Journal of Research and Practice on the Musculoskeletal System
JRPMS

Review Article

Clinical consequences of pseudotumors in hip arthroplasty

Georgios I. Karagiannis

4th Department of Trauma and Orthopaedics, KAT Hospital, Athens, Greece

Abstract

The occurrence of pseudotumors currently constitutes an important topic of interest among orthopaedic surgeons who prefer metal on metal arthroplasty and especially hip resurfacing arthroplasty. Adverse reactions to metal ions are associated with the formation of such lesions and the orientation of implants has also been implicated in their pathogenesis. The diagnosis of pseudotumors is as difficult as complex. There is a variety of symptoms and patients with mild or tolerable pain may not seek medical attention. Revision surgeries may be the only solution in some cases. The goal of this article is to review the clinical presentation, prognosis of pseudotumors and associated complications, based on evidence published in the literature.

Keywords: Total hip arthroplasty, Metal-on-metal, Pseudotumor, Hip revision, Metal ions

Introduction

Joint arthroplasty has increased over the last decades as an effective treatment option for hip and knee osteoarthritis. Significant evolution in techniques and materials offer a better quality of life and long-lasting improvement in well-selected patients.

Metal on metal (MoM) hip arthroplasty and especially resurfacing arthroplasty has gained a wide interest and the main reason is the increased head-neck implant ratio which provides an increased range of motion and decreased femoral neck impingement and dislocation rate[1,2]. Despite the fact that many surgeons tend to use implants like ceramic heads and High-density crosslinked polyethylene, the MoM articulation remains still appreciable.

Adverse effects can been seen to all types MoM arthroplasties, Including Total Hip Arthroplasty (THA) with small (<36 mm) or large (≥36 mm) head diameter and Resurfacing Hip Arthroplasty (HRA). The incidence of local reactions is higher in articulations with large diameter heads[3]. Some of these reactions include metallosis, aseptic lymphocytic vasculitis associated lesion (ALVAL) and pseudotumors. The term pseudotumor has been used to describe non neoplastic cystic or solid mass around a MoM hip arthroplasty. These masses form as a result of a reaction to metal debris from the implants surfaces[4].

Second and third generation MoM hip implants use new articulation surfaces made by improved materials and have been associated with only minimal problems concerning durability like wear which can lead to aseptic loosening and revision surgery[5]. Nonetheless side effects still exist. Metal ions release from the articulation surfaces especially when larger heads (larger loads) used lead on to local reactions which can present clinically in many ways.

In 2012 Natu et al. made an effort to investigate the Adverse Reactions to Metal Debris (ARMD) after MoM hip arthroplasty. This umbrella term includes conditions like metallosis ALVAL (perivascular inflammatory infiltration of lymphocytes), granulomatous inflammation and pseudotumors[6]. In this review are included only articles referring in the term pseudotumor and not the other reactions mentioned above.

Method

A thorough search of the Medline database was performed. A number of 36 out of 158 articles which examined the occurrence of pseudotumors following hip

The author has no conflict of interest.

Corresponding author: *Karagiannis I. Georgios, 4th Department of Trauma and Orthopaedics, KAT Hospital, Nikis 2, Kifissia, 14561, Athens, Greece*

E-mail: *drkaragiannisg@gmail.com*

Edited by: *Kostas Stathopoulos*

Accepted *4 May 2018*

arthroplasty in the last decade were identified. The terms of the search were "pseudotumors" combined with "metal on metal " and "hip arthroplasty". A second search in articles cited in the first results was performed excluding primary studies that have been updated. 7 (seven) case series, 3 (three) cohort studies, 2 (two) experts opinion articles and one meta-analysis are included in this review. The search consisted only of articles in the English language, and for studies performed in human subjects. Two studies were excluded because of manufacturer recall of the implants[7]. One of these studies was referring to ceramic-on-highly cross-linked polyethylene.

