

Dilated cardiomyopathy and left bundle branch block associated with ingestion of colloidal gold and silver is reversed by British antiLewisite and vitamin E: The potential toxicity of metals used as health supplements

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SL Archer. Dilated cardiomyopathy and left bundle branch block associated with ingestion of colloidal gold and silver is reversed by British antiLewisite and vitamin E: The potential toxicity of metals used as health supplements. *Can J Cardiol* 2008;24(5):397-399.

A case of left bundle branch block and a dilated, nonhypertrophic cardiomyopathy associated with ingestion of colloidal gold and silver as an 'energy tonic' is described. The cardiac disease was reversed within two months by a course of dimercaprol (Akorn Inc, USA) (British antiLewisite) and vitamin E. This is the first case of gold and silver cardiomyopathy in humans, and highlights the risks of these colloidal metal 'health supplements'.

Key Words: Alternative medicine; Cardiomyopathy; Chemical warfare; Dimercaprol (British antiLewisite, BAL); Health food supplements

CASE PRESENTATION

A 40-year-old woman was referred with a two-month history of fatigue, palpitations, fleeting retrosternal pains and a new left bundle branch block (LBBB). She denied paroxysmal nocturnal dyspnea, orthopnea, syncope, angina pectoris or edema and had no symptoms of infection. She did not smoke cigarettes, consume alcohol or use illicit drugs. Her family history was negative for cardiovascular disease. She had a healthy seven-year-old daughter. She took no prescription medications; however, on directed questioning, she acknowledged taking colloidal gold for approximately three months as a tonic to increase her energy level at the supplier-recommended dose (one teaspoon daily, 20 ppm) (Figure 1). She had also consumed colloidal silver intermittently for seven years. She had tolerated the silver but noted chest discomfort, palpitations and headache within one hour of each dose of gold.

A physical examination revealed a thin, Caucasian woman. Her vital signs included blood pressure of 104/60 mmHg, heart rate of 64 beats/min, temperature of 37°C and body mass index of 19.7 kg/m². A cardiovascular examination revealed normal first and second heart sounds, without a third heart sound. She had normal central venous pressure, with no peripheral edema. She had no organomegaly or ascites. A neurological examination was normal, and she had no argyria.

A 12-lead electrocardiogram (ECG) showed sinus rhythm, a normal axis and LBBB (QRS duration 138 ms). There was no LBBB on

Cardiomyopathie dilatée et bloc de branche gauche associés à l'ingestion d'or et d'argent colloïdaux corrigés par British AntiLewisite et vitamine E : Toxicité potentielle des métaux utilisés en suppléments

L'auteur présente ici un cas de bloc de branche gauche et de cardiomyopathie dilatée non hypertrophique associés à la prise d'or et d'argent colloïdaux sous forme de solution tonique. La maladie cardiaque a été corrigée en l'espace de deux mois au moyen de dimercaprol (aussi appelé BAL, de l'anglais British AntiLewisite, Akorn Inc, États-Unis) et de vitamine E. Il s'agit du premier cas de cardiomyopathie associée à la prise d'or et d'argent chez l'être humain, et il rappelle les risques inhérents à ces suppléments dits « naturels » à base de métaux colloïdaux.

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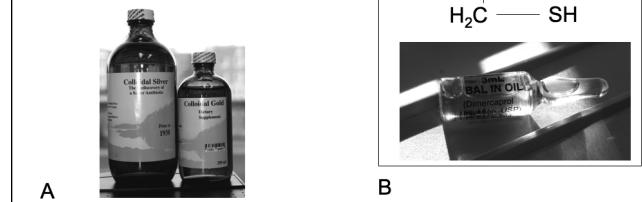


Figure 1) A Bottles of colloidal gold and silver as supplied by the vendor. Note the caveat appended by the vendor on their Web site (November 2005). B Figure showing the supplier, chemical structure and an image of a vial of British antiLewisite in peanut oil

an ECG performed in 2002, although diffuse T wave inversion and poor R wave progression were evident. On echocardiography, the left ventricle (LV) was dilated, thinned and globally hypokinetic (LV

