

Michael Tsokos · Sören Schröder

Black thyroid

Report of an autopsy case

Received: 4 May 2005 / Accepted: 5 July 2005 / Published online: 6 September 2005
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Abstract A distinctive but very rare side effect of exposure to minocycline is black pigmentation of the thyroid gland. Until 2002, not more than 30 cases of black thyroid had been reported in the English literature. We report on a 24-year-old woman with known antemortem ingestion of minocycline. The woman suffered from a depressive disorder with repeated suicide attempts and committed suicide by a gunshot to the head. At autopsy, the thyroid gland showed coal-black coloration. Upon histology, clumps of black-brown pigment were seen in the colloid, and a granular precipitate of this pigment was noted in the apical portions of the follicular epithelial cells. The diagnosis of minocycline-associated black thyroid was established. Forensic pathological significance of black thyroid may arise from the fact that hypothyroidism has been occasionally associated with minocycline-related black thyroid and that hypothyroidism may contribute to the development of depressive disorders (and thus, in given cases, may be responsible for suicide attempts). Under this assumption, the presence of black thyroid would represent more than just a morphological curiosity in specific cases.

Keywords Black thyroid · Minocycline · Suicide · Forensic pathology

Introduction

Black thyroid, characterized by a grossly evident black pigmentation of the thyroid gland, is a very rare pathological entity associated with long-term minocycline ingestion [9]. Until 2002, not more than 30 cases of black thyroid had been reported in the English literature [10]. We present an additional case of minocycline-associated black thyroid.

Case report

A 24-year-old woman committed suicide by a gunshot to the head. As reported by her family members, she had suffered from a depressive disorder with repeated suicide attempts with sedative and hypnotic drugs and was under continuous ambulatory psychiatric surveillance. The day before the finding of the body, she had taken two revolvers from her father and disappeared. As she had left a farewell letter at her father's house, a police search was started. The deceased was found lying fully dressed in a supine position in a wood with a .22 caliber revolver lying on her abdominal region.

Medico-legal autopsy revealed a close-range entrance wound in the right temporal region. The corresponding skull defect was circular in shape (0.6 cm in diameter) and showed internal beveling and powder blackening. The missile track passed through posterior parts of the right frontal lobe, crossed the midline through the corpus callosum where parts of the adjacent brain stem were injured, and then continued through the left temporal lobe, where the bullet was recovered.

The most remarkable autopsy finding was a coal-black coloration of the thyroid gland (Fig. 1). A small nodule that was also black-colored was situated outside the thyroid above the right upper lobe of the organ. Apart from edema of the brain and lungs, no other gross pathologic findings were found, and no black coloration of other organs or tissues was present at autopsy.

Microscopical examination of the thyroid (organ weight 11 g) showed flattened and cuboidal follicular epithelium.

S. Schröder
Institute of Immunology, Pathology,
and Molecular Biology,
Hamburg, Germany

M. Tsokos (✉)
Department of Forensic Pathology,
Institute of Legal Medicine, University of Hamburg,
Butenfeld 34,
22529 Hamburg, Germany
e-mail: mtsokos@web.de
Tel.: +49-40-428032748
Fax: +49-40-428033934



Fig. 1 Gross appearance of black thyroid

The thyrocytes contained numerous black-brown granules, variable in size and shape, which were for the most part located in the apical portion of the cytoplasm (Fig. 2). In addition, clumps of this pigment were deposited within the colloid. Interstitial fibrosis, signs of thyroiditis, or nodular changes were lacking. The histological diagnosis was given as most probably minocycline-associated black thyroid.

According to the deceased's family physician who was contacted after knowledge of the histopathological examination of the thyroid gland, the woman had received minocycline for treatment of acne vulgaris between the ages of 15 and 19. The family physician reported that no thyroid function tests had been performed in recent years. However, he stated that the woman's previous medical history had been unremarkable so far and that he had neither any knowledge about a depressive disorder nor had he prescribed any benzodiazepines.

Toxicologic analysis revealed benzodiazepines within the therapeutic range (citalopram, 0.09 $\mu\text{g/ml}$ in femoral venous blood and 4.52 $\mu\text{g/ml}$ in urine; lorazepam, 0.098 $\mu\text{g/ml}$ in femoral venous blood and 0.16 $\mu\text{g/ml}$ in urine).

