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## Case report

# Black pigmentation of both forearm bones after chronic minocycline antibiotic therapy for septic nonunion. A case report and literature review

## *Pigmentation noire des deux os de l'avant-bras après traitement par minocycline pour pseudarthrose septique. À propos d'un cas et revue de la littérature*

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### ABSTRACT

We report the case of a 28-year-old man with a septic forearm non-union treated with minocycline for 3 months. At the time of reconstructive surgery, the radius and ulna were entirely black. Surgical debridement until bleeding of both bone extremities resulted in a 5-cm defect that was filled with a cement spacer. Histology confirmed poorly vascularized bone with focal areas of acute inflammatory infiltrate at the non-union sites (highly suggestive of infection) and normal structure of the remaining diaphyseal bones, although black in color. Reconstruction with free vascularized fibula transfer was successful leading to complete bone healing. An incidental finding of minocycline-induced black bone discoloration should not change the surgeon's decision because there is no evidence of adverse effects on bone healing in the literature. Surgery can be performed safely at sites of minocycline-induced black bone pigmentation.

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### R É S U M É

Nous rapportons le cas d'un homme de 28 ans, traité par minocycline pendant 3 mois pour une pseudarthrose septique des deux os de l'avant-bras. Au cours de la chirurgie de reconstruction, le radius et l'ulna sont apparus entièrement colorés en noirs. Une résection osseuse de 5 cm a été réalisée sur chacun des deux os jusqu'à obtenir des extrémités saignantes à l'avivement. La perte de substance a été comblée par une entretoise en ciment. L'analyse histologique a confirmé au niveau des zones de résection un os dévascularisé avec des zones d'infiltrats inflammatoires (fortement compatible avec une infection osseuse évolutive) ainsi qu'un os de structure histologique normale au niveau d'autres zones de prélèvements diaphysaires également pigmentées. Une reconstruction secondaire par fibula vascularisée dédoublée a permis une consolidation osseuse complète. Au regard des données actuelles de la littérature, la découverte fortuite d'une pigmentation osseuse noire dans un contexte de traitement par minocycline ne devrait pas modifier l'indication chirurgicale initiale, car aucune preuve d'effet indésirable sur la structure osseuse n'a pu être établie. Une intervention chirurgicale sur un os coloré en noir dans un contexte de prise de minocycline au long cours peut être réalisée sans préjudice sur la consolidation ou l'ostéointégration.

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## 1. Introduction

Only a few cases of black bone pigmentation have been reported. Possible etiologies are chronic use of tetracycline antibiotics, ochronosis, metallosis, sequestrum and metastatic disease [1]. We report the case of a 28-year-old man with septic forearm non-union treated with minocycline for 3 months.

## 2. Case report

A 28-year-old male non-smoker had a motorcycle collision with car, which resulted in mild traumatic brain injury, chest wall trauma with fracture of four adjacent ribs and a flail chest complicated by pneumothorax. He also had an open right diaphyseal forearm fracture, which was managed by debridement, irrigation and titanium intramedullary nailing as a damage control procedure (Fig. 1a).

At day 11 after the surgery, a surgical site infection required revision surgery consisting of irrigation and debridement. Microbiology work-up isolated *Enterobacter cloacae*, *Bacillus cereus* and *Coagulase-negative staphylococci*. The patient received a 3-month course of levofloxacin, minocycline and rifadine.

When he was first referred to our septic surgery department, the wound was completely healed, and levels of inflammatory blood markers were not altered. Radiographs revealed a mid-shaft forearm non-union (the proximal fracture site of the radius was healed), with no evidence of underlying bone pathology. The multidisciplinary bone infection team recommended a one-stage reconstruction with locking plate and iliac-crest bone graft.

We used a standard anterior radius and dorsal ulna approach. The radius and ulna bones had an unusual dark appearance (Fig. 1b). This black bone coloring had no metallosis characteristic as titanium nails showed no evidence of wear and no metal debris was noted [2]. After removal of the intramedullary nails, surgical debridement until bleeding of the bone extremities resulting in a 5-cm defect in the radius and ulna that was filled with a gentamicin-loaded cement spacer (Fig. 1c). A detailed clinical examination did not reveal any skin or oral cavity discoloration

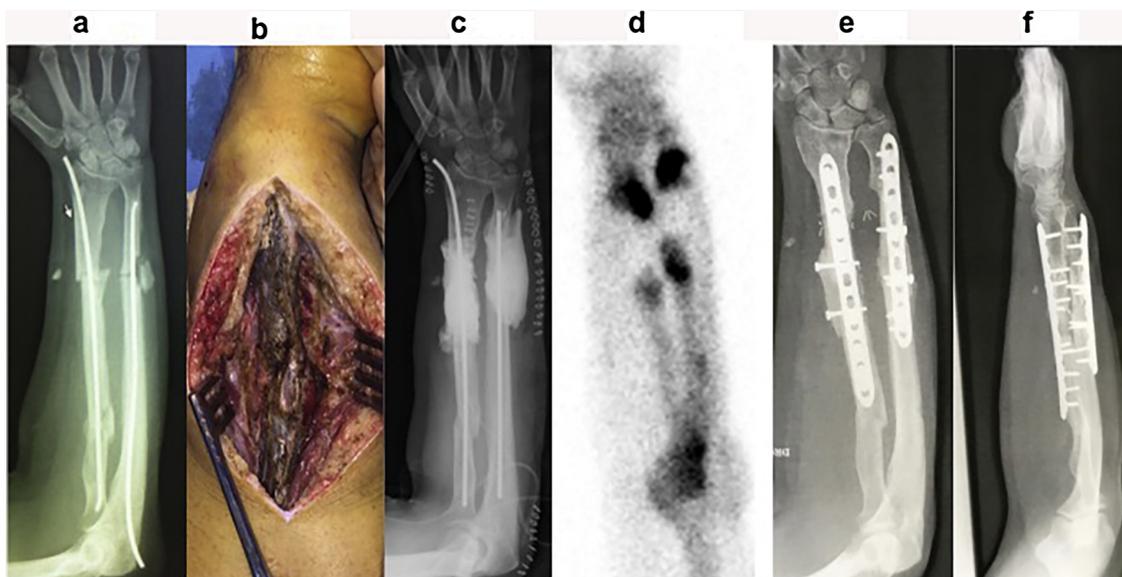
Microbiology testing revealed methicillin-resistant *Staphylococcus aureus* and *Cutibacterium acnes*. Histology confirmed poorly vascularized bone with focal areas of acute inflammatory infiltrate at the non-union sites (highly suggestive of infection) and normal structure of the remaining black diaphyseal bones. Neither granular particles nor metal fragments were noted. The patient took levofloxacin and rifadin for 3 months. Postoperative bone scintigraphy revealed increased uptake in both forearm bone extremities and normal diaphyseal uptake demonstrating normal bone perfusion and vitality (Fig. 1d).

