

Case Report

A case report of myolysis as an infrequent adverse effect of iopamidol

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Abstract: Iopamidol is commonly applied in computed tomography (CT) scan and cardiac catheterization as a contrast-enhancing agent. Compared to iodinated contrast agent, it will be more safe and there is only some adverse effects. Up to date, no information about muscle damage caused by iopamidol has been reported. Here, we report a case of myolysis by iopamidol and how to deal with this infrequent adverse effect.

Keywords: Iopamidol, myolysis, infrequent adverse effect, case report

Introduction

Iopamidol is a nonionic, low-osmolar iodinated contrast agent, and it is widely used in contrast enhancement computed tomography (CT) scan and cardiac catheterization. It shows a less cytotoxicity than the high-osmolar iodinated contrast agent [1]. However, it still has some adverse effects, such as nephrotoxicity, thrombogenicity, allergic reactions, etc. So far, there is no report about muscle damage caused by iopamidol. This article is to report a case of myolysis as an infrequent adverse effect of iopamidol.

Case report

The 60-year-old female patient was referred to our hospital for the symptoms of general fatigue, loss of appetite, icteric sclera and dark urine for over one month, which was showed after taking of some traditional Chinese medicine for therapy of a cold. The past medical history about this patient showed a "secondary tuberculosis at right upper lung", which diagnosed two months ago at another hospital. A combination of four anti-tuberculosis drugs (Isoniazid, Rifapentine, Pyrazinamide and Ethambutal) was used. In the body examination, a severe jaundice, shifting dullness and a mild pitting edema of both lower extremities

were found. The laboratory investigation showed: White Blood Cell: $6.2 \times 10^9/L$; Red Blood Cell: $2.64 \times 10^{12}/L$; Hemoglobin: 76 g/L; Platelet: $40 \times 10^9/L$; Total Bilirubin: 431.67 $\mu\text{mol}/L$; Conjugative bilirubin: 239.69 $\mu\text{mol}/L$; AST: 68 IU/L; ALT: 22 IU/L; Serum Albumin: 36.1 g/L; Prothrombin Time: 25.5 s; Prothrombin Activity: 32%; HAV-IgG(-); HEV-IgM(-); HEV-IgG(+); HBsAg(-); Anti-HBs(+); HBeAg(-); Anti-HBe(-); Anti-HBc(+); AFP: 21.5 ng/mL; ESR: 13.0 mm/H. Abdominal ultrasonic examination indicated an infection of biliary tract.

According to materials, the patient was diagnosed medicamentous liver lesion, secondary aplastic anemia, pulmonary infection and biliary tract infection. After a liver-protecting, cholagogic, jaundice removing, anti-infection, symptomatic and supportive treatment, the patient got improvements.

After the anti-infection treatment, the patient's condition got released, but still had cough and sputum. In Dec 30th 2009, an X ray and contrast enhancement CT scan of chesty were done to examine the condition of the pulmonary infection. It indicated an improvement of the pulmonary infection. However, in the second day, the patient started to complain about severe fatigue and a muscular soreness of the

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whole body. The laboratory investigation showed the liver function got improvement, which did not match to the severity of fatigue. At the same time, an increasing level of Creatine Kinase (CK) was found. In the following days, CK level was examined. The results of blood biochemistry examination in Jan 3rd 2010 showed: CK: 2521 U/L, LDH: 1147 U/L, CK-MB: 40 U/L, K⁺: 5.63 mmol/L.

These symptoms were regarded as an adverse effect of the contrast media of CT. The therapies of her basic diseases went on. At the same time, the management of nourishing muscle had been taken to the patient. In the few days, the muscular soreness lightened, and the creatases went down. After a few weeks, the patient recovered.

Discussion

CK is an enzyme exists in the cells of cardiac muscle, skeletal muscle and brain tissue. The increase of it usually indicates myocardial infarction, skeletal myolysis or a cerebrovascular disease. As the case discussed above, rare evidence suggests that the patient may suffer heart or brain diseases. Therefore, the increment of CK may probably relate to the disorder in skeletal muscle. As the cardiac enzymes are normal. So there is no evidence of heart and brain diseases. In addition, the patient has the symptoms of fatigue and muscular soreness. So we regard the abnormality of creatine kinase as a result of myolysis.

The adverse effects of contrast media are various.

Contrast media-induced nephropathy (CIN)

Contrast media-induced nephropathy (CIN) is a most common adverse effect of contrast media. CIN is defined as the acute deterioration of renal function after parenteral administration of contrast medium in the absence of any other cause. According to most materials, renal function deterioration is referred to an increase of serum creatinine concentration > 0.5 mg/dL (44 µmol/L) or 25% above baseline, within 48 hours after contrast medium administration [2].

The overall incidence of CIN is about 14.5%, but it may vary from 0% to 90%. In general pop-

ulation it is less than 2% [3]. But in the patient with the risk factor such as chronic renal insufficiency, diabetes mellitus, and high contrast volume administration, the incidence of CIN can reach up to 40%~90% [4].

Although the pathogenesis is not fully clear, the mechanisms of contrast media-induced nephropathy proposed mainly include: a) alternations in renal microcirculation and medullary oxygenation; b) direct cytotoxicity of contrast media.