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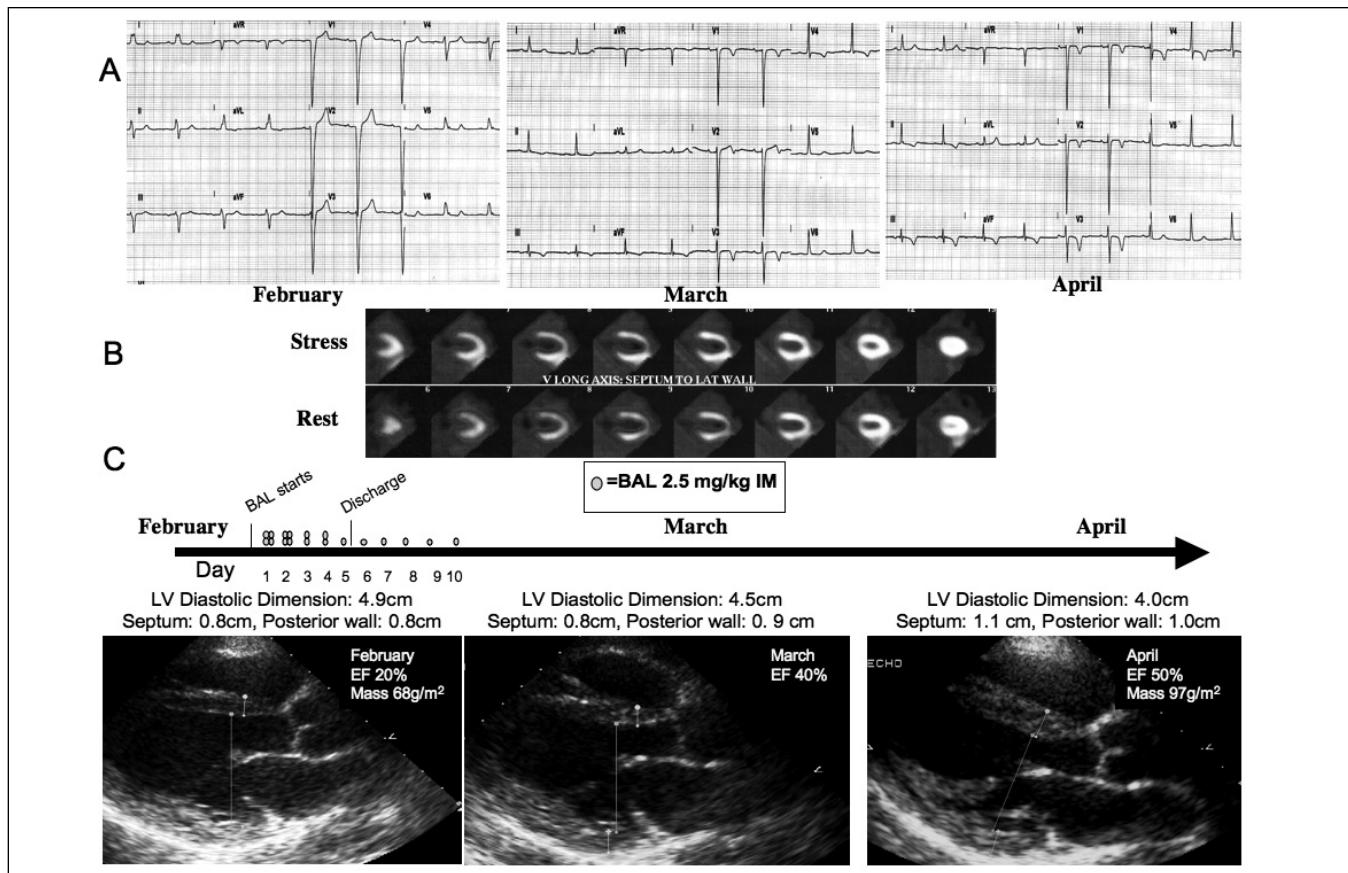


Figure 2) A Serial electrocardiograms showing resolution of left bundle branch block with British antiLewisite (BAL) and vitamin E. B Normal stress sestamibi test (confirmed by normal angiography results). C Serial echocardiography showing normalization of left ventricular (LV) ejection fraction (EF) and mass. IM Intramuscular

ejection fraction [LVEF] was approximately 20%; LV mass was 68 g/m^2). The right heart and cardiac valves were normal. A dipyridamole stress sestamibi scan and coronary angiography were normal. LV end-diastolic pressure was 14 mmHg with a LV dP/dt (first derivative of the change in ventricular pressure over time) of 1055 mmHg/s.