Two weeks after the antibiotic therapy ended, we performed surgical reconstruction with a double-barrel free vascularized fibula graft and locking plates. Microbiology at the time of surgical revision was negative. Complete bone healing was achieved 6 months later (Fig. 1e and f). The patient (a plumbing/heating contractor) resumed his full work activities without residual pain. He recovered a functional range of motion with full wrist and elbow flexion-extension, 60° pronation and 50° supination.

## 3. Discussion

Cases of black bone pigmentation have mainly been reported in oral and maxillofacial surgical reviews [2]. There are only a few case reports in the orthopedic literature of incidental findings during routine surgical procedures [3–15]. We are aware of 17 published cases (Table 1). Hyperpigmentation of various body sites such as the skin, oral mucosa, teeth, nails, eyes and thyroid is a well-known side effect of chronic minocycline use with dosage > 100 mg/day [16]. Yang et al. [8] reported 5 cases of periarticular bone pigmentation discovered during total joint arthroplasty after a mean minocycline dosage of 160 mg/day for 2.2 years.

The ability of tetracycline and its derivatives to chelate calcium ions allows for its incorporation into normal bone. Deposition of minocycline complexes results in black discoloration [17]. Minocycline may be responsible for dysosteogenesis of oral bone [16], particularly in children. However, whether minocycline-induced pigmentation has any adverse effect on bone quality in adults is unclear. To our knowledge, there are no published reports of



**Fig. 1.** Early postoperative X-rays from the first surgical procedure (a). Intraoperative photo showing black pigmentation of the ulna (b). Early postoperative X-rays after surgical revision with new intramedullary nailing and cement spacer (c). Bone scintigraphy revealing increased uptake in the extremity of both forearm bone and normal diaphyseal uptake (d). X-rays showing complete bone healing at 10 months after free vascularized fibula transfer (e, f).

**Table 1**

Cases of black bone discoloration related to minocycline use in orthopedic surgery.

Authors	Number of patients	Location	Procedure
Kerbleski et al. (2013) [3]	1	Foot	HV
Thiam et al. (2016) [4]	1	Femoral shaft	Fixation hardware removal
McCleskey and Littleton (2004) [1]	1	Knee	TKA
Hepburn et al. (2005) [5]	1	Femoral shaft	Revision surgery for late surgical site infection
Chauhan and McDougall (2014) [6]	1	Knee	TKA
Reed et al. (2012) [7]	1	Knee	TKA
Yang et al. (2012) [8]	4	2 hips, 2 knees, 1 ankle	2 THA, 1 TKA, 1 TAA, 1 revision THA, 1 revision TKA
Carter-Wale and Prior (2016) [9]	1	Foot	HV
Middleton et al. (2011) [10]	1	Foot	HV
Chan et al. (2012) [11]	1	Femoral neck	Arthroscopic treatment of femoroacetabular impingement syndrome
Pandit and Hadden (2004) [12]	1	Acromion and pelvic girdle	Subacromial decompression
Somayazula and Rogers (2010) [13]	1	Hand	Corrective metacarpal osteotomy
Wolfe and Reichmister (1984) [14]	1	Clavicle	Clavicle cyst removal
Rumbak et al. (1991) [15]	1	Vertebrae	Partial hemi-laminectomy

HV: hallux valgus; TKA: total knee arthroplasty; THA: total hip arthroplasty; TAA: total ankle arthroplasty.

structural bone damage or a histological abnormality related to long-term minocycline exposure in adults. In black bone case reports, the surgeons did not change their surgery plan and the patients had a normal postoperative course and recovery [3–15].

In this case, discoloration of the forearm bones is a potential consequence of long-term treatment with minocycline antibiotics. Normal histological structure of the black-colored diaphyseal bone suggests minocycline-related pigmentation. Poorly vascularized bone with focal areas of acute inflammatory infiltrate at the non-union sites may result from chronic infection. Reconstruction with a free vascularized fibula transfer was successful in our case, which underlines the benefit of free vascularized bone grafts in extensive forearm bone loss management.

#### 4. Conclusion

Orthopedic surgeons should be aware of black bone disease secondary to the chronic use of minocycline and patients should be systematically informed of possible skin, bone or tooth hyperpigmentation in addition to well-known adverse effects (photosensitivity, digestive disorders, teratogenicity). Recognition of this entity should be reassuring because of no evidence of adverse effects in adult bone. Surgery can be performed safely at sites of minocycline-related black bone pigmentation.

#### Disclosure of interest

The authors declare that they have no competing interest.

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