

Feeling blue? Minocycline-induced staining of the teeth, oral mucosa, sclerae and ears – a case report

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IN BRIEF

- Blue staining of the teeth, oral mucosa, sclerae and ears are rare side effects of minocycline use.
- Early detection and diagnosis allows cessation of the drug which could reduce the severity of the effects.
- Suggestions for the mechanisms of staining along with possible treatment options are given.

Minocycline is a broad-spectrum antibiotic belonging to the tetracycline family, often prescribed in infective skin conditions such as acne and rosacea. Minocycline-induced staining of the sclerae, ears, oral mucosa and teeth are rare but troublesome conditions. If patients already have concerns about their appearance due to an unsightly skin condition, careful consideration ought to be given to using minocycline as it could worsen the *status quo*, should potentially irreversible blue staining occur. This report describes one case and highlights some of the other dangers of long-term minocycline use which may present themselves to dentists.

INTRODUCTION

Minocycline-induced staining of the sclerae, ears, gingivae and teeth is a rare but troublesome condition. This report describes one such case and highlights the dangers of long-term minocycline use.

CASE REPORT

History

In this case a 51-year-old woman presented with a bluish discoloration of the pinna of both ears, sclera of both eyes, oral mucosa and teeth. The discoloration developed slowly over several years before her presentation and the patient's motivation for attending was derived from a loss in confidence at the workplace due to the stigma associated with the increasingly evident blue discoloration. Her medical history revealed hypertension, asthma and the patient's GP had diagnosed a combination of acne and/or rosacea for which the patient had a 20-year history of minocycline use. There was no known history of tetracycline use as a child.



Fig. 1 Bluish discoloration of the patient's ears



Fig. 2 Bluish discoloration of the patient's sclerae



Fig. 3 Bluish discoloration of the patient's teeth

Clinical features

On examination there was clearly evident bluish discoloration of the patient's ears (Fig. 1), sclerae, oral mucosa (Fig. 2) and teeth (Figs 2 and 3). The patient did not consent to a photograph of her eyes which is why no image is shown. The discoloration of the oral mucosa was confined to the buccal surface of the anterior, maxillary sextant of the mouth, above the mucogingival margin. Of the dentition the maxillary and mandibular incisors appeared to be the worst affected, notably the coronal thirds with the gingival third being spared.

Investigations

A dental panoramic radiograph excluded the presence of any radiographically detectable underlying bony pathology contributing to the oral discoloration and showed only localised dental pathology.

Treatment and outcomes

Unfortunately much of the literature describes minocycline-induced staining as irreversible^{1,2} thus limiting our treatment of the affected areas to cessation of minocycline to prevent any further deterioration. The exception to this was the

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dentition and the patient was referred on to a specialist in restorative dentistry for advice. Minocycline-induced staining of the teeth may be amenable to vital bleaching³ which is a relatively simple and inexpensive option when compared to other options such as crowns and veneers which are also more costly and more destructive.

DISCUSSION

Review of literature

Minocycline is a broad spectrum antibiotic belonging to the tetracycline family which is well absorbed into bodily tissues given its lipid solubility and ability to bind to plasma proteins.⁴ Minocycline is the drug of choice in the treatment of moderate to severe acne vulgaris⁵ and in the long term management of rosacea.⁶ Discoloration of the developing dentition following childhood tetracycline use is well documented and widely known among prescribing practitioners.^{7,8} Although minocycline-induced staining has been documented in the past, the dangers of long-term minocycline use do not appear to be as well known as its relative. The two differ in that minocycline can affect fully erupted teeth^{7,9,10} whereas tetracycline affects the unerupted, uncalcified dentition leading to avoidance of the drug during childhood.⁷ Indeed Cascio *et al.* demonstrated that a three-week course of minocycline during childhood has no ill effects on the developing or developed dentition.¹¹ Another difference, as seen in this case, is that the gingival third of the crown tends to be spared in minocycline staining.¹²

