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Delayed Hypersensitivity Reaction to Iodinated-Contrast Following Lumbar Epidural Steroid Injection: Case Report

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Background: Delayed hypersensitivity reactions to an iodinated radiologic contrast are a form of hypersensitivity reactions that occurs anywhere from one hour up to 10 days after exposure to the causative agent.

Case Report: We present a case of a 54-year-old woman with a history of a single minor reaction to an intravenous iodinated contrast consisting of only abdominal pain who developed a maculopapular exanthema 7 days after exposure to iohexol, an iodinated radiological contrast, during a lumbar epidural steroid injection. The patient was later treated with topical betamethasone with resolution of cutaneous symptoms within 2 weeks. The patient then underwent patch testing, which revealed a positive result for palladium (II) chloride; to date, there has been no documented association in the literature between palladium (II) chloride and iohexol.

Conclusion: DHRs to an iodinated radiologic contrast can range from cutaneous manifestations to lethal presentations, such as Stevens-Johnson syndrome and toxic epidermal necrolysis, with the most common form being a maculopapular exanthema as experienced by our patient. Testing can be performed to determine the causative agent of the DHR and to find an alternative agent if a radiologic contrast is required. Caution must be taken if using an alternative contrast agent as there is significant cross-reactivity to other iodinated radiologic contrasts.

Key words: Delayed hypersensitivity reaction, iodinated contrast, maculopapular exanthema, palladium, case report

BACKGROUND

Epidural steroid injections (ESIs) have long been leveraged as an important therapeutic intervention in patients with chronic back pain, especially for diagnoses of lumbar radiculopathy and spinal stenosis (1,2). Steroid medications are injected into the epidural space under fluoroscopic guidance to optimize needle accuracy and precision (3). As part of the procedure, a contrast agent is injected once the needle is presumed to be in the correct space to confirm needle location. Though the use of the contrast is relatively safe, it is not without risks.

Although radiologic contrast agents are available in different formulations, the primary contrast agent used in ESIs is iodine based. Adverse reactions to iodinated contrasts are rare; however, acute kidney injury and hypersensitivity reactions may occur (4-8). Hypersensitivity reactions to iodinated contrast agents can be classified into immediate and delayed hypersensitivity reactions (DHRs) (6). Furthermore, DHRs can present in many forms with the most common being maculopapular exanthema, which accounts for > 50% of cases (6,9). Though less common, other types that can occur include delayed-onset urticaria/angioedema, drug reaction with eosinophilia and systemic symptoms syndrome, Stevens-

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Johnson syndrome, and toxic epidermal necrolysis (9,10). The mechanism for DHRs is via a T-cell mediated reaction, and if a biopsy is taken of the cutaneous lesions, CD4+ and CD8+ T-cell infiltration may be present (6). The timing of DHRs varies from 1 hour after contrast exposure up to 10 days (9-11). With subsequent exposures, the reactions can occur much quicker (12).

Historically, shellfish allergy was thought to increase the risk of allergic reactions to iodinated contrast; however, studies (13-15) suggest there is no increased risk of reaction to iodinated contrast with very little evidence to support this claim of an increased risk. Moreover, iodine cannot be an allergen as it is found throughout our bodies in thyroid hormones and amino acids (14-16). Patients who are allergic to shellfish are not allergic to the iodine in shellfish, but the fish tropomyosin which is unrelated to iodine (14). The reaction may not necessarily be related to free elemental iodine or the anion, but the combination of the iodine bound to the aromatic ring of the contrast. Here, we present a case of a 54-year-old woman who developed maculopapular exanthema 7 days after a lumbar ESI (LESI) was performed using an iodinated contrast, iohexol.

CASE

Our patient is a 54-year-old woman with a past medical history of depression, anxiety, morbid obesity, fatty liver disease, asthma, eczema, allergic rhinitis, diabetes mellitus, and chronic lower back pain treated with opioids who presents for a LESI for chronic lower back pain with right radiculopathy. The patient had previously experienced a motor vehicle accident 4 years ago in which she began to experience lower back pain that radiated down the back of the right leg to the sole of the foot. The pain's average daily pain on the Visual Analog Scale was an 8-10/10. Magnetic resonance imaging of the lumbar spine revealed severe stenosis at L3-L4 with mild impingement of the traversing right L4 nerve root.