Discussion

The association of black pigmentation of the thyroid with prolonged use of minocycline, a tetracycline antibiotic, was first described by Benitz and coworkers in 1967 [2]. Since then, different investigators have tried to clarify the pathogenesis of minocycline-associated black coloration of the thyroid and to identify the nature of the black thyroid

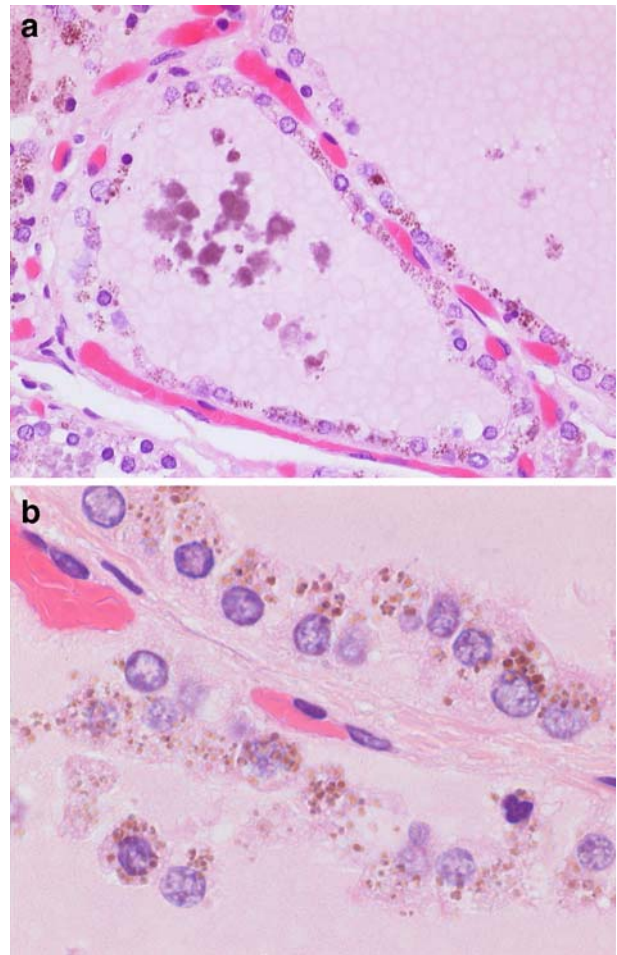


Fig. 2 Histology of black thyroid. **a** Dark brown granules in flattened follicular cells and blackish-brownish pigment deposits in the colloid (hematoxylin–eosin, $\times 100$); **b** Numerous brownish-blackish granules in the cytoplasm of cuboid follicular epithelial cells in the apical portion of the cytoplasm (hematoxylin–eosin, $\times 800$)

pigment by animal experiments and a paucity of investigations carried out on human surgical specimens. Based on the results of electron microscopy and histochemistry, Reid [11] suggested that the black pigment located in intracytoplasmic granules of follicular epithelial cells and in colloid represents lipofuscin. This assumption was essentially supported by the results of Gordon and coworkers [7] who proposed that the pigment is predominantly composed of lipofuscins, but with a small amount of another, possibly minocycline-related pigment. In marked contrast to these theories, more recent in vitro experiments suggest that the black thyroid pigment is a synthetic polymeric substance generated by oxidation of minocycline by thyroid peroxidase [6, 13]. However, the precise pathophysiological mechanisms and underlying biochemical pathways of minocycline-related black pigmentation of the thyroid are not clear at present.

Despite the widespread use of minocycline, most often for the treatment of acne vulgaris, black thyroid is an ex-

tremely rare pathological finding [9]. The phenomenon seems to develop regardless of dose or duration of therapy with minocycline [5], hence, additional individual factors such as a preexisting imbalance in thyroid lysosomal function in the affected individuals may account for pigmentation in one person but not in the other [1].

Apart from black coloration of the thyroid, pigment changes of the skin, nails, teeth, blood vessels, heart valves, and bones have also been reported in patients chronically taking minocycline [3, 5, 8, 12]. In addition, black discoloration phenomena of other organs in the course of natural diseases, such as “black esophagus” [14], may occasionally be observed at autopsy. However, none of the aforementioned changes were seen in the present case.

Although clinical studies monitoring thyroid function in patients receiving long-term minocycline therapy are totally lacking in the literature, some case reports have associated hypothyroidism with minocycline-related black thyroid [1, 10], and potent antithyroid effects of minocycline have been observed in vitro, too [4, 13]. Hypothyroidism occurred, however, only when a black pigmentation of the thyroid was observed histologically in combination with thyroiditis [1]. Our case lacked any signs of thyroiditis, and no thyroid function tests had been performed in the young woman before death. Therefore, we are unable to comment on whether any hypothyroidism was present in this case and, under the assumption that hypothyroidism was manifest here, whether this condition has contributed to the development of her depressive disorder with repeated suicide attempts. However, in specific cases where the combination of minocycline-induced black thyroid and thyroiditis can be established, the presence of black thyroid would represent more than just an incidental autopsy finding and morphological curiosity in the case investigated here.

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