

Neuropsychiatric symptoms following bismuth intoxication

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Summary: A number of seemingly neurotic symptoms, similar to those reported in bismuth intoxication, occurred in a patient taking a proprietary dyspeptic preparation, tri-potassium di-citrate bismuthate (De-Nol), over 2 years. The symptoms remitted over 10-12 months after stopping the drug - a similar period to that described in bismuth intoxication, and the patient has remained symptom-free for 7 years. Possible mechanisms are discussed.

Introduction

The term psychosomatic implies that psychological processes cause or exacerbate physical symptoms and dyspepsia is generally regarded under this rubric. Occasionally physical treatment can become a perpetuating factor for the symptoms and the source of seemingly neurotic symptoms. 'Seemingly' because one is tempted to regard such symptoms as 'functional', a term that today implies an absence of organic determinants. A case is described that illustrates such a process.

Case report

A 41 year old professional man with a previously healed duodenal ulcer, radiologically demonstrated, took a bismuth preparation tri-potassium di-citrate bismuthate (De-Nol) for approximately 2 years, intermittently as and when dyspeptic symptoms were troublesome. The manufacturers recommend only two courses, and only in the case of proven peptic ulceration. Initially two successive 28 day courses were taken as recommended, of 600 mg four times a day, 1/2 hour before meals or snacks, consisting of 5 ml of the preparation at a concentration of 120 mg/ml, diluted with 15 ml water. The patient continued to take the preparation at a reduced, estimated dose of 240 mg/day, diluted as before, after completing the two courses. The manufacturers recommend that milk and antacids are avoided during treatment and this recommendation was largely observed.

In the last 4 months of the 2 years' treatment the

patient began to experience increasingly troublesome numbness and paraesthesiae in both hands; the problem was particularly troublesome at night, creating difficulties in finding a sleeping posture which did not aggravate the condition. On one occasion he was obliged to sit down when he felt his heart beating irregularly while walking up a hill and generally felt unusually irritable and fatigued. He was troubled with restless insomnia and early morning waking and felt increasingly uneasy, particularly when driving his car. His concentration was poor and his short term memory was so impaired that he had difficulty remembering telephone numbers for long enough to dial them.

The paraesthesiae were readily induced by carrying a briefcase and were most noticeable in the right hand, largely confined to the ulnar distribution. On the left they varied between the ulnar and radial distribution.

On examination the hand paraesthesiae could be readily elicited by lightly rolling the ulnar nerve over the medial epicondyle of the humerus. A blue line could be seen in a small area of gum surrounding a crown. All reflexes were brisk and symmetrical. Radiological examination of the epicondyle region and wrist failed to reveal any abnormality.

The bismuth preparation was stopped and replaced with calcium and magnesium salts. All symptoms gradually disappeared. The dyspepsia remitted so completely that antacids were quickly discontinued. The hand paraesthesiae slowly improved, as did the insomnia and irritability. Short term memory, measured by digit span, increased, from six to eight digits, over a period of 10 months and was sustained at this level for the next 7 years. The patient began to enjoy an enhanced sense of well being and in retrospect saw

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Accepted: 24 November 1987

how handicapped he had insidiously become. No psychotropic medication was prescribed. The blue line faded but was still apparent, with a less sharply demarcated edge, a year later; eventually the gum retracted and a cosmetic extension was made to the crown.

Discussion

Similar symptoms to those reported here have been described by patients taking bismuth subgallate for colostomy management.¹⁻⁴ The suggestion that the gallic acid in bismuth subgallate may be responsible¹⁻³ seems unlikely in view of the French experience with bismuth subnitrate^{5,6} and the present report where similar symptoms were seen with a bismuth chelate.

Buge *et al.*⁷ describe a series of twenty cases of myoclonic encephalopathies following intoxication with bismuth subnitrate. Goule *et al.*,⁶ reviewing this work, together with Burns' original five cases and their own series of eight patients, conclude that the clinical picture is stereotyped, characterized by an asthenic, depressive state, with insomnia, disturbance of mood, extreme impairment of concentration, slowing of thought process, memory disturbances, headache, vertigo and unsteadiness of gait. An exacerbation of the gastrointestinal symptoms was also noted.

Difficulty in driving a car was a common complaint, which was observed in this present case and which seemed to arise out of an uncomfortable, exaggerated startle response, which took perhaps a minute to settle after it was triggered. The hand paraesthesiae may be examples of peripheral nerve irritability, neuritis being a recognized symptom of bismuth intoxication.⁸

It is alleged that bismuth is not generally

absorbed from the intestinal tract, as soluble salts are converted into insoluble bismuth compounds.⁹ Some absorption, however, does take place, the plasma level rising to 137 mmol/l (28.6 mg/l) following De-Nol ingestion in humans¹⁰ and the soluble salt, trimethyl bismuth, resulted in toxic neurological symptoms in experimental animals.¹¹ Solubility is increased in the presence of wine and ascorbic acid,⁶ both taken occasionally by the patient. Even minute absorption can produce cumulative effects. Kruger *et al.*¹² report two cases of intoxication due to a cosmetic cream containing bismuth.

The neurological and higher cerebral process are impaired for a long time and high intracerebral levels of bismuth have been found in patients who had recovered from bismuth encephalopathy and who died later of unrelated illness, after their blood level had returned to normal values.⁵

This case illustrates an organic cause for apparently neurotic complaints and sounds a note of caution for the prolonged use of oral bismuth preparations. Three hundred and sixty cases of poisoning, with 16 deaths were filed in France.¹³ The pattern of symptoms conformed to other surveys, but anomalies in the epidemiological distribution, and the variability of toxicity in relation to the dose, suggested to the authors that some extraneous factor, such as a microorganism, might sometimes modify the ingested bismuth salts and convert them into a toxic substance.

Acknowledgements

I am grateful to Dr I.I. Dainow for drawing my attention to the French literature and providing unpublished information, Dr J. Swale and an anonymous reviewer for advice and Friern Hospital Library for assistance.

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