Metallic Discoloration on the Right Shin Caused by Titanium Alloy Prostheses in a Patient with Right Total Knee Replacement

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The differential diagnosis of bluish-gray discoloration of the skin includes benign melanocytic nevi, such as Mongolian spots, blue nevi, junctional nevi, or nevi of Ito and Ota, and malignant melanoma as well as metallic discoloration. Although histopathologic findings are important for differentiating benign melanocytic nevi from malignant melanomas or metallic discoloration, a thorough history and physical examination may also provide significant information. Metallic discoloration is an uncommon disorder defined by the accumulation of metallic particles in the skin through the blood stream or surface application, while metallosis refers to the deposition of metallic particles after being worn out by artificial articulation after total joint replacement.

To the best of our knowledge, only 2 cases of titanium pigmentation have been reported in dermatologic literature and orthopedic literature. Here, we describe a case of metallic discoloration induced by titanium-aluminium alloy in a patient with a history of bilateral total knee replacements, presenting with symptoms of bluish-gray pigmentation of the right shin.

CASE REPORT

A 75-year-old woman had a large blue patch on the right shin for 3 years. She underwent a left total knee replacement 18 years ago and a right total knee replacement 14 years ago due to severe osteoarthritis of both knees. Each of the operations was carried out successfully without any serious adverse events. Eleven years after the right total knee replacement, she noticed a discoloration of her...
right shin, and the lesion continued to enlarge slowly over time. She was referred to a dermatology clinic where a large, well-demarcated bluish-gray patch was noted on her right shin. The surface of the skin was smooth with no palpable infiltration. For 1 year, she experienced pain when walking on the right shin. She had a 10×15 cm well-demarcated bluish-gray patch on the extensor surface of her right shin (Fig. 1). Routine laboratory tests, including complete blood count, liver function tests and urine analysis, yielded normal findings. Histopathologic findings from the skin lesion showed perivascular, fine black particles in the dermis (Fig. 2). The black particles were stained positive with both melanin and demelanin stains. Polarizing microscopy of the skin specimen revealed refractile foreign materials in the perivascular area of the dermis (Fig. 3). Further, energy-dispersive X-ray spectroscopy revealed the presence of titanium and alumi-

![Fig. 1.](image1.jpg) (A) A 10×15 cm sized skin lesion is observed on the right shin. (B) The skin lesion show blue to gray colored patch.

![Fig. 2.](image2.jpg) (A, B) Black particle deposits on the perivascular area in the dermis (black circles) (A: H&E, ×40; B: H&E, ×400). (C) Melanin in the epidermal basal layer (arrows) and black particles around vessels in the dermis (circle) are positive for melanin stain (×200). (D) Positive staining of black particles around vessels in the dermis (circle) and negative staining of melanin in the epidermal basal layer (Demelanin, ×200).

![Fig. 3.](image3.jpg) Findings from polarizing microscopy reveal refractile foreign materials (arrows) in the skin specimen (H&E, ×200).
Fig. 4. Findings from energy dispersive X-ray analysis of black particles around vessels in the dermis show peaks for titanium (Ti), aluminium (Al), carbon (C), sodium (Na), chlorine (Cl) and vanadium (V).

Fig. 5. During the revision operation, periprosthetic tissues from the interface to the joint capsule showed black pigments.

Metallic discoloration was diagnosed on the basis of clinical, histopathological, polarizing microscopy and energy dispersive X-ray spectrophotometer findings. The radiographs revealed loosened and dislocated tibial components of the right knee prostheses. Preoperative and intraoperative cultures were negative for bacteria. During surgical revision, marked loosening of the tibial component and wearing of polyethylene were found. Additionally, an intense black staining of a substantial amount of wear debris adjacent to the tibial components and tibial bone defect was observed (Fig. 5). The patient was treated by debridement, and the right tibial component was replaced. After the revision procedure, metallic discoloration disappeared and has not reoccurred over the past 4 years.

DISCUSSION

Metallic discoloration is caused by a deposition of metallic particles in the skin, mostly via the blood stream, external exposure or rarely, by metallosis of the prostheses. This pigment change takes place via the deposition of metal particles and induction of epidermal melanin production. Metallic discoloration by copper, silver and thallium has been reported in dermatologic literature. This case presented several interesting features: (i) localized bluish-gray pigmentation mimicking the clinical picture of dermal melanocytosis caused by metallosis of an artificial joint in the knee, and (ii) the importance of considering the history of joint replacement surgery when there are bluish-gray skin lesions in an elderly patient in order to differentiate dermal melanocytosis from blue nevi or malignant melanoma.

Titanium alloy (Ti-Al6-V4) has been widely used as a material for total knee replacement surgery ever since 1985. It is composed of 90% titanium, 6% aluminium and 4% vanadium. Metallosis of titanium alloy has frequently been reported in orthopedic literature as black staining of the periprosthetic tissue due to debris from the metallic wear and tissue reaction after knee or hip replacement surgery. Metallosis is usually confined to the joint capsule or around the prosthesis. Metallosis of the overlying skin is quite rare.

