Letter to the Editor

A Case of Megaloblastic Anemia Due to Vitamin B₁₂ Deficiency Precipitated in a Totally Gastrectomized Type II Diabetic Patient Following the Introduction of Metformin Therapy

To the Editor;

We wish to report a totally gastrectomized type II diabetic patient, a 67-year-old woman, who developed megaloblastic anemia due to vitamin B₁₂ deficiency precipitated by the introduction of metformin therapy. She was diagnosed with type II diabetes at the age of 50, and glibenclamide administration was started. At the age of 60, she received a total gastrectomy because of gastric cancer. Following gastrectomy, she was switched to insulin therapy. In June 2000, since she hoped to be switched to oral anti-hyperglycemic therapy, 250 mg metformin was administered two times a day instead of the insulin therapy. She had not been clinically anemic until

she had started the metformin therapy (Fig. 1). Six months later, she stopped visiting our hospital because of her husband's illness. However, she continued to take metformin for an additional four months. In April 2001, when she revisited our hospital, we found that she had developed megaloblastic anemia. While receiving the metformin therapy, she did not show any marked body weight loss and/or diarrhea. Her hematological data were as follows: hemoglobin 10.7 g/dL, red blood cell count $2.61 \times 10^{12}/L$, mean corpuscular volume 120.3 fl (normal 78–110), and mean corpuscular hemoglobin 41.8 pg (normal 28.0–35.0). Her serum vitamin B₁₂ level fell to 131 pg/mL (normal 233–914). Since we believe that this patient's megaloblastic anemia may have been triggered by the introduction of metformin therapy, metformin administration was immediately terminated. In addition, mecobalamin was intramuscularly or orally administered as a vitamin B₁₂ supplementation over a period of three months. Her megaloblastic anemia gradually improved, and was cured within three months (Fig. 1). Since July 2001, our patient has been treated with 90mg nateglinide three times daily to control her blood glucose level. After the discontinuation of the metformin therapy, she has not been clinically anemic, and her serum vitamin B₁₂ levels have returned to

Fig. 1. Changes in hemoglobin (●), MCV (□), and MCH (■) in a type II diabetic patient with gastrectomy. MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin.

near-normal values between 200 to 250 pg/mL.

It is well known that long-term metformin therapy often decreases intestinal absorption of vitamin B₁₂ [1]. However, since very few patients develop megaloblastic anemia due to vitamin B₁₂ deficiency [2], this effect of metformin does not seem to cause serious clinical problems. Patients who have had a gastrectomy tend to have vitamin B₁₂ malabsorption problems due to the loss of intrinsic factors. Therefore, from our clinical experiences, the introduction of metformin therapy in gastrectomized patients appears to accelerate the vitamin B₁₂ deficiency state. In previously published studies [2, 3], it has not been clarified whether metformin can be administered to gastrectomized patients. Since it can sometimes take several years to develop clinical vitamin B₁₂ deficiency following gastrectomy, we cannot entirely exclude the suggestion that megaloblastic anemia observed in the present case may only be a long-term consequence of total gastrectomy. However, considering that our patient did not develop megaloblastic anemia due to vitamin B₁₂ deficiency following the discontinuation of metformin therapy, together with the finding that megaloblastic anemia was precipitated by the intro-

duction of metformin therapy, it seems likely that metformin administration may have contributed to the development of megaloblastic anemia in the present case. We suggest that metformin administration should be carefully performed in type II diabetic patients with gastrectomy.

References

1. Tomkin GH, Hadden DR, Weaver JA, Montgomery DAD (1971) Vitamin-B₁₂ status of patients on long-term metformin therapy. *BMJ* 2: 685–687.
2. Bailey CJ, Turner RC (1996) Metformin. *N Engl J Med* 334: 574–579.
3. Bailey CJ (1992) Biguanides and NIDDM. *Diabetes Care* 15: 755–772.

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