Case Report | Journal of Orthopaedic Case Reports 2020 March-April: 10(2):Page 73-75

Procalcitonin –Vital Tool to Differentiate Septic Progression of Spondylodiscitis from Drug Hypersensitivity: A Case Report and Brief Review of Literature

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Learning Point of the Article:

Pro-calcitonin proves to be vital tool to differentiate between acute septic spondylodiscitis and drug hypersensitivity.

Abstract

Introduction: Drug hypersensitivity is an important differential diagnosis in patients of infective spondylodiscitis, who develop systemic symptoms such as fever, rash, and arthralgia while on treatment with antibiotics. As these symptoms may also be present in sepsis progression, differentiation between two is very difficult. Procalcitonin (PCT) is one of the important and specific biomarkers of early sepsis.

Case Report: We present a case of a 33-year-old male with deep post-operative spinal infection complicated by drug hypersensitivity and worsening of systemic parameters. Serum PCT levels helped us to make correct diagnosis and prevent unnecessary surgical debridement.

Conclusion: PCT, as a biomarker, can help distinguish the septic progression of spondylodiscitis from drug hypersensitivity and prove vital in clinical decision-making in these difficult scenarios.

Keywords: Procalcitonin, spondylodiscitis, sepsis, drug hypersensitivity.

Introduction

Procalcitonin (PCT) is normally produced in the C cells of the thyroid, but microbial infections induce the release of PCT from all cell types throughout the body [1]. PCT is superior to C-reactive protein (CRP), tumor necrosis factor-α, and interleukin-6 in the early diagnosis of sepsis [1, 2]. Drug hypersensitivity is an important differential diagnosis in patients of infective spondylodiscitis who develop systemic symptoms such as fever, rash, and arthralgia while on treatment with antibiotics. Such symptoms may also arise as a result of septic progression of a localized spinal infection. This creates confusion and can lead to overuse of antibiotics or even a debridement surgery resulting in increased costs of treatment and potential morbidity. Furthermore, it can damage the confidence of the patient on the quality of treatment being given by the spinal team. We present a case where PCT levels helped us take a correct decision in managing a case of antibiotic-related drug hypersensitivity. Informed consent was obtained from the patient.

Case Report

A 35-year-oldpreviously fit male patient underwent uncomplicated lumbar interbody fusion for leg and back pain secondary to a spondylolisthesis (Fig. 1). The patient returned to clinic after 3 weeks complaining of increasing nocturnal back pain and arthralgia. Magnetic resonance imaging scan demonstrated non-specific post-operative appearances. CRP was elevated at 22. Computed tomography(CT) scan showed no evidence of bone resorption or screw loosening. A differential diagnosis of either intercurrent illness or early discitis was made. A plan was made for observation. After 2 weeks, the CRP was repeated and had elevated to 38. Repeat CT

Access this article online

Website: www.jocr.co.in

DOI: 10.13107/jocr.2020.v10.i02.1704

Author's Photo Gallery


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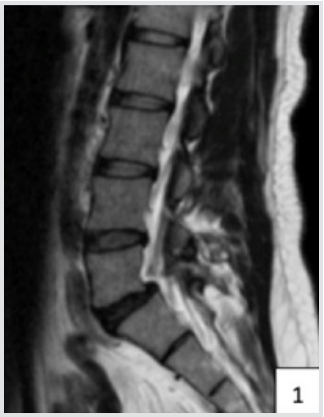

Figure 1: Pre-operative magnetic resonance imaging showing L5-S1 spondylolisthesis.

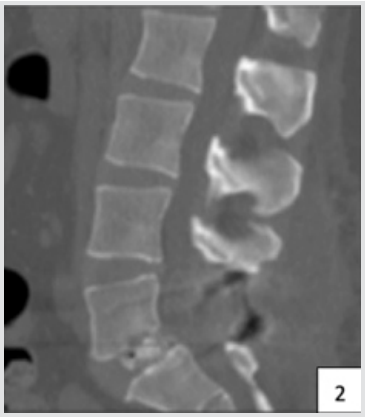

Figure 2: Post-operative computed tomography showing resorption of L5 inferior end plate.

(Fig. 2) demonstrated bone resorption around one of the interbody cages. A diagnosis of discitis was made. As there was no clear target for biopsy (Fig. 3), a plan was made for empiric intravenous antibiotics for 6 weeks. A peripherally inserted central catheter (PICC) line was inserted and teicoplanin prescribed. Thepatient reported a dramatic improvement in symptoms within 48 h of starting antibiotics. Oral rifampicin was added after 4 days. On day 7 of commencing the antibiotics, the patient developed temperatures spiking above 39.0°C. CRP increased to over 200. Repeat CT scan demonstrated the progression of the previous appearances (Fig. 4). The differential diagnosis at this stage was either PICC line sepsis, progression of discitis, or immune-mediated drug reaction. Repeated blood cultures and line tip culture did not reveal an infective source. A case discussion was held with spinal surgery colleagues and microbiology. The surgical consensus was that debridement of the disc space was required as this was thought to represent the progression of infection. The microbiology team advised that drug reactions were uncommon in the 1stweek after commencing antibiotics. To discriminate between sepsis and immune reaction, PCT levels were checked. The level below 0.5ng/ml is thought to exclude sepsis. The patient's level was 0.3ng/ml. Rifampicin and teicoplanin were stopped and after a further 48 h temperatures and CRP normalized. (Fig. 5) depicts the timeline of CRP values of the patient.