Laboratory tests

The patient's serum silver levels were elevated (16 nmol/L; normal 0 nmol/L to 3 nmol/L), while serum gold level were less than 0.1 $\mu\text{mol/L}$ (normal 0 $\mu\text{mol/L}$ to 0.5 $\mu\text{mol/L}$). She had a hemoglobin level of 134 g/L, platelet count of $286 \times 10^9 \text{ L}$, white blood cell count of $8.0 \times 10^9 \text{ L}$, total protein concentration of 65 g/L and a creatinine level of 68 $\mu\text{mol/L}$; serum protein electrophoresis was normal. She had a total cholesterol level of 3.85 mmol/L, high-density lipoprotein cholesterol level of 1.34 mmol/L and low-density lipoprotein cholesterol level of 2.17 mmol/L; her ferritin level was 42 $\mu\text{g/L}$ and her troponin level was lower than 0.15 $\mu\text{g/L}$. She had a negative creatine kinase muscle-brain test and an erythrocyte sedimentation rate of 8 mm/h. A urine screen was negative for excess aluminum, arsenic, barium, beryllium, cadmium, copper, manganese, thallium and zinc. There was no selenium deficiency.

DISCUSSION

Therapy

Based on the onset of symptoms shortly after commencing gold ingestion, and the absence of other explanations for her dilated cardiomyopathy with LBBB, a presumptive diagnosis of gold and/or silver toxicity was made. Because the silver ingestion had been sporadic, although prolonged, and because her symptom onset better coincided with onset of gold ingestion, she was admitted to hospital for gold

chelation using a low-dose regimen of British antiLewisite (BAL) (Akorn Inc, USA) (2.5 mg/kg in lidocaine, by deep intramuscular injection). She received a 10-day course of BAL (four times daily for two days, twice daily for one day and once daily for seven days). Vitamin E 50 U/day was administered orally to counteract possible silver toxicity. Carvedilol 3.125 mg twice daily and ramipril 2.5 mg once daily by mouth were administered several days after onset of chelation therapy. Her LBBB resolved within 10 days, but T wave inversion persisted (Figure 2). Two weeks following discharge, her LVEF had increased to 35% (Figure 2), and her fatigue and palpitations had resolved. After approximately two months, her LV dimensions and mass were nearly normal (Figure 2), and cardiac magnetic resonance angiography confirmed normal chamber sizes, function (LV end-diastolic and end-systolic volumes were 152 mL and 75 mL, respectively; LVEF 51%), myocardial perfusion and LV mass (88 g/m^2). At the time of writing, she was 12 months postdischarge and had returned to work without functional limitations; her LVEF remained at 50% and she had no LBBB.

Literature review

This was the first report of gold- and silver-associated dilated cardiomyopathy and LBBB, and demonstrates a therapeutic response to BAL and vitamin E. Colloidal gold is a water-based suspension of microparticles created by the chemical reduction of gold chloride. It has acquired the unsubstantiated reputation of 'elixir of life'. In rheumatoid arthritis patients, repeated gold injection creates a plateau gold level. Over 80% of injected gold is retained in the body one week after injection. Although cleared through the urine, many patients on chronic, high-dose, parenteral therapy have detectable gold in their plasma and urine months after administration is stopped (1).

However, oral colloidal gold results in lower plasma and urine concentrations and a lower incidence of toxicity. On average, patients receiving 60 mg of oral colloidal gold per week have serum concentrations of approximately 3.6 µmol/L (1). When colloidal gold sulphide is administered orally, the plasma and urine values vary widely, and may even be undetectable despite large doses of colloidal gold (1), as in the present case. Gold levels in the blood are often not concordant with levels in the tissue, where gold may accumulate.

