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Mahmood, Muhammad N

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Histopathological features of iatrogenic occlusive vasculopathy caused by intra-articular hyaluronic acid injection for osteoarthritis

Muhammad N Mahmood MD

Affiliations: Department of Laboratory Medicine & Pathology, University of Alberta Hospital, Edmonton, Alberta, Canada

Corresponding Author: Muhammad N Mahmood MD, University of Alberta Hospital, Laboratory Medicine & Pathology, 5B4.55 WMC, 8440-112 Street, Edmonton, AB T6G2B7, Canada, Tel: 780-407-2145, Fax: 780-407-3009, Email: noshpath97@gmail.com

Abstract

Occlusive vasculopathy may rarely occur after intra-articular injection with hyaluronic acid. The associated histological changes are not well described. Herein, we would like to present representative histology of this phenomenon.

Keywords: dermatopathology, hyaluronic acid, iatrogenic, occlusive vasculopathy, osteoarthritis

Introduction

In an interesting report in this journal, Toussi et al. highlight iatrogenic vascular occlusion secondary to intra-articular injection of hyaluronic acid (HA) in a patient with osteoarthritis [1]. Occlusive vasculopathy related to HA injections is typically described in association with cosmetic facial procedures, with only rare reports in the setting of intra-articular injections in patients with osteoarthritis. Toussi et al. describe the clinical parameters and treatment options very well; however, the histopathological profile is not discussed. Owing to the rare reporting of this phenomenon, the histopathological profile in this particular setting has only been discussed in occasional case reports [2-4]. We would like to add to this and describe the histopathological changes associated with this uncommon iatrogenic condition.

Discussion

Many diverse conditions can produce non-vasculitic occlusive vasculopathy of cutaneous vasculature [5].

Embolization phenomena related to various underlying etiologies are known to cause a number of such vasculopathies. In vasculopathies secondary to embolization, recognition of pathognomonic elements occluding vascular lumina in the dermis and subcutis are usually required to establish the cause. Accurate recognition of underlying etiology is of utmost importance as a number of these disorders can be associated with systemic involvement and visceral damage. Examples of conditions in this category include cholesterol and oxalate embolus, intravascular metastasis from visceral malignancies, endocarditis, atrial myxomas and intimal angiosarcomas, and inoculated foreign materials. Hyaluronic acid induced vasculopathy can be categorized in the embolization of foreign material subgroup. Some other similar examples in this subgroup include transarterial chemoembolization with drug-eluting microspheres, such as doxorubicin beads, and hydrophilic polymer microemboli from coatings developed to reduce friction between catheters and vessel walls [6, 7].

The histopathological changes associated with this adverse event in this particular setting have been reported in the past [2-4]. Hyaluronic acid gains access to cutaneous vessels possibly secondary to injection at incorrect anatomic site or extravasation from inside the joint cavity into the surrounding tissue and vasculature. On microscopic examination, amorphous lightly basophilic foreign material representing HA is noted within the vascular lumina in the lower dermis and subcutis (**Figure 1**). The vessels appear dilated and associated thrombosis can be seen. Owing to vascular obstruction and resulting ischemia, cutaneous necrosis can be seen

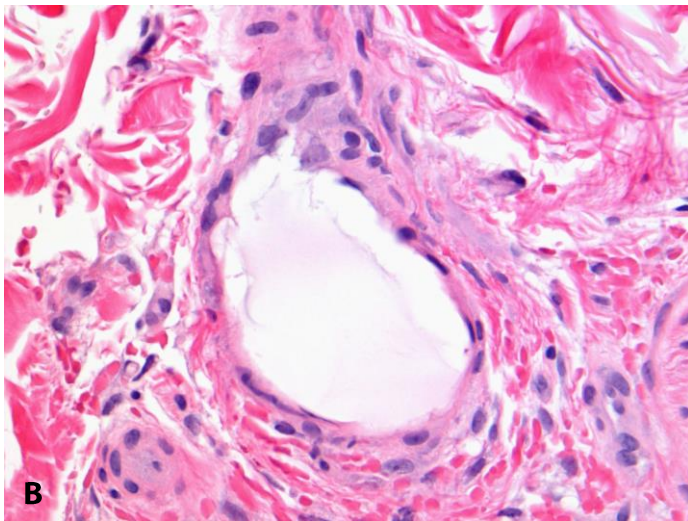
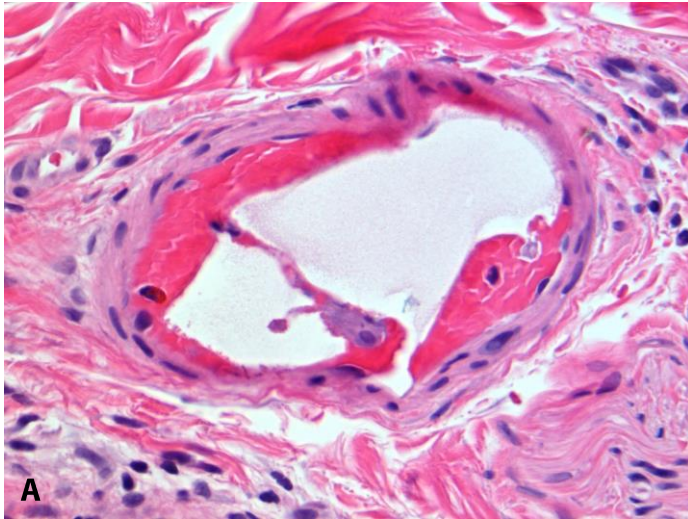


