Aseptic femoral head necrosis in a patient receiving long term courses of inhaled and intranasal corticosteroids

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ÖZET

Uzun süreli inhale ve intranazal kortikosteroid kullanan bir hastada aseptik femur başı nekrozu

Aseptik (avasküler) femur başı nekrozu erişkinlerde farklı hastalıklarla ilişkilidir. Aynı zamanda sistemik kortikosteroid tedavinin olası bir komplikasyonu olarak bilinir. Astımın uzun süreli tedavisinde inhale steroidler ilk basamak antiinflamatuvar tedavidir. Astımın inhale steroidlerle uzun süreli tedavisinde hem sistemik hem de topikal yan etkileri olabildiği dikkate alınmalıdır. En önemli olası sistemik etkileri adrenal yetmezliği, büyüme geriliği, glokom ve osteoporozdur. Flutikazon propionat diğer inhale steroidlere oranla daha az yan etkisi olduğu düşüncesiyle solunum semptomlarını kontrol etmek için yüksek dozlarda yazılabilir. Çalışmalar beklametazon veya budesonide göre oral absorbsiyonun sınırlı olması ve karaciğerden ilk geçiş etkisine bağlı olarak daha düşük sistemik biyogeçerliliğinin olması nedeniyle daha güvenilir olduğunu göstermiştir. Buna rağmen büyüme geriliği ve semptomatik adrenal baskılanması yüksek doz flutikazon alan çocuklarda bildirilmiştir. Uzun süreli inhale flutikazon ile birlikte intranazal triamsinolon asetonid kullanımına bağlı gelişen nadir bir femur başı avasküler nekrozu olgusunu bildiriyoruz.

Anahtar Kelimeler: *Aseptik nekroz, kortikosteroidler, femur başı.*

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SUMMARY

Aseptic femoral head necrosis in a patient receiving long term courses of inhaled and intranasal corticosteroids

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Aseptic (avascular) necrosis of the femoral head in adults has been associated with a variety of disease entities. It is also recognized as a potential complication of systemic corticosteroid therapy. Inhaled corticosteroids are the first line anti-inflammatory agents for the long term treatment of asthma. However, long term treatment of asthma with inhaled corticosteroids has been accompanied by concern about both systemic and topical side effects. The most worrying potential systemic effects are adrenal insufficiency, growth suppression, glaucoma and osteoporosis. Fluticasone proprionate may be prescribed at higher doses to relieve respiratory symptoms in the belief that it generates fewer side effects than other inhaled steroids. Studies have shown that fluticasone is safer than beclomethasone or budesonide, with limited oral absorption and extensive hepatic first pass metabolism leading to a lower systemic bioavailability. However growth retardation and asymptomatic adrenal suppression in children receiving high-dose fluticasone have been reported. We report a rare case of avascular osteonecrosis of the femoral head associated with the use of long term inhaled fluticasone propionate along with the intranasal application of triamcinolone acetonide.

Key Words: *Aseptic necrosis, corticosteroids, femoral head.*

Aseptic (avascular) necrosis (AVN) of the femoral head in adults has been associated with a variety of disease entities (1). It is also recognized as a potential complication of systemic corticosteroid therapy (2). Inhaled corticosteroids are the first line anti-inflammatory agents for the long term treatment of asthma (3). However, long term treatment of asthma with inhaled corticosteroids has been accompanied by concern about both systemic and topical side effects (4). The most worrying potential systemic effects are adrenal insufficiency, growth suppression, glaucoma and osteoporosis (4).

Fluticasone proprionate may be prescribed at higher doses to relieve respiratory symptoms in the belief that it generates fewer side effects than other inhaled steroids (5). Studies have shown that fluticasone is safer than beclomethasone or budesonide, with limited oral absorption and extensive hepatic first pass metabolism leading to a lower systemic bioavailability (6,7). However growth retardation and asymptomatic adrenal suppression in children receiving high-dose fluticasone have been reported (8).

We report a rare case of avascular osteonecrosis of the femoral head associated with the use of long term inhaled fluticasone propionate along with the intranasal application of triamcinolone acetonide.

CASE REPORT

A 38-years old male had a history of asthma and allergic rhinitis diagnosed at the age of 20 years, with known sensitization to grass pollens. He received treatment with an inhaled short-acting β_2-agonist (salbutamol) that kept his disease in good control until the age of 25 years when a moderate asthmatic exacerbation developed. Apart from a slight modification in treatment which consisted of a higher dose of the same bronchodilator plus ipratropium bromide he was discharged and had a follow-up on an outpatient basis. No inhaled corticosteroids were given at that time. At the age of 46, he started having complaints of persistent nasal stuffiness and further examination disclosed nasal polyps. The polyps were successfully removed endoscopically and the patient required maintenance do-

ses of triamcinolone acetonide twice daily (each dose consists of 55 μg of triamcinolone acetonide), treatment he followed ever since.

At the age of 35 years, he was admitted to the chest clinic, with a severe exacerbation of his asthma requiring hospitalization. He was given a combination of ipratropium bromide plus salbutamol and methylprednisolone 40 mg twice a day. After he was discharged, he was prescribed inhaled fluticasone at a dose of 1000 μg a day plus an inhaled long acting β_2-agonist (salmeterol). The above medication was continued for a period of three years.