Definition

Most authors define Pseudotumor as a cystic or solid mass which is non neoplastic and is formed around a hip prosthesis[4,8] with or without communication to the joint. These masses are usually discovered in patients with metal on metal hip arthroplasties. Their formation is the result of the inflammatory reaction to the release of metal debris from the articulating surface. Revising surgeons have described these lesions as aseptic soft tissue masses among many other definitions. Pseudotumors may range from small asymptomatic tissue reactions to severe destructive masses of bone and soft tissues. Based on experts' opinions their formation takes place at sites with decreased tissue resistance from surgical approach and dissection[9]. They can occur months after surgery even becoming evident after a relatively long period with an incidence of 1% at five years[10,11]. The histological specimens of pseudotumors include macrophages with particles, lymphocytic aggregates, granulomas and extensive necrosis of connective tissue[10]. The differential diagnosis from low grade infection may be difficult.

Epidemiology

The 2016 annual registry of joint replacement in USA (AJRR) show that year by year surgeons are moving away from MoM that predominated. Ceramic head usage continues to grow each year[12]. In 2012 the compotiton of CoCr femoral heads was 63.1% (7.513) and ceramic 36.2% (4.317). In 2015 CoCr usage was 49.6% (30.368) and ceramic 48.8% (29.878). Hip resurfacing also decline, in 2015 were performed 1.560 procedures out of 169.060 (0.9%). A meta-analysis in 2013 by Wiley et al. reported the incidence of pseudotumors to be 0.3% in a total of 13898 MoM hip arthroplasties[13]. Pandit et al. in 2008 estimate the incidence of pseudotumor in patients with MoM HRA at 1% within 5 years[10]. They performed over 1300 resurfacing hip arthroplasties over a period of nine years and identified a group of 17 patients with pseudotumors.

Implants size and type

HRA is designed to minimize the changes in hip joint kinematics by replacing only the surfaces been affected, thus maintaining a greater amount of bone stock than conventional hip arthroplasty, however, it is technically more demanding than THR and the positioning of acetabular implant is more critical[14].

Many studies report the presence of pseudotumors after large diametral metal on metal total hip replacement. Bosker et all (2012) show an incidence of 39% in a total of 108 patients. Primary uncemented MoM THRs were performed with a mean follow up of 3.6 years but patients with body mass index (BMI) >30 kg/m^2 were excluded[3].

The prevalence of these tumor-like lesions is reduced with the use of smaller implants. W. van der Weegen et al. performed a one year follow up with metal artifact reduction sequence-magnetic resonance imaging (MARS MRI) in 37 patients. The first MRI was performed at a mean post operative time of 4.3 (2.2-8.3) years and the second 8 months later. Little to no change has been shown in symptomatics pseudotumors with 28 mm MoM hip resurfacing arthroplasty[15].

Risk factors

Implants malposition, bearing surfaces, diametral clearance and sector angle are associated with high ions level. Position of the implants is vital for the outcome of MoM HRA. Mal-positioning of the implants and especially the acetabular component, increase the risk of impingement and edge loading[16]. Daily living activities affect the forces applied to the implants in a different way. While walking, the edge loading area is in the outer superior zone of acetabular implant at 12.00 o clock. During stair climbing and rising from a chair, the edge loading predominates at the same zone at 10.00 o clock position. Edge loading etiology is multifactorial but in a small group of MoM HRA (33 cases) the patients presenting with pseudotumors had an increased angle of anteversion and inclination of acetabular components with 67% outside the safe zone of Lewinnek[17]. Hartmann et all in a 10 year follow up of HRA identified that high cup inclination was associated with high cobalt levels[18].

An other risk factor is the corrosion on the taper and trunnion contributing to the formation of metal debris also in well-positioned implants[3]. On the other hand, the free motion between bearing surfaces is also a reason for producing wear debris. Diametral clearance is the gap between the two mating metal surfaces forming a gland's internal cavity. The low clearance of the implant is associated with increased wear due to reduced fluid film formation[19].

There is no significant association of metal allergy to pseudotumors, but the result of that study was based on a small group of cases[20]. Patients age seems to be another factor. The younger the patient, the greater the risk for revision surgery[21]. A study of 1419 MoM HRA with a follow up of 8 years shows a greater risk for patients under the age of 40. Maybe this can be explained by the higher activity level. Finally, as for the gender but not as an independent risk factor, most of the patients affected are women[10,21].