Many cases within the literature describe the dental discoloration caused by minocycline as irreversible,^{1,2,12} however, Dr I. Caro described a case where partial resolution was seen within one month of cessation of the drug after 4-5 years of 200-300 mg daily minocycline.¹³ The incidence of dental staining in patients using long term minocycline has been estimated at around 3-6% if a daily dose of 100 mg is exceeded.^{14,15} The effect of minocycline on teeth tends to be less severe than that of tetracycline but the mechanism of the tooth staining is not fully known. One theory proposed involves minocycline attaching itself to the acquired pellicle and forming black quinone.¹⁵ A theory involving the breakdown of minocycline to form

haemosiderin which then combines with iron to form the pigment was proposed by Poliak *et al.* in 1985.¹⁰ In 1997 Bowles *et al.* suggested a third theory where minocycline binds to plasma proteins which are subsequently deposited in the pulp of the tooth.¹⁶ Although several theories exist, further work is required to establish the true process. In this case the third theory is supported by the absence of discoloration in the non-vital mandibular right central incisor. Interestingly, Kim *et al.* carried out *in vitro* experiments on extracted teeth to establish the causative agent in the discoloration of teeth treated with an intracanal triple antibiotic mixture and found minocycline to be the causative agent.¹⁷

It is also worth noting here that doxycycline, another of the tetracycline family, has also been known to cause post-eruption staining of the teeth¹⁸ and ciprofloxacin has been associated with a greenish discoloration of teeth following neonatal administration of the drug.¹⁹ The patient in this case, however, did not have a history of use of either of the latter therefore they were excluded from the differential diagnosis. Given the spared root-treated mandibular incisor, extrinsic sources of dark discoloration can also be excluded.

The mucosa in the anterior maxilla is relatively thin and discoloration of the gingivae is thought to be related to discoloration of the underlying bone transmitting through the mucosa.^{2,7,9,20} Siller *et al.* described one such example in a case affecting lingual mucosa where upon lifting a muco-periosteal flap it was found the mucosa has a normal colour but the underlying bone exhibited a blue-green discoloration.²¹ Kelly *et al.* proposed that the discoloration could be due to the deposition of insoluble black salts within the bone.²² Minocycline induced pigmentation of bone at various other sites, termed 'black bone disease', has also been documented.²³ The incidence of pigmentation of alveolar bone in patients taking between 100-200 mg minocycline per day is 10% after one year, increasing to 20% after four years,²⁴ indicating the duration of use is important. A reduction in the severity of the discoloration has been described following cessation of minocycline.^{21,24}

There have been reported cases of staining of the tongue and buccal mucosa itself; however, these are much less common

and the mechanism of such discoloration is largely unknown.^{24,25} It is thought that a complex of minocycline and a metabolite or granules of calcium, melanin or iron result in deposits of pigment²¹ and Eisen *et al.* proposed that the staining was more commonly seen in sites predisposed to trauma.²⁴

Bluish staining of the sclerae following minocycline use has been documented to varying degrees of severity²⁶ and upon cessation of minocycline therapy, may take several years to resolve or may persist indefinitely.²⁴ In each of the cases reviewed by Sabroe *et al.* the patients each had other sites affected²⁶ and Pepine *et al.* described one such case with discoloration of the skin, sclerae and nails which, after a 3-4-year period of discontinuation of minocycline, had faded.²⁷

Staining of the pinnae of the ear has been documented only a few times within the literature and therefore it is assumed this side effect is very rare.^{28,29} The mechanism for ear staining is still unclear and is difficult to study given such low numbers of patients affected but given the proposed mechanisms for other sites which are also affected, one would propose it is related to either to the underlying cartilage or staining of the skin itself.

In addition to the sites described in the case report above, minocycline has also been known to cause pigmentation in the thyroid, nails, bone, subcutaneous fat and skin.^{2,7,10,15,16,26,30,31} There have been suggestions that there may a relationship with thyroid function and Vitamin C use.³ Therefore it may be worthwhile considering these factors before prescribing long-term minocycline, but further evidence is required to support these theories. Alternatives to minocycline such as azithromycin should be considered³² or perhaps a reduced dose if possible.³³

CONCLUSION

If patients already have concerns regarding their appearance due to facial acne vulgaris or rosacea, careful consideration ought to be given to using minocycline as the medicament as it could lead to potentially irreversible discoloration. Patients commencing long-term minocycline therapy of greater than 100 mg per day should be informed of the risk of developing staining before commencing therapy and dental

practitioners with patients taking minocycline ought to be vigilant in identifying discoloration of the sites described above as early cessation could reduce severity of the effect. This case report adds to the few reports of minocycline-induced staining of the teeth, oral mucosa, sclerae and ears in the literature and provides support for the theory of an intrinsic mechanism for the staining of the dentition.

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