

Intra-Articular Pigmentation of Synovium: An Unusual Cause

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An unusual grayish brown discoloration of the synovium was found during a knee arthroscopy of a 72-year-old man. He also had similar pigmentation affecting the skin on the legs, arms, hands, and face. It was found he had been taking 400 mg of amiodarone hydrochloride daily for last 7 years. Amiodarone is known to cause a slate grey pigmentation of skin and cornea, but we believe this is the first report of amiodarone-induced pigmentation of the synovium. The arthroscopist should be aware of the possibility of drug-related synovial pigmentation and include this in differential diagnosis.

Keywords: *Knee, Arthroscopy, Synovium, Pigmentation, Articular*

Intra-articular pigmentation is uncommon. It may be due to conditions such as pigmented villonodular synovitis or alkaptonuria. It has also been noted after carbon-reinforced synthetic anterior cruciate ligament reconstruction.

CASE REPORT

A 72-year-old man underwent arthroscopy for symptoms of mechanical locking of his left knee. He had been taking amiodarone hydrochloride for the last 7 years for treatment of cardiac arrhythmia. He had areas of blue grey pigmentation on the face, forearms, hands, and legs (Fig. 1). He did not have a storage disease and his only other medications were warfarin and aspirin. During knee arthroscopy, widespread pigmentation of the synovium similar to that on his skin was seen. The menisci and articular cartilage were not affected. He underwent debridement of a lateral meniscal tear (Fig. 2). The debrided meniscus and synovial tissue obtained during arthroscopy was sampled

and sent for histopathological examination, which showed the presence of periodic acid–Schiff-positive aggregates of yellowish brown granules within histiocytes consistent with the usual microscopic presentation of such deposits in the cornea and skin described by various authors previously.^{1,2)} The histopathological examination ruled out any pigmented villonodular synovitis. Considering the history, clinical picture and histological findings, the pigmentation seemed to have no other possible etiology but amiodarone.

DISCUSSION

Amiodarone hydrochloride is a coronary vasodilator used in the treatment of cardiac arrhythmias and can induce a blue-gray or violaceous pigmentation of the skin and yellow-brown stippling of the cornea.³⁾ The pigmentation of the skin and cornea in patients on long-term amiodarone therapy is well established and usually develops after 6 months or more of the therapy.^{4,5)} The cutaneous effects are more likely to manifest with longer durations of use and at doses greater than 400 mg per day.³⁾ The pigmentation on the skin and cornea may slowly resolve months to years after withdrawal of the therapy, although it can be permanent.^{2,5)}

Delage, a Belgian ophthalmologist, was the first to report a gray pigmentation of the cornea secondary to amiodarone use.¹⁾ The pathogenesis of this side effect is poorly understood. In 1975, Delage et al.¹⁾ described light

Received February 15, 2016; Accepted April 9, 2016

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Fig. 1. Clinical pictures of cutaneous pigmentation due to amiodarone.

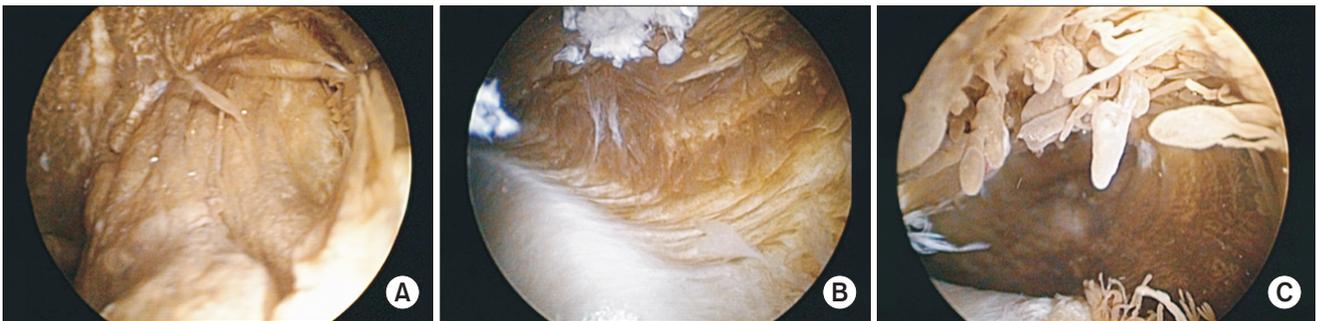


Fig. 2. Arthroscopic views of synovial pigmentation in the knee joint and meniscal sparing.

and electron microscopic findings of tissues affected by amiodarone as deposition of yellow-brown granules and lipofuscin within dermal macrophages. Electron microscopy also demonstrated granules contained within intralysosomal laminated inclusion bodies, and they suggested a storage abnormality involving the drug or its metabolites as the mechanism.⁴⁾ They also hypothesized that amiodarone accelerates normal cellular autophagocytosis resulting in increased production of lipofuscin which accumulates in lysosomes because of a deficiency in lipolytic enzymes and concluded that pigmentation in the skin and cornea may develop because the drug or its metabolites accumulate in the histiocytes between the collagen fibres. How-

ever, Brazzelli et al.,⁶⁾ in their article, suggested that the pathogenesis may be related to the action of the drug on cell membranes causing local metabolic damage, accumulation of the drug in the lysosomes, and acceleration of the physiological aging process. We think that drugs should be included in the differential diagnoses of pigmentation of the synovium and the arthroscopist should be aware of this condition.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported

REFERENCES

1. Delage C, Lagace R, Huard J. Pseudocyanotic pigmentation of the skin induced by amiodarone: a light and electron microscopic study. *Can Med Assoc J.* 1975;112(10):1205-8.
2. Quintanilla E, Tunon T, Fernandez-Berridi D, Pardo-Mindan FJ. Cutaneous pigmentation caused by amiodarone: optical and ultrastructural study. *Med Cutan Ibero Lat Am.* 1982;10(3):177-82.
3. MIMS [Internet]. St Leonards, AU: MIMS; 2016 [cited 2016 May 1]. Available from: <http://www.mims.com.au/>.

4. Zachary CB, Slater DN, Holt DW, Storey GC, MacDonald DM. The pathogenesis of amiodarone-induced pigmentation and photosensitivity. *Br J Dermatol.* 1984;110(4):451-6.
5. Weiss SR, Lim HW, Curtis G. Slate-gray pigmentation of sun-exposed skin induced by amiodarone. *J Am Acad Dermatol.* 1984;11(5 Pt 1):898-900.
6. Brazzelli V, Borroni G, Dal Tio R, Riva R, Bollati A, Rabbiosi G. Amiodarone-induced pigmentation: a histological, ultrastructural study and review of the literature. *G Ital Dermatol Venereol.* 1990;125(11):521-6.