Without having sufficient evidence women tent to edge-load more than men because at the standing gait phase the hip remains in a more adducted position. In 2009 S. Glyn-Jones et all found that the coexistence of young age (<40), woman gender and small size implants increase the risk of failure and the need for revision (13.1% in six years).

Metal Ions

The bearing surfaces of MoM implants are mostly made of chromium (Cr) cobalt (Co) and molybdenum (Mo). Additionally, in smaller amounts, they contain nickel (Ni), iron (Fe), manganese (Mn), silicon (Si) and vanadium (V). Metal on metal wear releases metal particles and metal ions enter the systemic circulation but as long as renal clearance mechanism is effective the levels of ions remain low. Some of the metal particles are phagocytosed by macrophages and giant cells. Through the lymphatic system, these particles are deposited in the lymph nodes, liver, and spleen. The metal particles or ions originate either from the bearing articulation surface or the taper junction between prosthesis head and stem as a result of corrosive process or mechanical wear. They consist mostly of chromium (Cr) and cobalt (Co). Their blood levels can use as markers for screening patients with MoM implants. Inductively coupled plasma mass spectrometry (ICPMS) and electrothermal atomization atomic absorption spectrometry (ETAAS) are used for the measurement of metal ions in biological samples. ICPMS is preferable having lower detection limits.

Pseudotumors are associated with elevated metal ions in blood sample. Kwon et all. Measure the levels of metal ions in a study performed in 158 patients who underwent a MoM HRA at least 3 years before. In 7 patients, most of them females, pseudotumors were found. This group compared with a control group of MoP THA and a non pseudotumors group was associated with significantly higher median metal ion levels: cobalt 9.2 μg/L, chromium 12.0 μg/L. Additionally, hip aspirate metal ion levels were elevated (cobalt 1182 μg/L chromium 883 μg/L). This group was found having mild pain and a mean Oxford hip score at 41. None of them reported mass lesion symptoms8. Bosker et al. also identify an increased risk developing a pseudotumour in patients with serum cobalt levels >5 μg/l.

In 2014 the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) determined critical threshold ranges for Co at 2 to 7 μg/L in whole blood. As some metals, particular chromium, tend to concentrate within erythrocytes serum analysis may have underestimated the metal levels. The appropriate blood fraction for the measurement of metal ions remains controversial[22]. The use of metal needles for collecting blood sample may show higher metal ion than reality.

Local symptoms

Pain is the essential predictor of the presence of a pseudotumor with a variety of locations, in the thigh, groin or buttock. Bosker et all performed a follow up in 706 MoM concluding that pain dominates to cobalt levels and swelling[9]. Patients with mild or tolerable pain may not seek medical attention but follow up is essential for everyone[8]. Osteolysis and aseptic loosening give rise to pain and loss of function of the hip and the need for a revision arthroplasty to prevent it from progressing on to extensive bone loss and catastrophic structural failure. Signs of swelling, discomfort or pain in the groin may indicate a sizeable pseudotumor with local tissue distraction, pressure effects on vital structures and the need for revision. Symptoms may develop slowly and the patient will report good to excellent scores. Pandit et al. report a common symptom of discomfort and pain in the groin, buttock or at the lateral side of the hip. A smaller group describe symptoms from Irritation of the femoral and lateral cutaneous nerve of the thigh[10]. If the lesion is superficially and enlarged it may be palpable or visible as a lump.

A deeper forming lesion can potentially cause local pressure effects causing necrosis and compression of nearby structures such as the iliac vessels, femoral vessels, and the femoral or sciatic nerve[23]. A case report of Werner Maurer-Ertl et al. presented with swelling of the leg and hip discomfort with no evidence of deep venous thrombosis (DVT). They underwent a u/s, and CT found a solid mass compressing the external iliac vein. In an other case of Daniel J. Parfitt et al. with the same CT findings, the patient presented with DVT. This patient was older and presented with symptoms 16 months after arthroplasty also he had a medical history with ischemic heart disease.