Figure 1. Amorphous basophilic foreign material representing hyaluronic acid is present in the vascular lumina **A)** at dermal-subcutis border, **B)** in dermis. H&E, 400 \times .

with patchy epidermal necrosis. Prominent neutrophilic infiltrate with leukocytoclasia has not been described. Hyaluronic acid may also be present in the dermal stroma or around the vasculature, with focal multinucleated histiocytic response (**Figure 2**). Alcian blue stain (pH of 2.5) highlights HA (**Figure 3**).

Conclusion

Dermatopathologists should be mindful of this rare, albeit potentially serious, adverse event. Availability of clinical history of intra-articular HA injection close

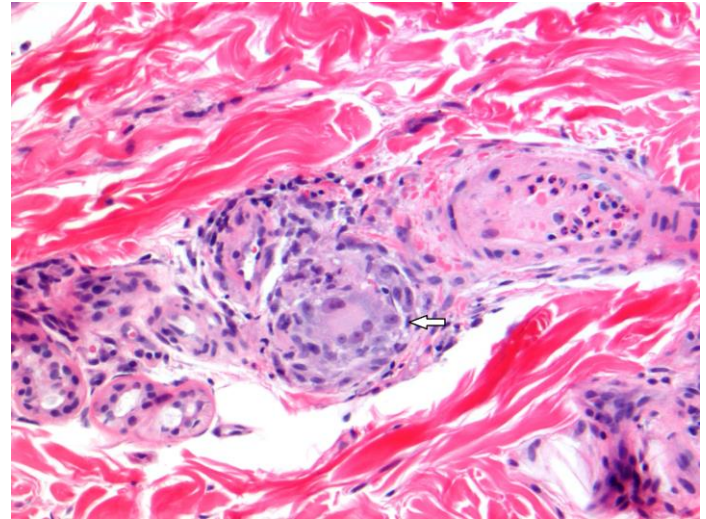


Figure 2. Focal multinucleated histiocytes (arrow) are seen around involved vessels. H&E, 200 \times .

to the area of involvement is critical in establishing correct pathological diagnosis. As complete clinical history may not be available in all cases, a dermatopathologist should be aware of this diagnostic possibility as a potential rare cause of occlusive vasculopathy.

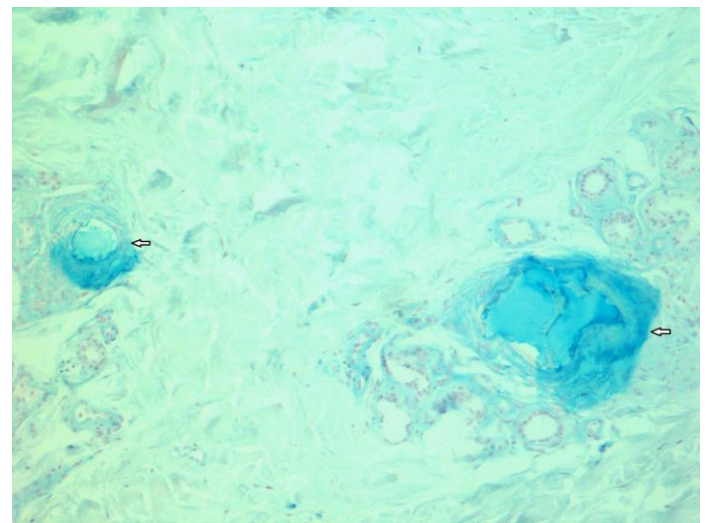


Figure 3. Alcian blue stain (pH 2.5) highlights hyaluronic acid (arrows), 50 \times .

Potential conflicts of interest

The author declares no conflicts of interest.

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