At the age of 38 years, without apparent trauma, he experienced left hip pain. It was initially misdiagnosed as sciatica and he was prescribed non-steroidal anti-inflammatory drugs for two months but with no objective improvement. He was seen by the orthopedic department and was subsequently hospitalized. At presentation, range of motion was restricted and walking was painful. X-rays revealed a radiolucent area in the left femoral epiphysis with slight flattening of the head, along with signs of sclerosis. The bone scan with Technetium 99m revealed increased uptake in the same area, whereas the rest of the skeleton showed normal radioisotope distribution. A magnetic resonance imaging (MRI) scan was then ordered which showed evidence consistent of bilateral avascular necrosis of femoral head (Figure 1).

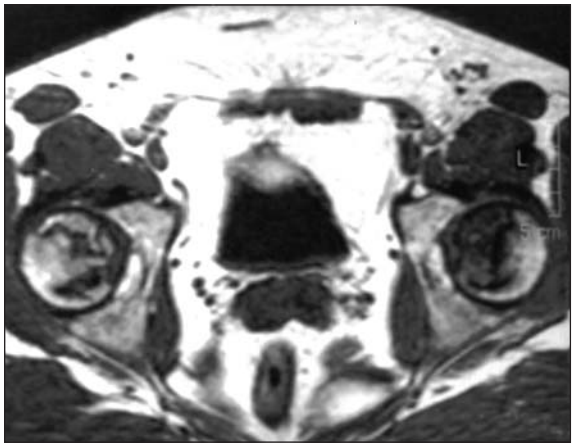

Figure 1. MRI scan image revealing evidence consistent of bilateral avascular necrosis of femoral head.

Because of the known association of avascular necrosis with numerous risk factors, a thorough history and physical examination were obtained. He was neither a drinker nor a smoker and the biochemistry of the liver was normal, along with a normal value for glucose, cholesterol, urea and creatinine. Findings were negative for a hypercoagulable state, including blood clotting time, prothrombin time and activated partial thromboplastin time, along with normal levels for D-dimer. No blood cell disorders that would account for blood vessel occlusion were found and the bilirubin level was normal. Findings were also negative from tests for antibodies associated with connective tissue disease, including ANA, ANCA, anti-ds DNA, anti-ENA and anti-cardiolipin antibodies (both IgM and IgG titers). Serum complement levels were normal.

The patient required bilateral total hip replacement with porous tantalum prostheses, which combine the effectiveness of core decompression with that of mechanical support of the femoral head, therefore, theoretically decreasing the tendency to collapse. His condition is presently stable, with a follow up on an outpatient basis.

DISCUSSION

Our patient had been receiving 1000 μg a day of fluticasone propionate for a period of three years. The cumulative dose for fluticasone therefore would be 1100 mg. He was also receiving for a period of five years 0.11 mg of triamcinolone acetonide for which the cumulative dose was about 800 mg. If we accept the fact that fluticasone is about 3.5 times as potent as triamcinolone (4,9). 800 mg of the latter would equal about 230 mg of the former. That brings about to the total sum of 1330 mg of fluticasone. Taking into consideration the fact that no other risk factors were identified to account for the development of osteonecrosis, the additive effect of the two steroids could be responsible. The risk of adverse effects becomes disproportionately high in patients who require long-term, high-dose glucocorticoid therapy to control their asthma, and the related atopic diseases (4,9).

AVN of the femoral head is a common disorder and occurs in about one third of patients on long

term systemic corticosteroid therapy (6,7). Steroids are now the second most common cause of osteonecrosis after trauma and the prevalence in studies of (AVN) varies between 3-38% (1).

Systemic glucocorticoids are known inhibitors of angiogenesis and revascularization, and the femoral head is vulnerable to these effects because of the stress of weight bearing. Can impede bone remodeling (10). Abnormalities in femoral head blood vessel patterns have been reported in patients taking glucocorticoids (1,11). It has also been shown that inhaled corticosteroids can impede bone remodeling, decrease bone mineral density and levels of bone formation markers as compared to controls (1). Fluticasone proprionate is the most potent inhaled corticosteroid available, and with the longest half-life (9). A meta-analysis of studies of adrenal suppression among patients who used inhaled corticosteroids demonstrated that fluticasone was nearly twice as likely to cause adrenal suppression compared to beclomethasone, triamcinolone or budesonide at equivalent doses (4,9). Fluticasone exhibits greater dose-related systemic bioactivity compared with other inhaled corticosteroids particularly at doses above 0.8 mg/d (4).

If we take into account the aforementioned bioactivity characteristics of a potent glucocorticoid such as fluticasone, combined with a potentiation effect from the part of triamcinolone, a strong link between a known glucocorticoid adverse effect as osteonecrosis and the therapy of our patient can be made. Although no reports of osteonecrosis associated with combined intranasal and inhaled glucocorticoid therapy exist, physicians must be aware when using at the same time formulations containing these drugs, especially with high dose inhaled fluticasone proprionate used over a period of six months. Their combination can cause osteonecrosis in the long-term.

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