Discussion

Drug hypersensitivity is essentially a diagnosis of exclusion; however, a biomarker is necessary to rule out septic progression of spondylodiscitis in the post-operative setting, while the patient is on antibiotic therapy. PCT has been shown to be less sensitive than CRP in the diagnosis of spinal infection by Jeong et al. [3]. About 80% of their patients who had elevated PCT levels had evidence of concurrent infection elsewhere in the body, predominantly sepsis. They recommended that patients with spinal infection who showed elevated serum PCT level should be investigated for combined infection, and proper antibiotics should be given. Maus et al. [4], in their paper, concluded that PCT is not useful as a diagnostic tool or monitoring parameter for spondylodiscitis. PCT was not elevated in any of their 17 patients of spondylodiscitis except in one patient with infection of cardiac pacemaker. The common observation in both the studies was that elevated PCT in a patient with spondylodiscitis is more likely in the presence of a concurrent infection, including sepsis. Yoon et al.[5] analyzed PCT as a biomarker to differentiate between delayed-type drug hypersensitivity and systemic bacterial infection. Their study showed that 91% of patients with bacterial infection had serum PCT levels above 0.5 ng/ml, while only 21% in the drug hypersensitivity group exceeded this value. The best cutoff value in their study was 1.67ng/ml. Furthermore, the patients with drug hypersensitivity who exceeded 0.5ng/ml limit had more severe presentations including Stevens–Johnson syndrome, toxic epidermal necrolysis, drug reaction and eosinophilia with systemic symptoms, and one with maculopapular rash. Our patient had fever and arthralgia as his symptoms and was unlikely to exceed levels of 0.5ng/ml.

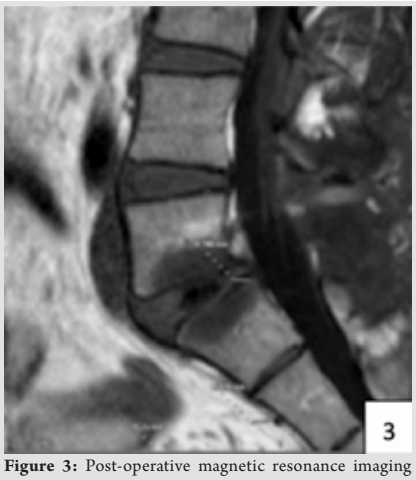

Figure 3: Post-operative magnetic resonance imaging showing non-specific marrow edema and absence of fluid for targeted computed tomography-guided biopsy.

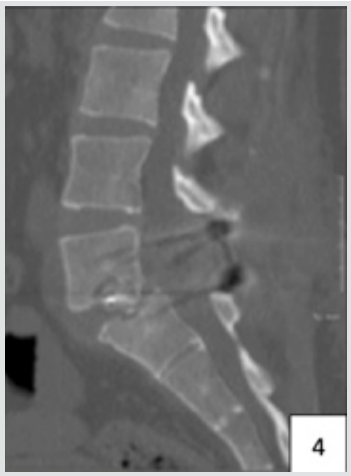

Figure 4: Progression of bony resorption around the cage.

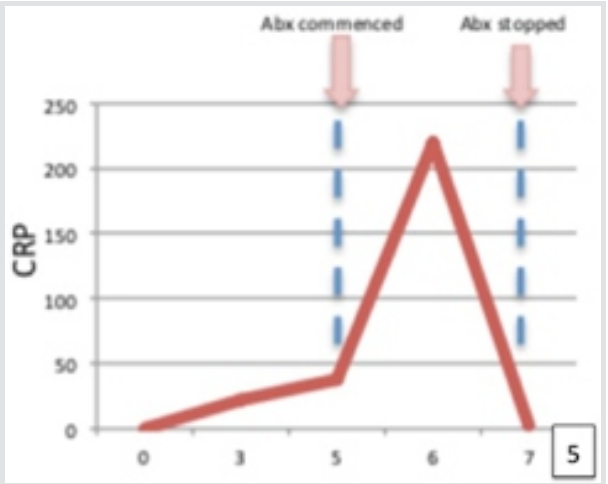

Figure 5: Timeline of C-reactive protein values of the patient.

Another study by Oshita et al.[6] showed that in 56 patients with systemic inflammatory responses including malignancy, viral infection, allergy, and drug-induced inflammation, the frequency of positive PCT tests (>0.5 ng/mL) was significantly lower compared to a bacterial infection group.

Hence, it is clear that although the role of PCT is limited in diagnosing infective spondylodiscitis, it is highly likely to be elevated when it is complicated by sepsis and other concurrent infections. It is essential to diagnose drug hypersensitivity early enough as it is a potentially life-threatening complication.

Conclusion

Drug hypersensitivity reaction is a rare but important differential diagnosis in patients being treated for infective spondylodiscitis. PCT, as a biomarker, can help distinguish septic progression of spondylodiscitis from drug hypersensitivity and prove vital in clinical decision-making in these difficult scenarios.

Clinical Message

Although drug hypersensitivity reaction is rare, it is important to have a strong clinical suspicion as an alternative diagnosis to acute septic spondylodiscitis. In such a scenario, PCT proves to be a vital tool to differentiate between the two clinical entities.

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Conflict of Interest: Nil
Source of Support: Nil

Consent: The authors confirm that Informed consent of the patient is taken for publication of this case report

How to Cite this Article

Kapoor S, Gadiya AD, Rasul FT, Bell D. Procalcitonin – Vital Tool to Differentiate Septic Progression of Spondylodiscitis from Drug Hypersensitivity: A Case Report and Brief Review of Literature. Journal of Orthopaedic Case Reports 2020 Mar-Apr;10(2): 73-75.