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Reversible Dysphagia and Dementia in a Patient with Bromide Intoxication

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Sirs: Bromide intoxication is nowadays rarely seen in Western society because its medical use was to a large extent replaced by much safer and more effective medications [1]. However, in Asian countries bromide is still available as an ingredient of many over-the-counter (OTC) medications [2–4]. A variety of neuropsychiatric and dermatological manifestations arise from bromide intoxication but dysphagia has never been reported as a key manifestation.

We report a 73-year-old man with bromvalyrelurea intoxication manifesting as reversible dysphagia, dementia and pseudo-hyperchloremia. The patient was admitted after a falling accident and a delirious episode 10 days previously. He had noticed a gradual mental deterioration during the past year. He had a history of impaired recent memory, difficulty in finding his way home and occasional incoherent speech. He had become partially dependent for activities of daily living for 6 months. During the same period, dysarthria and dysphagia were also noticed, and he lost about 15 kg of his body weight. On examination, the patient did not have dermatological manifestations of bromoderma such as generalized rash or acneiform eruptions. Neurological examination showed poor attention span with fluctuating consciousness, dysarthria with staccato speech and dysphagia, particularly choking on liquids. Bilateral gag reflexes were preserved. Both limb and trunk ataxia with a wide-based gait were noted. He scored 8/30 on the Mini Mental State Examination (MMSE). No weakness, rigidity or abnormal reflexes were detected. He was given nasogastric tube feeding soon after the admission. During the hospitalization, he also had psychotic symptoms with visual and auditory hallucinations and persecutory delusions so that a low dose quetiapine 12.5 mg per day was given. Brain computed tomography was unremarkable. An electroencephalogram (EEG) on the day of admission showed nearly continuous slow waves with intermittent generalized delta waves and positive photoparoxysmal responses. The peak frequency of the EEG power spectrum obtained from the artifact free background activity was 2.3 Hz, compatible with a moderate to severe diffuse cortical dysfunction. The findings of video fluoroscopic swallowing study (VFSS), that was recorded after swallowing 5 ml barium of various consistencies, disclosed a moderate oropharyngeal dysphagia. The patient had prominent abnormal bolus holding in the oral phase, impaired swallowing trigger and mild vallecular and pyriform stasis in the pharyngeal phase (Fig. 1a). Marked hyperchloremia (179 mmol/L) with a significant negative anion gap (–67.1 mmol/L) was found in his biochemistry studies, but there was no evidence of hyperlipidemia, multiple myeloma or lithium overdose to account for the hyperchloremia.

Reviewed his drug history, we found that he habitually used an OTC analgesic, the Ming-Ton Pain Killer, for more than a decade. Each gram of the analgesic consists of 200 mg bromvalerylurea, 350 mg ethoxybenzamide, 200 mg acetaminophen, and 50 mg caffeine anhydrous. He had taken up to 15 packs a day (bromvalerylurea 3 g/day) in the past six months in order to relieve his intractable chronic headache. His bromide levels were 12.69 ± 0.24 mmol/L in serum and 5.69 ± 0.08 mmol/L in urine on the admission day (Table 1). Forced diuresis was achieved with intravenous saline and intermittent boluses of furosemide (20 mg/ampoule). These were administered to maintain high daily urine output (3~4 liters). His impaired consciousness, psychotic symptoms, dysarthria, dysphagia and cerebellar ataxia re-

Table 1 Blood chemistry data

	Hospitalization Day		
Mmol/L	Day 1	Day 7	Day 21
Sodium (serum)	142	139.6	141.2
Chloride[a] (serum)	179	134	103
Carbon dioxide (serum)	30.1	21.8	23.2
Anion gap[b] (serum)	–67.1	–16.2	15
Bromide[c, d] (serum)	12.69 ± 0.24	0.77 ± 0.08	
Bromide[c] (urine)	5.69 ± 0.08	0.61 ± 0.03	

[a] measured by an ion-selective electrode with a bromide interference ratio of 3.0
[b] calculated as sodium – (chloride + carbon dioxide)
[c] measured spectrophoto metrically using the gold chloride method
[d] toxic level of serum > 12.5 to 18.8 mmol/L

