Systemic argyria

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Abstract

A 74 year old man presented with signs and symptoms of mild cardiac failure. His face and chest were severely discoloured, which was thought to be due to cyanosis. He deteriorated and died of bronchopneumonia. At post mortem examination multiple organs, including the skin, showed silver pigment deposition; he also had a gastric malignant neuroendocrine tumour. He gave no history of contact with silver compounds. Systemic argyria caused by chronic ingestion of silver compounds is a rare condition which, apart from its cosmetic effects, is thought to be relatively harmless; it is not thought to be carcinogenic. This condition can pose diagnostic problems for both clinicians and pathologists.

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Case report

A 74 year old white man presented with a one year history of general ill health, exertional dyspnoea, and ankle oedema. He had gone to hospital two years earlier complaining of breathlessness when an abnormal complex, thought to be due to central cyanosis, was noted. He gave no drug history and, in particular, he denied contact with any compounds containing silver in his occupation as an engineer in the textile industry. He had, in the past, worked on a sheep farm in Australia.

On examination he showed a bluish discolouration of the skin of his face, neck, and upper chest which he claimed had been present for seven to eight years. Clinically, he was in mild cardiac failure and his blood tests revealed a hypochromic, microcytic anaemia (haemoglobin = 108 g/l), a raised erythrocyte sedimentation rate 34 mm/first hour and abnormal liver function tests (aspartate transaminase 159 U/l (normal is <55), lactate dehydrogenase 762 U/l (normal is <300), alkaline phosphatase 720 U/l (normal is 30-135). His serum iron, methaemoglobin, and sulphaemoglobin concentrations were within the normal range.

An ultrasound scan showed that his liver was enlarged with multiple space occupying lesions, consistent with metastatic tumour. Argyria was diagnosed from a skin biopsy specimen and he subsequently deteriorated and developed terminal bronchopneumonia.

Post mortem findings

The body showed marked blue-grey discolouration of the face, neck, and anterior chest wall. Bilateral arcus senilis was noted. The oesophagus showed four small polypoid nodules measuring up to 1 cm, located above the oesophago-gastric junction. The stomach contained a 6 cm in diameter ulcerated tumour on the greater curvature of the gastric fundus. The liver contained multiple large metastatic tumour nodules.

The lungs showed bronchopneumonic consolidation of the right lower lobe and pronounced oedema. The heart was of normal size but showed scarring of the anteroseptal left ventricular wall. The right coronary artery was completely occluded by atheroma. The other organs were grossly normal.

Microscopically, the skin showed fine granular deposits of black pigment within the basement membranes of the epidermis and sweat ducts. The pigment was bleached by a solution of 1% potassium ferricyanide in 20% sodium thiosulphate, thus proving it contained silver ions.¹ Similar pigment was also found in the pars anterior of the pituitary gland, myocardium, liver, spleen, adrenals, prostate, thyroid and kidneys (figure).

The oesophageal polypi were tubulovillous adenomas. The gastric tumour showed features of a malignant neuroendocrine tumour in which no argyrophilia was demonstrable. The liver contained metastatic neuroendocrine tumour deposits.

Fine granular deposits of silver pigment in a renal glomerulus.

The lungs showed bronchopneumonia, mild emphysema, focal mild interstitial fibrosis, and a foreign body giant cell reaction to aspirated food particles. The heart showed myocardial fibrosis. The cause of death was bronchopneumonia.

Discussion

Argyria was recorded in ancient times due to the usage of silver compounds in treating various nervous system disorders. Sola in 1647 advocated silver nitrate for treating epilepsy, tabes, and chorea.² The prevalence of argyria increased until the late 19th century when silver toxicity was described.³ Acute silver poisoning may cause haemorrhage and erosive intestinal lesions,⁴ but in small doses silver compounds are thought to be harmless despite widespread systemic deposition, though the cosmetic disability can be psychologically traumatic.

The main route of absorption is through the gastrointestinal tract, but the respiratory mucosa or broken skin are other alternative routes. Substances which include silver compounds include antimicrobial, astringent, and caustic agents which produce systemic deposition, but, localised argyria can be seen in the eye or oral mucosa following topical application⁵ or as an occupational disease in silver workers. Dental amalgam displaced into oral tissues during drilling may produce localised argyria. There is a report of anti-smoking lozenges causing argyria.⁶

Although any organs may be the site of silver deposition, the skin and connective tissues are said to have the highest concentrations. The silver granules preferentially localise in the basal lamina of the secretory portion of eccrine glands, elastic fibres of the papillary dermis, dermal collagen and, to a lesser extent, in connective tissues surrounding pilosebaceous units, arteriolar walls, perineural tissues and arrector pili muscles.

The cutaneous pigment may be silver sulphide, chloride, or metallic silver which results from photoactivated reduction of silver salts within tissues.⁷ A direct stimulatory effect of silver on melanocytes increases the degree of skin pigmentation in areas exposed to sun which is permanent and irreversible.⁸

Systemic argyria has not been associated with any neoplasia and, in our case, the neuroendocrine tumour must have been a coincidental finding. In our patient no source of the silver ingestion could be found and the skin discolouration was mistakenly thought to be solely due to cardiac cyanosis, an error which has been documented before.^{5 9 10}

Other conditions which can lead to similar skin pigmentation are methaemoglobinuria, metastatic melanoma with melanogenuria, and haemochromatosis.¹¹

Pathologists and clinicians alike should be aware of this rare condition which can pose diagnostic difficulties.

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