



Black thyroid: a note for the surgeon, the pathologist and the dermatologist

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Color and consistency of the thyroid gland can vary and delivers important information on the nature of an underlying thyroid pathology (1). The healthy thyroid has typically a homogeneous pinkish-red color. Hypervascularisation, characteristic for Graves' disease, can confer an intense beefy red color, Hashimoto thyroiditis a tannish yellow discoloration and fibrotic changes, malignant lesions are often pale gray scars with firm consistency, while adenomas generally appear like pale gray, soft, gelatinous or fleshy masses, and oncocytic lesions (formerly known as Huerthle-Cell-Lesions) are mahogany brown tumors with frequent parenchymal hemorrhages (1). A dark red discoloration may be seen in patients taking psychotropic drugs such as doxepin, lithium carbonate or tricyclic antidepressants (2).

The accumulation of dark brown to black pigment in the thyroid gland called "black thyroid" was first described in laboratory animals in 1967 and in humans in 1976 (3). It was also described in a few hundred reports as a rare side effect of minocycline (MN) therapy or related tetracyclines (4) and, more recently, after intraoperative indocyanine green administration during transoral robotic-assisted surgery (5).

It seems to be caused by a deposition of lipofuscin, melanin/neuromelanin or an oxidation product of MN in the thyroid gland (6) but can also be found in bone, teeth, skin, nails and oral mucosa of patients undergoing this

treatment (often administered for chronic acne) (7,8). As a possible pathophysiologic mechanism, it has been suggested that MN reacts with the thyroid peroxidase and forms a black pigment, which deposits in lysosomes and can be seen in histological examinations (1). It is said to be possibly prevented by the coadministration of the antioxidant ascorbic acid (4).

The black discoloration typically does not affect thyroid function, despite some rare reports of hyperthyroidism (9). Some authors have claimed a high rate of papillary thyroid cancer (4), but no causal relationship has been established so far. In contrast, there are even reports on some anticancer activity of MN instead (10-13). Interestingly however, tumors arising in a pigmented thyroid have been described to lack the black pigment, and discolored foci in an otherwise dark thyroid should be thoroughly examined (14,15).

In their case report entitled "*Papillary thyroid cancer in black thyroid: a case report and literature review*" (16), Kim *et al.* describe the case of a 29-year-old woman with metastatic papillary thyroid microcarcinoma involving level IV lymph nodes in the neck, whose thyroid was incidentally found to be "black" intraoperatively and review the current literature on this subject. The young woman had been on MN for the previous 19 months. Neither the tumor nor the lymph nodes were found to be "black" by histopathology (see their *Figs. 1,2*), and in fact malignant cells notably display

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decreased pigmentation compared to the surrounding tissue as previously described also in other reports (17). The reason for this is still unclear. An altered lysosomal metabolism of cancer cells, including their relocation of lysosomes at the plasma membrane and increased exocytosis, meant to adapt the extracellular membrane for their survival (18) as well as the nuclear inclusion of heterolysosomes lacking contact with the cytoplasm (19) might offer possible explanations for this phenomenon.

Although this is only a single case description (the first in the authors' institution), it draws attention on a rare but striking finding, which is of relevance both for the thyroid surgeon and the endocrine pathologist. The authors correctly conclude that there is currently no sufficient evidence of a causative relationship between black thyroid and cancer. A MEDLINE search delivers no more than 250 cases and there is a relevant bias to take into consideration: "black thyroid" is not diagnosed preoperatively by sonography or fine needle biopsy but it represents a mere incidental intraoperative finding during procedures performed for other reasons, such as malignant or suspicious nodules (20).

In the lack of strong data, it is unclear if a sonographic and biochemical thyroid screening should possibly be recommended in patients undergoing long-term MN treatment, in patients presenting discoloration in any part of the body or in patients incidentally diagnosed with "black thyroid" by hemithyroidectomy performed for other reasons (21). It remains also unclear if long-term MN therapy or MN associated discoloration in any part of the body should encourage to simultaneously prescribe ascorbic acid to the patients (22). Nevertheless, this case report raises further awareness in dermatologists, surgeons and pathologists for this rare but striking incidental finding and its possible correlations.

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