MEDICAL MEMORANDA

Sensitivity to Cyanocobalamin and Hydroxocobalamin

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The purpose of this paper is to draw attention to sensitivity to cyanocobalamin and hydroxocobalamin as a cause of chronic urticaria and to report the case of a patient who also reacted to vitamin B₁₂ given by mouth.

Reports on sensitivity to cyanocobalamin are few, though sensitivity reactions to parenteral liver extracts are well recognized. Anaphylactic reactions to vitamin B₁₂ injections, which in some cases were severe and included peripheral circulatory collapse, shivering, and death, have been recorded by Young *et al.* (1950), Borodulin (1961), Roy (1961), and Marinkovic (1962). Bedford (1952), Gillhespy (1955), and Ungley (1955) reported less severe allergic reactions. These findings were noted by Høvdning (1968) in his report of a case of anaphylaxis after intramuscular injection of vitamin B₁₂ in a patient who gave positive prick-test reactions to cyanocobalamin and hydroxocobalamin. Gillhespy (1955) reported that large doses of vitamin B₁₂ can be tolerated by these patients when given by mouth.

Case Report

A woman aged 50 presented with symptoms of subacute combined degeneration of the cord in 1960 and was found to have pernicious anaemia, with a megaloblastic blood picture and a positive Schilling test. She was successfully treated with cyanocobalamin injections for the next eight years. In January 1968, however, she had two episodes of swelling of the face, shivering, bronchospasm, dyspnoea, and aphonia after injections of vitamin B₁₂, and developed persistent urticaria, which was treated with antihistamines.

In October 1968 she was admitted to hospital for investigation of the chronic urticaria. Her blood picture was normal. Intradermal and prick tests with aseptically diluted proprietary preparations of cyanocobalamin and hydroxocobalamin *B.P.* giving a concentration of 100 µg/ml resulted in a negative immediate allergic response, but a very small erythematous papule of doubtful significance was observed at this site five hours later. It was felt that her symptoms might be due to a "suggestion" effect of the vitamin B₁₂ injections to which she attributed her symptoms; a change was therefore made, and cyanocobalamin cytamene 1,000 µg was given once monthly by intramuscular injection. The first injection given in

hospital caused no symptoms, but after the second she again had an attack of shivering and bronchospasm, and her urticaria lesions were present for about four days in every week.

In January 1969 a further change was made and she was given Distivit 100 µg by mouth twice daily (a vitamin B₁₂ peptide, orally active and a fomented product of cyanocobalamin); again she had symptoms of bronchospasm, dyspnoea, flushing, dizziness, and headache, and her urticaria persisted. She then stopped all treatment herself for two months, with subsequent return of symptoms of subacute combined degeneration and peripheral neuritis. She was then given Anahaemin 2 ml intramuscularly each week (liver extract containing cyanocobalamin) and later Neo-Cytamen (hydroxocobalamin). Though she had no anaphylactic symptoms the urticaria was persistent and widespread in spite of treatment with antihistamines. Her treatment was then changed to Bifactor (25 mg of intrinsic factor plus vitamin B₁₂ 7.5 µg = ½ U.S.P. anti-anaemia unit), but once more her urticaria persisted.

In November 1969 she was readmitted to hospital and found to have a normal blood count, but the pernicious anaemia was again confirmed by a Schilling test augmented with intrinsic factor. A glucose tolerance test was within normal limits and a barium-meal examination showed nothing abnormal apart from a small hiatus hernia. Her urticaria at this time was continuous and severe. She was treated with intrinsic factor 40 mg three times daily (supplied by Armour Pharmaceutical, Eastbourne), as Hogastrin had been out of production for several years, and her urticaria immediately subsided. In January 1970 she reported that she had not felt so well for years. Her serum vitamin B₁₂ was 816 µg/ml (normal 150-925), but she reported some tingling of the fingers. X-ray examination of the cervical spine showed posterior disc lesion space narrowing of C 3/4, C 4/5, C 5/6, and osteophytes, but no narrowing of the intervertebral foramina. In February 1970 she had no symptoms of peripheral neuritis, anaphylaxis, or urticaria.

Comment

It appears that this patient was indeed sensitive to cyanocobalamin and hydroxocobalamin, responding with anaphylaxis and chronic severe urticaria. We cannot explain her negative response to intradermal prick tests with cyanocobalamin and hydroxocobalamin. She was unable to tolerate the drug administered by injection or by mouth, though Gillhespy (1955) reported that the latter route is tolerated by patients sensitive to the injection. At the time of writing the urticaria seemed to have cleared completely since taking intrinsic factor alone, and the pernicious anaemia appeared to be under control.

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