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Etiology of Craniofacial Bone Hyperpigmentation and an Algorithm for Addressing Intraoperative Discovery

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Intraoperative discovery of previously undiagnosed calvarial bone hyperpigmentation, or "black bone," is a relatively uncommon occurrence but can be a confounding encounter. The literature is sparse and limited to case reports.[1] At the time of writing, the authors found only 6 reported cases dating back to 1962, 3 of which were autopsy findings.[2] The most commonly reported cause of osseous hyperpigmentation is tetracycline use. At cumulative doses of 100 g or greater—as typically prescribed for acne vulgaris and other chronic conditions—the risk is 10% after 1 year and 40% after 4 years.[3] The mechanism occurs during bone growth, in which tetracycline molecules chelate to calcium and are incorporated into actively mineralizing tissues forming a tetracycline-calcium orthophosphate complex.[4] Osseous discoloration is a result of subsequent oxidization and deposition of various endogenous products of degradation. It has a predilection for well-vascularized areas. There are no reported radiological abnormalities attributed to tetracycline-related hyperpigmentation. Histologically, in adults, tetracycline appears to be innocuous.[3]

Despite tetracycline use being the most common underlying etiology, a number of additional uncommon and more sinister diagnoses must be excluded. Potential causes include congenital metabolic conditions, malignancy, infection, metallosis from implanted material,[1] and additional medications such as some chemotherapeutic and antileprosy agents. Ochronosis, the skeletal manifestation of the autosomal recessive condition alkaptonuria, is a well-described but rare cause of bone hyperpigmentation. It is characterized by accumulation of polymerized homogentisic acid and may remain undiagnosed until adulthood. A family medical history or a personal history of early-onset large joint osteoarthritis or osteoporosis can aid in making the diagnosis which can be confirmed with a urinary homogentisic acid test. Other causes require a careful histological and radiological diagnosis.

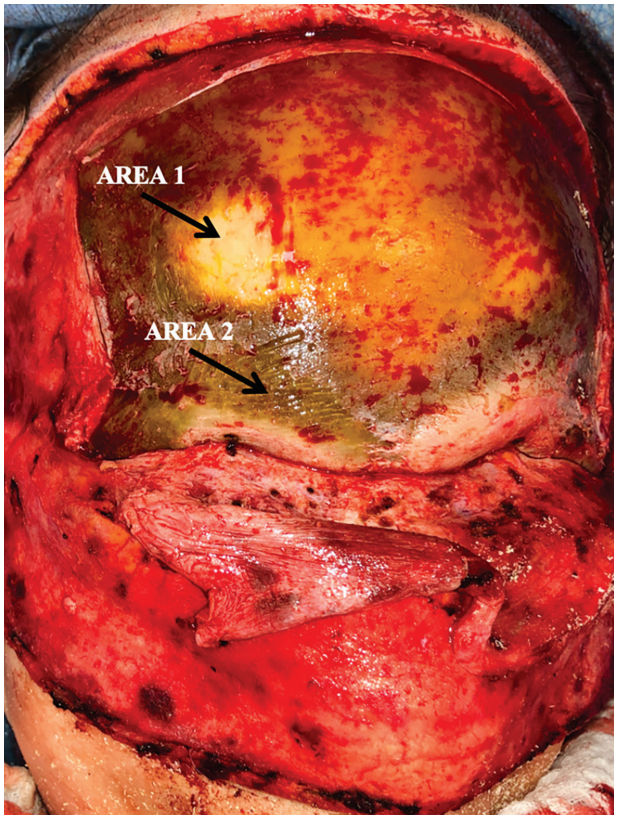

Fig. 1. Intraoperative photograph following bicoronal exposure and pericranial flap reconstruction for brow recontouring during a facial feminization procedure. The image demonstrates yellow and black-green bone discoloration. Only the right side has undergone recontouring with a mechanized burr at this point. The right frontal bone has been superficially burred, revealing a normal appearing bone at a relatively shallow level (area 1), whereas the right brow region has been extensively burred showing darker staining and increased depth of involvement (area 2).

The illustrative case presented is of a 47-year-old patient who is undergoing facial feminization as part of a male-to-female gender transition. She is otherwise well with a medication history significant for multiple courses of tetracycline as an adolescent for treatment of acne vulgaris. A bicoronal exposure and a pericranial flap reconstruction were performed for brow recontouring—which revealed a striking hyperpigmentation of the frontal bones (Fig. 1). A preoperative computed tomography (CT) imaging revealed normal bone structure (Fig. 2).

Intraoperatively, the bone was macroscopically normal beside the hyperpigmentation with expected integrity and resilience. Interestingly, the depth and degree of pigmentation were not uniform (Fig. 1). It has been shown that tetracyclines will preferentially involve areas of new

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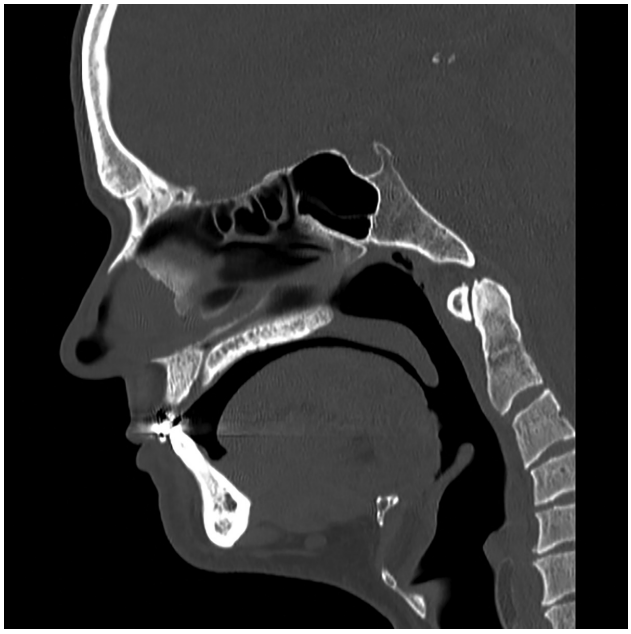

Fig. 2. A sagittal view of a preoperative computed tomographic image demonstrating normal radiological appearance of the frontal bone and the remaining craniofacial skeleton.

bone formation.[5] We hypothesized that the superficial involvement of the calvarial frontal bone stems from the appositional growth of adolescence where tetracycline was preferentially chelated in bone matrix at the outer surface of the calvaria.

When encountered, hyperpigmented craniofacial bone requires a thorough investigation to find its cause. A detailed history and clinical examination are essential even if performed in a focused, retrospective fashion. A full medication history should be sought—in particular, the use, dose, and duration of tetracycline-class medications. Physical examination may reveal pigmentation of dentition or transmucosal discoloration of the mandibular or maxillary bone, highly suggestive of tetracycline use.[3] However, a history of tetracycline use does not exclude other causes, particularly where pigmentation is focal. For instance, yellow fluorescence from localized tetracycline uptake has been noted in malignant bone tumors.[2] We recommend an algorithm that includes both perioperative CT imaging and histological examination where a clear medication history is not elucidated or where focal pigmentation is present.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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