Gold, used to treat rheumatoid arthritis, is known to cause dermatitis, nephritis, stomatitis, gastrointestinal discomfort, alveolitis and hepatic toxicity (1). However, gold-induced cardiomyopathy or LBBB have not previously been reported. The apparent lack of toxicity in rheumatoid arthritis patients may relate in part to the lack of systematic cardiac monitoring or to the lack of concomitant silver ingestion.

There is biological plausibility for the contention that this patient's cardiac disease resulted from gold-induced oxidant injury. Gold inhibits two selenocysteine-based myocardial antioxidant enzymes, thioredoxin and glutathione peroxidase. The enzymes are crucial for myocardial protection from reactive oxygen species. While high doses of gold inhibit both enzymes, low doses only inhibit thioredoxin (2). Auranofin (S-triethylphosphinegold(I)-2,3,4,6-tetra-o-acetyl-1-thio-beta-d-glucopyranoside), used to treat rheumatoid arthritis, exacerbates ischemia-reperfusion injury in rats by enhancing apoptosis through a caspase-3-dependent mechanism (2). Gold may also increase apoptosis by opening the mitochondrial transition pore, resulting in mitochondrial swelling and depolarization (3). A gold-containing, experimental antineoplastic drug, bis(1,2-bis(diphenylphosphino)ethane gold(I) chloride, causes myocardial contraction band necrosis, associated with a loss of mitochondrial function (4).

BAL (Figure 1B) is a disulphide that was synthesized in 1940 as an antidote to the arsenic-containing chemical warfare gas Lewisite (5). BAL can treat gold, lead and arsenic poisoning, and copper overload (5). At doses of greater than 5 mg/kg, BAL causes modest toxicity in 50% of subjects (hypertension, tachycardia and fever) (5). However, at lower doses (3.6 mg/kg to 5.0 mg/kg), adverse effects are rare. Our patient experienced only gluteal discomfort from the intramuscular injections.

Our patient was also ingesting colloidal silver and had elevated silver levels. Silver can impair antioxidant defenses by antagonizing selenium, and can cause a selenium and vitamin E deficiency (6). The relative contribution of the two metals to her cardiomyopathy and

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LBBB is unclear. However, the fact that gold ingestion was temporally associated with her symptom onset, and the rapid resolution of her LBBB with BAL (before significant vitamin E ingestion) implicates gold as the predominant toxin. It is likely that the elevated silver levels in this patient's blood promoted a synergistic toxicity with the gold, constituting a second oxidant stress that led to overt cardiac disease.

The National Health Interview Survey (7), which assessed alternative medicine use in 31,000 subjects, found that 21% of individuals use one or more biological nonprescription medications, most of whom did not spontaneously inform their physicians of this fact. Patients are usually unaware of the untested nature and potential toxicity of these chemicals, which often lack a trial-based body of evidence to support their purported benefits (Figure 1A). The gold and silver vendor portrays colloidal metals as dietary supplements and, while issuing a safety disclaimer (Figure 1A), implies that they have healing properties, and that they prolong life, reduce weight and act as an energy tonic.

The concomitant use of low-dose angiotensin-converting enzyme inhibitors and beta-blockers is unlikely to have caused our patient's rapid improvement, and neither agent should reverse LBBB. In patients with heart failure and reduced LVEF, carvedilol (at twice the dose our patient received) increased LVEF by only 5% after six months (8). Likewise, in patients with reduced LVEF, ramipril increased LVEF by only 5% (9). While these mean increases in LVEF achieved with medical therapy for chronic heart failure are much smaller than those observed in the present patient, occasional cardiomyopathy patients may have a larger therapeutic response to angiotensin-converting enzyme inhibitors, and the LVEF can rise significantly due to spontaneous disease remission.

CONCLUSIONS

We describe a case of LBBB and dilated cardiomyopathy due to ingestion of colloidal gold and silver that was successfully reversed by BAL and vitamin E. Systematic inquiry for the ingestion of gold and silver should be included in the investigation of patients with unexplained cardiomyopathy or conduction system abnormalities. The prevalence with which these metals are used is unknown and merits definition.

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