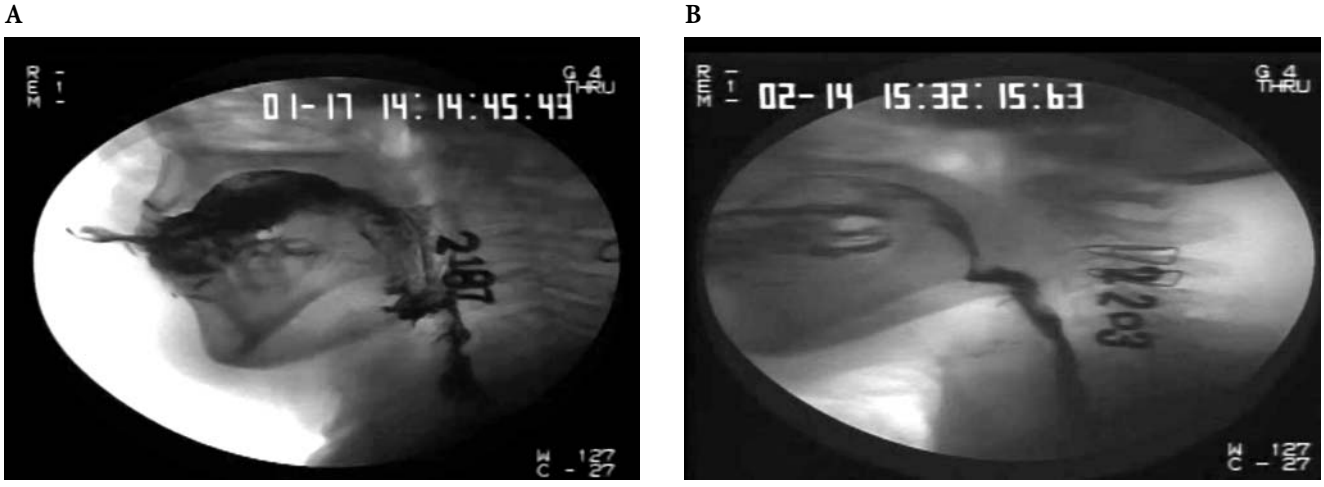

Fig. 1 (**A**) Video fluoroscopic swallowing study (VFSS) on day 3 of the hospitalization shows markedly abnormal bolus holding, piecemeal swallowing and abnormal oral mucosa coating; (**B**) Follow-up VFSS at about 4 weeks shows near normal swallowing except mildly abnormal bolus holding

solved gradually while the serum bromide returned to normal limits (0.77 ± 0.08 mmol/L). The MMSE score improved by 20 points (from 8/30 to 28/30) and the EEG showed diminished slow waves with normalization of the background activities (peak frequency of the EEG power spectrum 8.2 Hz). Follow-up VFSS in about 4 weeks revealed only mild dysphagia (Fig. 1b). He then resumed oral feeding and gained 4 kg of body weight in 1 month.

Bromism refers to a chronic bromide intoxication characterized by neuro-psychiatric and dermatological disturbances [5], which usually develop after ingestion of excessive amounts over a 2–4 week or longer period. Bromvalerylurea is an organic bromide with hypnotic-sedative effects that is still used as an ingredient in many OTC analgesics in Asian countries such as Japan, Thailand and Taiwan. The neuropsychiatric symptoms of bromism usually resolve when bromide is effectively excreted. However, irreversible cerebellar atrophy may occasionally occur [6, 7]. Pseudohyperchloremia is the result of an interaction between bromide and the reagent used to measure serum chloride by the ion-specific method yielding a false high serum chloride level and thus a decreased or negative anion gap. Colorimetric titration may accurately measure the chloride level [8]. Direct measurement of the bromide level may be achieved by using the gold chloride method of spectrometry to confirm the diagnosis [9]. In general, obvious clinical symptoms and signs appear when the serum level is more than 12.5 mmol/L and the condition is probably lethal when level exceeds 37.5 mmol/L [10]. The serum level of our patient was 12.69 ± 0.24 mmol/L, which was almost certainly associated with the clinical toxicity.

To the best of our knowledge, dysphagia caused by bromism has never been reported as a key feature of bromism. The three phases of deglutition, including oral, pharyngeal and esophageal phases, require the neural integrity from supranuclear, nuclear to peripheral neuromuscular levels. Clinical observations and cortical mapping using magnetic stimulation [11, 12] demonstrate the role of the inferior frontal gyrus in modulating swallowing. Dysphagia is also frequently seen in basal ganglia and cerebellar lesions which attest the involvement of these systems in normal deglutition [13]. In terms of bromism, high cortical as well as cerebellar functions are impaired, and this is probably the basis for the observed dysphagia. In our patient, the gag reflexes were preserved and the stasis in vallecular and pyriform sinuses disclosed by VFSS was mild, which further suggests that brainstem dysfunction did not contribute much to the symptoms.

In conclusion, bromide intoxication should be considered as a differential diagnosis of dysphagia and dementia especially in the face of an unexplained hyperchloremia.

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