Muscles atrophy and their irreversible destruction is another conserve which may lead to revision. Soft-tissue abnormalities can identify with the use of MRI. These findings are the results of local distraction causing by pseudotumors and by an inflammatory response to metal wear debris. A study of Berber et al. based on MARS MRI findings, report an increase in atrophy of the gluteus minimus or medius in 17 out of 74 cases .progressive atrophy was more obvious in female patients with metal ion levels above 7 ppb[15]. This study has some limitations considering the small number of cases, the different surgeons and hip approaches and the absence of preoperative MRI evaluation for muscle atrophy. Despite that, it is the only study evaluating the changes of muscle atrophy in large diameter MoM implants with MRI scanning. In 2015 Aleksi Reito et al. reported a low prevalence of gluteal muscle atrophy in 263 patient with no association with elevated metal ions in blood sample.

Toxicity

Metal ions like chromium cobalt, nickel and molybdenum are essential microelements found in our body in traces being a part of a normal cell function.

Chromium aids in glucose metabolism and glucose tolerance[25,26]. Molybdenum works as an enzyme catalyst for certain amino acids breakdown and its deficiency have linked with esophageal carcinoma[27]. Cobalt contained in vitamin

B12 essential in red blood cell formation. The chemical form of these elements seems to be responsible for the systemic effects. Hexavalent Cr[Cr(VI)] is a well-known carcinogen, and some studies relate it with MOM, but evidence is not supported by others[28]. Cobalt has been associated with cardiomyopathy[29,30]. Seven cases have been described having peripheral neuropathy do to co levels above 250 μg/L in blood sample[31]. Ikeda et all performed a biopsy in suran nerve with the finding of axonal degeneration, such findings in central nervous system can affect cranial nerves[32]. Hearing loses, also in co poisoning, may coexist with headache vertigo tinnitus[31,33]. These symptoms are rarely presented[34] and in some cases seem to subside after revision surgery[35].

Diagnosis

The diagnosis of pseudotumor is as difficult as complex, when they occur the progression is slow and annually imaging is sufficient to identify any change. Every patient must perform a systematic infection workup because an infection may confound the clinical picture. Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP) and standard infection lab test must be performed followed up by hip aspiration and imaging. Metal ion measurement is advisable for systemic exposure and wears rate. They reach a peak 6 to 12 months postoperatively. Based on Effort guidelines, all MoM large diameter arthroplasties with risk factors need an annual follow up. Risk factors include femoral head size <50 mm, female gender. HR asymptomatic arthroplasty needs an annual follow up for the first 5 years. Imaging rather than x-rays are needed if metal ions are >2 μg./l or abnormal findings in x rays

X rays include anteroposterior (AP) and lateral views of the hip and an AP view of the pelvis are needed for long-term surveillance, but radiographs have poor sensitivity for detection of Pseudotumors. Ultrasonography is a good initial examination in the suspicion of pseudotumor it can also identify abnormalities in tendons. CT scanning has the advantage over ultrasound that is less operative dependent and more readily available than MRI MARS[3], it has a lower cost, and the surgeon can observe the position of the implant and identify osteolysis. MARS MRI has greater sensitivity and specificity for lesions detection at any depth.

Based on experts opinion large heads implants, as well as THR, need an annual follow up and if metal ions level is normal after two years postoperatively, the following investigation is based on local protocols for conventional THR[36]. Consider revision in symptomatic patients with progressive osteolysis or other imaging abnormalities, large pseudotumors or metal ions concentration above 7 μg/L or progressive rising at follow-ups. Co levels above 20 μg/L associated with severe cardiac and neurological complications from metal poisoning and is an indication for revision by itself[37]. Metal ion concentration can reduce to close to normal levels after one year of MOM removal[38].

Hartmann et al. in 2012 reviewed 100 HRA with a 10 year follow up. The survivorship for revision was 88%. Revision due to pseudotumor presence was performed in 3 female patients after 10.2 to 10.5 years. In these patients, the primary implant was small in size (46 mm head size)[18]. Complications of malpositioning will be reduced by placing the acetabular implant in 40° of abduction (30° to 50°) and 20° of anteversion (15° to 25°)[36].