To the best of our knowledge, there have been only a few cases of titanium pigmentation of the skin in the literature. Seong et al. reported 6 cases of failed total knee replacement with titanium-induced tissue response in 5 patients. Of the 5 patients, only 1 presented symptoms with metallic discoloration. Akimoto et al. reported an 80-year-old woman with solid red-brown nodules and papules with scattered bluish-black macules on her right lower leg after a total lateral replacement of the right hip 6 years ago.

Histopathologically, metallosis of skin shows fine brown/black particles consistent with metallic debris throughout the dermis in the subcutaneous tissue. They are mainly phagocytosed by macrophages, but can also be seen as dispersed particles. In addition, metallosis of periprosthetic tissue is usually composed of fibroblastic tissues, with a heavy deposition of black fragments lying extracellularly and within histiocytes and foreign-body giant cells. It is well known that metallosis has been implicated in implant failure by causing a darkly stained proliferative soft-tissue reaction. Unfortunately, in our case, studies to identify
titanium in the affected periprosthetic tissue were not performed.
The mechanism of metallic pigmentation caused by metal-wear debris in the overlying skin remains unclear. Agins et al.\textsuperscript{11} discovered that there was no correlation between the titanium content of the tissue and the length of time that the implant had been in the body. Moran et al.\textsuperscript{13} reported 4 patients who were presented with titanium dioxide in the lungs caused by inhalation. These patients had large quantities of dark pigments in the macrophages of the peribronchial lymph nodes, liver, spleen, alveolar spaces, and around the bronchioles and blood vessels\textsuperscript{11}. This suggests that macrophage-laden or free black metallic particles may spread to adjacent blood vessels and lymph nodes. In our case, the histologic appearance of the skin lesion showed black pigments predominantly in the perivascular area of the dermal and subcutaneous tissue. Further, it demonstrated a titanium and aluminium peak on the energy dispersive X-ray spectrophotometer unit attached to a transmission electron microscope. A vanadium (V) peak could not be identified because it is quickly released from tissues due to its high solubility (Fig. 4)\textsuperscript{14}. Presumably, we suggest that the periprosthetic tissue reaction of metallosis gradually spreads via lymphatic or blood vessels, and bluish-gray pigmentation subsequently develops on the overlying skin.

In summary, wear debris from a total knee joint prosthesis produced sufficient clinical symptoms, prompting the need for operative revision 14 years after implantation and 3 years after skin pigmentation on the right knee. Even though metallosis of titanium alloy is a relatively well-known disease in orthopedic literature, metallic discoloration of the skin is quite rare, mimicking the clinical picture of blue nevi or malignant melanoma. Therefore, the possibility of metallic discoloration must be included in the differential diagnosis of bluish-gray pigmentation.

REFERENCES

1. Tseng SS, Whittier S, Miller SR, Zalar GL. Bilateral tinea nigra plantaris and tinea nigra plantaris mimicking melanoma. Cutis 1999;64:265-268.
2. Goncharuk V, Mulvany M, Carlson JA. Bednár tumor associated with dermal melanocytosis: melanocytic colonization or neuroectodermal multidirectional differentiation? J Cutan Pathol 2003;30:147-151.
3. James WD, Berger TG, Elston DM, Odom RB. Andrews’ diseases of the skin: clinical dermatology. 10th ed. Philadelphia: Elsevier, 2006:858-860.
4. Breen DJ, Stoker DJ. Titanium lines: a manifestation of metallosis and tissue response to titanium alloy megaprostheses at the knee. Clin Radiol 1993;47:274-277.
5. Akimoto M, Hara H, Suzuki H. Metallosis of the skin mimicking malignant skin tumour. Br J Dermatol 2003;149:653.
6. Seong SC, Lee MC, Moon YW, Lee JC. Failed TKA with Titanium-induced tissue response. Korean J Orthop 1996; 31:720-729.
7. Peterson J, Shook BA, Wells MJ, Rodriguez M. Cupric keratosis: green seborrheic keratoses secondary to external copper exposure. Cutis 2006;77:39-41.
8. Jonas L, Bloch C, Zimmermann R, Stadie V, Gross GE, Schäd SG. Detection of silver sulfide deposits in the skin of patients with argyria after long-term use of silver-containing drugs. Ultrastruct Pathol 2007;31:379-384.
9. Aasly JO. Thallium intoxication with metallic skin discoloration. Neurology 2007;68:1869.
10. Witt JD, Swann M. Metal wear and tissue response in failed titanium alloy total hip replacements. J Bone Joint Surg Br 1991;73:559-563.
11. Agins HJ, Alcock NW, Bansal M, Salvati EA, Wilson PD Jr, Pellicci PM, et al. Metallic wear in failed titanium-alloy total hip replacements. A histological and quantitative analysis. J Bone Joint Surg Am 1988;70:347-356.
12. Asahina A, Fujita H, Fukuda S, Kai H, Yamamoto M, Hattori N, et al. Extensive skin pigmentation caused by deposits of metallic particles following total elbow arthroplasty: metallosis or not? Br J Dermatol 2007;157:1074-1076.
13. Moran CA, Mullick FG, Ishak KG, Johnson FB, Hummer WB. Identification of titanium in human tissues: probable role in pathologic processes. Hum Pathol 1991;22:450-454.
14. Lalor PA, Revell PA, Gray AB, Wright S, Railton GT, Freeman MA. Sensitivity to titanium. A cause of implant failure? J Bone Joint Surg Br 1991;73:25-28.