus Development Conference} [2]. As red cell life time is about 120 days, HbA_{1c} reflects the glycemic state of the past three months. Responsiveness of dapsone in lowering HbA_{1c} percentage has been shown in NOD mice [3]. Such an effect on HbA_{1c} can be secondary to hemolysis induced by N-hydroxy metabolites of dapsone responsive of hemolytic activity of dapsone [4] as in our observation. Thus dapsone affects the life span of erythrocytes and HbA_{1c} level. The fall in HbA_{1c} concentration is explained by increased erythrocytopoiesis as a product of drug-induced hemolysis [5]. Plasma fructosamine concentration is another method for evaluating intermediate-standing glycemic control and is not affected by hemolysis. So our case recalls that in patients presenting chronic hemolysis such as those treated with Dapsone, HbA_{1c} evaluation gives false low level and fructosamine evaluation may be preferred to estimate glycemic control.

REFERENCES

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