Conclusion

In 2012 the European Federation of National Associations of Orthopaedics and Traumatology (EFORT) made a common statement with European Hip Society (EHS), German Arbeitsgemeinschaft Endoprothetik (AE) and Deutsche Arthrosehilfe (DAH) based on experts opinion and concerning the management of MoM bearings. These implants have the total commercial control on surface replacement preserving bone stock compared to conventional total hip replacement. Comparing with ceramic on ceramic (CoC) they have smaller risk of fracture, and the availability of large heads (≥36 mm) minimize the risk of dislocation. In contrast, the risk for adverse reaction to metal debris (ARMD) is bigger than conventional bearings when large heads are used. HRA has a risk of femoral neck fracture in nonwell-selected patients (lower femoral neck bone quality and coverage) and finally health effects when metal products entering blood circulation causing organ disfunction

Some implants have been recalled because of the large number of complaints of pain and the increased need for revision surgery[7]. Longitudinal study is required to determine whether asymptomatic pseudotumors will progress to destructive lesions causing severe symptoms.

The definition of pseudotumors remains controversial making it difficult to search medical databases. The need for the establishment of a term of pseudotumors is essential.

The number of patient with artificial joints is rapidly increasing. Therefore more attention and investigation is needed to find the proper material to minimize local and systemic side effects.

References

1. Wiley KF, Ding K, Stoner JA, Teague DC, Yousuf KM. Incidence of pseudotumor and acute lymphocytic vasculitis associated lesion (ALVAL) reactions in metal-on-metal hip articulations: A meta-analysis. J Arthroplasty 2013;28(7):1238-45.
2. Cameron HU, Keppler L, McTighe T. The role of modularity in primary total hip arthroplasty. J Arthroplasty 2006;21(4)(Suppl 1):89-92.
3. Bosker BH, Ettema HB, Boomsma MF, Kollen BJ, Maas M, Verheyen CC. High incidence of pseudotumour formation after large-diameter Metal-on-Metal total hip replacement: a prospective cohort study. J Bone Joint Surg Br 2012;94(6):755-61
4. Campbell P, Ebramzadeh E, Nelson S, Takamura K, De Smet K, Amstutz HC. Histological features of pseudotumor-like tissues from metal-on-metal hips. Clin Orthop Relat Res 2010;468(9):2321-7.
5. Haddad FS, Thakrar RR, Hart AJ, Skinner JA, Nargol AV, NolanJF, Gill HS, Murray DW, Blom AW, Case CP. Metal-on-metal bearings: the evidence so far. J Bone Joint Surg Br 2011;93(5):572-9.

