Radio-opaque punctate opacities on the chest radiograph following intravenous injection of a bismuth compound

Doreen J Addrizzo-Harris, Andrew Churg, William N Rom

Abstract
The case history is described of a patient who presented with small rounded punctate metallic opacities widely dispersed on the chest radiograph with accumulation of metallic particles in the right ventricle. Energy dispersive x-ray spectroscopy of alveolar macrophages identified a major predominant peak as bismuth. The patient had been injected with a health tonic in Honduras two years earlier.

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Bismuth compounds have been used as medical agents since 1733 when bismuth salve was first introduced, followed in 1799 by their use for dyspepsia. Bismuth subnatrate paste was promoted in 1910 as a treatment modality for chronic abscesses. The paste was injected directly into cavities and its distribution documented with the developing radiographic technology. Currently, the most commonly used bismuth agents worldwide are bismuth subsalicylate (BSS, Pepto-Bismol, The Proctor and Gamble Company, Cincinnati, Ohio, USA) and colloidal bismuth subcitrate (CBS, De-Nol, Gist Brocades, Delft, The Netherlands). BSS is reported to be in more than 60% of homes in the USA and more than 10 billion doses have been consumed. Bismuth compounds have been reported to have adverse effects on various organ systems. Between 1973 and 1980 neurotoxicity was described in approximately 1000 cases in Europe and Australia following large doses (700 mg to 20 g/day) of bismuth subnitrate or bismuth subgallate given for long periods (four weeks to 30 years) for gastrointestinal conditions. Only four case reports of neurotoxicity to BSS have occurred—all in patients who took amounts above the recommended dosage. Given that more than 99% of the bismuth in an oral dose of BSS is excreted in the faeces, these reports suggest that diffuse colonic abnormalities may result in enhanced absorption through a diffusely abnormal mucosa. We describe an unusual case, not previously reported, of intravenous bismuth exposure in a 39 year-old patient who presented with metallic opacities on his chest radiograph.

Case report
A 39 year old man from Honduras who emigrated to the USA two years previously sought medical attention for evaluation of headache, myalgias, weight loss of 4.5 kg (10 lb), intermittent abdominal pain, back pain, and cough. He had been well until he was injected intravenously in his left forearm while in Honduras two years previously, after which he was ill for several days with a flu-like illness. He denied any other medical problems including a previous history of venereal disease. He was not taking medications and had no known allergies. He was an ex-smoker with a 20 pack year history who had stopped two years previously. He had taken cocaine in the past but denied any intravenous drug use. He had been employed in the agricultural industry picking fruits and vegetables for more than 10 years and had worked for eight months in a jewellery store, and had no inhalational exposures. Blood evaluation revealed normal serum electrolytes including a normal creatinine of 1.1 mg/dl. The haemogram was within normal limits except for mild thrombocytopenia of 131 000 cells/l. Arterial blood gas tension on room air showed a pH of 7.43, PaCO₂ of 37 mm torr and a PaO₂ of 100 mm torr with 98% saturation. The chest radiograph revealed multiple punctate 1 mm metallic densities scattered throughout the lung fields (fig 1) and lining the contour of the right atrium and ventricle (fig 2). A computed tomographic scan of the chest revealed discrete 1 mm punctate dense opacities scattered in both lungs with a subpleural distribution. Pulmonary function testing revealed forced vital capacity (FVC) of 5.141 (116% of predicted), forced expiratory volume in one second (FEV₁) of 3.861 (105%), total lung capacity (TLC) 7.091 (109%), and a lung transfer factor (Tlco) adjusted to haemoglobin of 139% predicted. Fibreoptic bronchoscopic examination was normal. Bronchoalveolar lavage recovered 14.6 x 10⁶ cells with 87% macrophages, 10% lymphocytes, 3% neutrophils, and no eosinophils. Histological examination of the transbronchial biopsy specimen revealed normal bronchial wall and lung parenchyma. Alveolar macrophages were evaluated for particles by morphology and energy dispersive x-ray spectroscopy. Most of the particles gave a single peak for bismuth. Rare particles of iron, titanium, and iron-chromium were also present.

Figure 1 Posterior-anterior chest radiograph showing punctate 1 mm metallic densities scattered throughout the lung fields.
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and 10 with no known history of dust exposure\textsuperscript{10} without finding bismuth. Churg and Stevens\textsuperscript{11} examined both lung parenchyma and airway mucosa from 12 non-smokers and 10 smokers. Although particle concentrations for both types of tissue were in the range of 106 particles/g, with particles of iron and titanium as well as a host of other known ambient atmospheric contaminants commonly observed, no bismuth particles were seen. These studies indicate that bismuth particles are not normally found in the lungs of either the general population or those with most types of common occupational exposures. Thus, the presence of numerous bismuth particles in the alveolar macrophages and the finding of extremely radiodense nodules on chest radiographic examination suggest that the substance with which this patient was injected was bismuth. Finally, the patient’s systemic symptoms were unlikely to be related to the intravenous injection of a bismuth compound since bismuth toxicity is associated with encephalopathy.\textsuperscript{4-7}

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Discussion
Analysis of particles from alveolar macrophages recovered by bronchoalveolar lavage in this case revealed numerous particles of bismuth. Takemura \textit{et al} evaluated inorganic particles in lavaged cells from 43 non-smokers, ex-smokers, and normal volunteers\textsuperscript{8} without identifying bismuth. Rom and colleagues used transmission electron microscopy and energy dispersive x-ray spectroscopy to determine the particle burden in 42 dust exposed subjects and non-exposed controls.\textsuperscript{9} Individuals with dust exposure had a fourfold increase in the numbers of particles per alveolar macrophage compared with controls but, again, bismuth was not found in either group. Johnson \textit{et al} performed a similar analysis on lavage fluid from 12 patients with occupational exposure

8 Takemura T, Rom WN, Ferraro VJ, Crystal RG. Morphological characterization of alveolar macrophages from individuals with occupational exposure to inorganic particles. \textit{Am Rev Respir Dis} 1989;140:1674–82.
10 Johnson NF, Haslam PL, Dewar A, Newman-Taylor M. Identification of inorganic dust particles in bronchoalveolar lavage macrophages by energy dispersive x-ray microanalysis. \textit{Arch Environ Health} 1986;41:133–44.
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