The patient was trialed on neuropathics (gabapentin and nortriptyline), nonsteroidal anti-inflammatories (ibuprofen and meloxicam), acetaminophen, and muscle relaxants (tizanidine and baclofen) to reduce her opioid consumption taken prior to bedtime. She received only minimal pain relief from the nonopioid medications, and the patient declined physical therapy due to the severity of her pain.

The patient was offered an L4-L5 ESI annually, but she declined each year for 2 years due to anxiety caused by the planned procedure. Of note, the patient did endorse only abdominal pain with a previous contrast injection with prior imaging, but the patient was unsure if the abdominal pain was due to the contrast administration, nor was it further investigated due to the minor symptoms. Given the worsening of her chronic lower back pain and the previous possible minor reaction to the contrast, the patient finally agreed to a LESI with the use of anxiolysis (lorazepam) prior to the procedure.

A right-biased LESI at L4-L5 was performed without any immediate complications. The amount of iohexol injected into the epidural space was 0.5 mL with a good spread followed by 80 mg of methylprednisolone and 1 mL of preservative-free 1% lidocaine (Fig. 1). On postoperative day 4, the patient noted increased pain in the lower back, but no red flag symptoms were present. On postoperative day 7, a pruritic, scaly, maculopapular purple eruption occurred over the arms, legs, and upper and lower back. Patient denied any shortness of breath or difficulty breathing. The patient was prescribed a topical steroid (0.05% betamethasone) with resolution of her eruption within 2 weeks.

The patient was referred to patch testing by Dermatology department using 172 patches (80 patches from the North American 80 Comprehensive Series, 42 patches from the cosmetic series, and 55 patches from the metal series). After 96 hours, the final patch test was read demonstrating a positive test to palladium (II) chloride (Fig. 2). Dermatology concluded that her reaction was most likely a DHR and advised the patient to avoid any exposure to her allergens.

DISCUSSION

The incidence of DHRs is widely variable ranging from 0.52% to 51%, but the incidence for cutaneous reactions is < 4% (17-19). The wide variability in the incidence seen in DHRs can be due to many reasons. The greater the time from the initial exposure to the development of the reaction can result in uncertainty as to what the actual cause was, improperly labeling an incorrect event as the cause, or the reaction may be very mild and the patient may not seek out medical attention.

DHRs typically occur anywhere from one hour up to 10 days later lasting up to one week, but can occur much quicker if the patient was previously exposed (12). A previous contrast DHR is the number one predisposing factor for an additional DHR; whereas, a previous immediate reaction does not increase the risk (20). Though this patient did have a previous possible

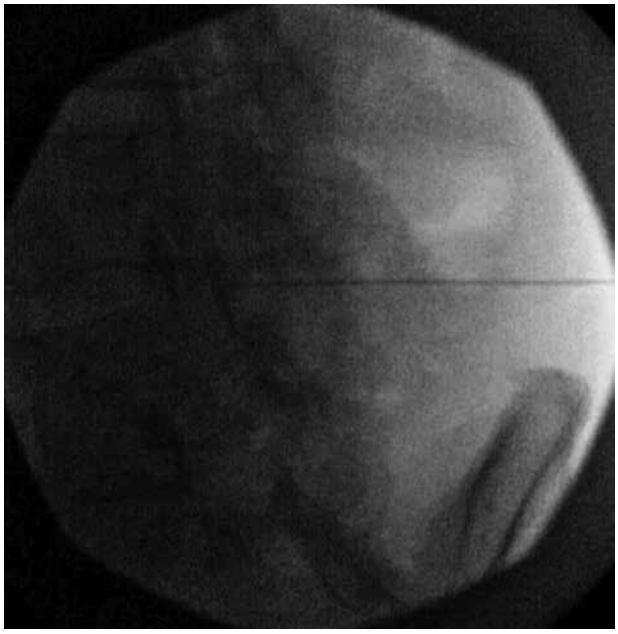

Fig. 1. Fluoroscopic image taken in lateral view during contrast injection demonstrating the spread of contrast in the epidural space.