Experimental models of animals predisposed to ischemic injury have demonstrated that after parenteral administration of contrast media they exhibit short-term renal vasodilatation, which followed by prolonged vasoconstriction, resulting in a decrease in total renal blood flow (RBF) and a reduction of glomerular filtration rate (GFR). The contrast agents decrease local prostaglandin- and nitric oxide (NO)-mediated vasodilatation, and increase endothelin-1- and adenosine-mediated vasoconstriction. Reactive oxygen species (ROS) and endothelial dysfunction due to oxygen free-radical generation during post-ischemic reperfusion, leading to medullary vasoconstriction, have also been implicated in the pathogenesis of CIN [2, 3].

Apart from haemodynamic alterations, the direct toxicity of contrast media on proximal tubular cell is still under investigation as a major contributor to the development of CIN. Cell vacuolisation is commonly observed in CIN. Rapid loss of cellular proteins, such as sodium-potassium ATPase pump, and mitochondrial proteins, such as cytochrome C, as well as increased susceptibility of the cell membrane to phospholipase A2, has been documented as a result of direct contact of tubular cells with contrast media [2].

Prophylaxis should be paid attention to. Adequate hydration is the simplest and most effective way to protect renal function. At the same time, using a lowest possible quantity of a low- or iso-osmolar radiocontrast agent is also a good way.

Thrombogenicity

In 1990s, some studies proposed that contrast media may have the possibility of increasing the risk of thrombogenicity which aroused peo-

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ple's attention. Since contrast media have been using in the cardiac catheterization, its thrombogenicity maybe likely to influent the prognosis of the patients. Because of the vantage of less adverse effects, nonionic, low-osmolar contrast agents gradually replace the ionic, high-osmolar ones. Many studies in vitro, however, have indicated that nonionic contrast media exhibit fewer inhibitory effects on platelets and therefore may be more thrombogenic. James's study showed there was no detectable platelet activation in vivo in the group of patients studied, possibly reflecting the absence of these conditions in the coronary circulation where coronary blood flow rapidly dilutes the contrast [5, 6]. In 2008, the study of Alexander Georgakis in the Journal of Invasive Cardiology is aim to investigate the thrombogenicity of the 6 different nonionic radiocontrast media in terms of their platelet reactivity. It shows that in the 50% contrast concentration group, all of the nonionic contrast agents inhibited aggregation, whereas in 10% contrast concentration group, all agents showed similar aggregation curves in comparison to the normal control [7]. Gabriel DA et al showed us that contrast media actually have some effects on the coagulation system. Although iopamidol is not shown to be thrombogenic, iopamidol does appear to reduce platelet surface charge, bind fibrinogen, and modify fibrin clot structure [8]. There may be not enough evidence to improve the contrast media induced thrombogenicity. However, it cannot be neglected in clinic work.

Seizure

Fedutes BA's study showed that available data supported the incidence of increased seizure risk with nonionic, water-soluble contrast media agents and concomitant medication administration that lowered the seizure threshold are anecdotal. However, because of product labeling and additive potential to decrease the seizure threshold, discontinuation of such medications should be considered to avoid the presumed increased risk of seizures [9]. Karl martin klein showed that seizure induction by iopamidoal are not only in epileptic patients but also in non-epileptic patients. And interestingly, Karl's two non-epileptic patients developed seizures induced by cervical myelography despite antiepileptic prophylaxis with phenytoin or sodium valproate [10]. Singh reported a case of

generalized tonic-clonic seizure after cervical myelography with iopamidol even in a previously healthy young man [11].

Pulmonary adverse effects

A review about effects of radiographic contrast media on the lung was published in 2003 [12]. It listed a number of pulmonary adverse effects, such as bronchospasm, pulmonary edema and increase in the pulmonary arterial blood pressure (Ppa). Symptomatic bronchospasm is rare but subclinical increase in airways resistance is common after intravascular injection of radiographic contrast media. The mechanisms responsible for the effects of radiographic contrast media on airway resistance and pulmonary circulation remain unclear. Pretreatment with corticosteroids or antihistamine does not appear to prevent radiographic contrast media induced bronchospasm, but the administration of beta-2 adrenergic agonist can abolish this adverse effect. Martin R Tramèr have done a systematic review which demonstrated that severe allergic reactions due to contrast media seem to be rare. Therefore, radiology departments should be staffed with the necessary equipment for resuscitation. And physicians dealing with patients receiving contrast media should not rely on the efficacy of pre-medication; routine prophylaxis should be abandoned [13].

Others

There are some other adverse effects besides the ones referred above. Skin reaction can be a manifestation of the anaphylactic reactions of the iodinated contrast media. The study of Mikkonen R showed that 52 of 4,875 patients (1.07%) had experienced a late skin reaction (urticaria or rash); this number exceeds the reports on spontaneous occurrence of such reactions by a factor of 300. Most of the reactions in a known location occurred on sun-exposed areas of the body [14]. Fränkle S reported a case on acute sialadenitis after percutaneous coronary intervention [15].

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Disclosure of conflict of interest

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