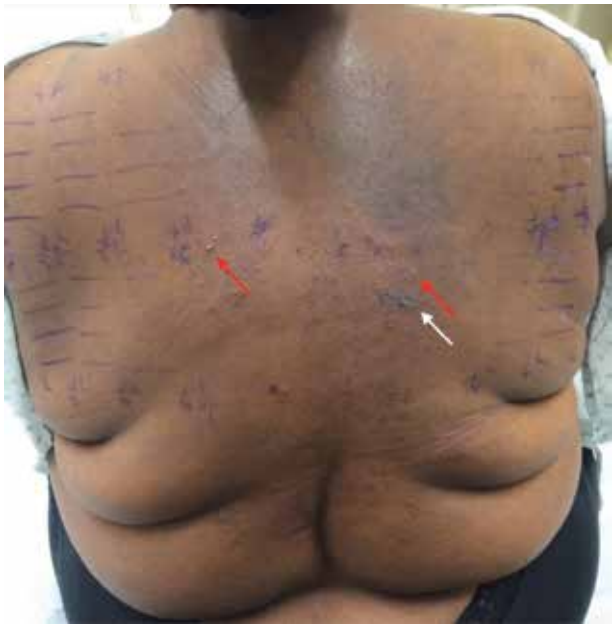

Fig. 2. Patch testing revealing a positive result to palladium (II) chloride (white arrow) and residual exanthematous pustulosis (red arrow).

contrast reaction, it was unclear if it was immediate or delayed or even due to the contrast. Other risk factors include a history of allergies or drug or contact allergies (18,21,22).

This patient most likely experienced a maculopapular exanthema, the most common presentation for DHRs, which can appear within 6 hours of exposure and up to 10 days after contrast exposure (10). The reaction is primarily mediated by T-cells primarily targeting the structure of the contrast agent as opposed to the actual iodine molecule (23).

To evaluate if an immediate or DHR did occur, allergy testing with either intradermal and patch testing should be performed within 1-6 months (10,24-26). If the testing is performed after 6 months, the percentage of positive reactions decreases by nearly half (24). Despite the testing, there is cross-reactivity with iohexol and other contrast agents, such as iodixanol and iomeprol; thus, care must be taken when using alternative agents (7,27,28). Though testing can be performed, it is not always definitive as the cause may not always be determined. Since the maculopapular exanthema is self-limited, only topical corticosteroid treatments may be needed as oral glucocorticoids are reserved if the maculopapular exanthema is severe.

Our patient developed a maculopapular exanthema secondary to iohexol administration after receiving a LESI. Though patch testing was performed, the only result was a reaction to palladium (II) chloride. Despite the cross-reactivities with iohexol, palladium (II) chloride does not have any documented cross-reactivity with iohexol in the literature, and there was no report of exposure to palladium (II) chloride in our patient though it has been widely used to plate metals, create catalysts, remove stains from stainless steel, and make carbon dioxide detectors (27). As to whether the positive test result for palladium (II) chloride is associated with iohexol remains to be determined or the result may be unrelated to the iohexol DHR.

CONCLUSIONS

A type of hypersensitivity reaction, DHR can occur anywhere from one hour up to 10 days after iodinated contrast exposure. Though patch and intradermal testing can assist in determining the possible cause, it does not always lead to detection of the causative agent as in our patient with a palladium (II) chloride positive patch result (Fig. 2). Despite the positive result, palladium (II) chloride has not been found to be associated with an iodinated-contrast allergy nor has it been found

to cross-react. Care should be used when considering alternative agents as iohexol has cross-reactivity with numerous alternative agents (27). Drug provocation tests, the gold standard for diagnosing DHRs, can also be performed if an alternative contrast is required, though they are not without their own risks as the patient will be reexposed to the possible culprit (26,29). Overall, the patient's cutaneous symptoms improved after 2 weeks with topical steroids. Our case demonstrates the difficulty with diagnosing DHRs as they often occur much later after the exposure, and there may not always be a definitive causative agent.

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