6. Natu S, Sidaginamale RP, Gandhi J, Langton DJ, Nargol AV. Adverse reactions to metal debris: histopathological features of periprosthetic soft tissue reactions seen in association with failed metal on metal arthroplasties. J Clin Pathol 2012;65(5):409-418.
7. Young-Min Kwon, Sariah Khormaee, Ming Han Lincoln Liow, Tsung-Yuan Tsai, Andrew A. Freiberg, , and Harry E. Rubash. Asymptomatic Pseudotumors in Patients with Taper Corrosion of a Dual-Taper Modular Femoral Stem MARS-MRI and Metal Ion Study. J Bone Joint Surg Am 2016;98:1735-40.
8. Kwon YM, Ostlere SJ, McLardy-Smith P, Athanasou NA, Gill HS, Murray DW. "Asymptomatic" pseudotumors after metal-on-metal hip resurfacing arthroplasty: Prevalence and metal ion study. J Arthroplasty 2011;26:511-8.
9. Bosker, B.H. Ettema, H.B. van Rossum, M. Boomsma, M.F. Kollen, B.J. Maas, M. Verheyen, C.C.P.M. Pseudotumor formation and serum ions after large head metal-on-metal stemmed total hip replacement. Risk factors, time course and revisions in 706 hips. Arch. Orthop. Trauma Surg 2015;135:417-425.
10. Pandit H, Glyn-Jones S, McLardy-Smith P, Gundle R, Whitwell D, Gibbons CL, Ostlere S, Athanasou N, Gill HS, Murray DW. Pseudotumours associated with metal-on-metal hip resurfacings. J Bone Joint Surg Br 2008;90(7):847-51.
11. Griffiths HJ, Burke J, Bonfiglio TA. Granulomatous pseudotumors in total joint replacement. Skeletal Radiol 1987;16(2):146-52.
12. American Joint Replacement Registry 2016 Annual Report.
13. Wiley KF, Ding K, Stoner JA, Teague DC, Yousuf KM. Incidence of pseudotumor and acute lymphocytic vasculitis associated lesion (ALVAL) reactions in metal-on-metal hip articulations: a meta-analysis. J Arthroplasty 2013;28(7):1238-45.
14. De Haan R, Pattyn C, Gill HS, et al. Correlation between inclination of the acetabular component and metal ion levels in metal-on-metal hip resurfacing replacement. J Bone Joint Surg Br. 2008; 90:1291-1297.
15. Van der Weegen W, Brakel K, Horn RJ, Hoekstra HJ, Sijbesma T, Pilot P, Nelissen RG. Asymptomatic pseudotumours after metal-on-metal hip resurfacing show little change within one year. Bone Joint J 2013;95-B(12):1626-31
16. De Haan R, Campbell PA, Su EP, et al. Revision of metal-on-metal resurfacing arthroplasty of the hip:The influence of malpositioning of the components. J Bone Joint Surg Br 2008;90:1158-1163.
17. Kwon YM, Mellon SJ, Monk P, et al. In vivo evaluation of edge-loading in metal-on-metal hip resurfacing patients with pseudotumours. Bone Joint Res 2012;1:42-49.
18. Hartmann A, Lutzner J, Kirschner S, Witzleb WC, Gunther KP. Do Survival Rate and Serum Ion Concentrations 10 Years After Metal-on-Metal Hip Resurfacing Provide Evidence for Continued Use? Clin Orthop Relat Res 2012;470(11):3118-26.
19. Tuke MA, Scott G, Roques A, Hu XQ, Taylor A. Design considerations and life prediction of metal-on-metal bearings: the effect of clearance. J Bone Joint Surg [Am] 2008;90-A(Suppl):134-141.
20. Hjorth MH, Stilling M, Soballe K, Bolvig LH, Thyssen JP, Mechlenburg I, Jakobsen SS (2015) No association between pseudotumors, high serum metal-ion levels and metal hypersensitivity in large-head metal-on-metal total hip arthroplasty at 5-7-year follow-up. Skeletal Radiology 2016;45(1):115-125.
21. S. Glyn-Jones, H. Pandit, Y.-M. Kwon, H. Doll, H. S. Gill, D.W. Murray. Risk factors for inflammatory pseudotumour formation following hip resurfacing. J Bone Joint Surg [Br] 2009;91-B:1566-74.
22. Walter LR, Marel E, Harbury R, et al. Distribution of chromium and cobalt ions in various blood fractions afterresurfacing hip arthroplasty. J Arthroplasty 2008;23-6:814.
23. Clayton RAE, Beggs I, Salter DM, Grant MH, Patton JT, Porter DE. Inflammatory pseudotumor associated with femoral nerve palsy following metal-on-metal resurfacing of the hip. A case report. Journal of Bone and Joint Surgery-American Volume 2008; 90(9): 1988-93.
24. Berber R, Khoo M, Cook E, Guppy A, Hua J, Miles J, Carrington R, Skinner J, Hart A. Muscle atrophy and metal-on-metal hip implants: a serial MRI study of 74 hips. Acta Orthop 2015;86:351-357.
25. Balk EM, Tatsioni A, Lichtenstein AH, Lau J, Pittas AG. Effect of chromium supplementation on glucose metabolism and lipids: a systematic review of randomized controlled trials. Diabetes Care 2007;30(8):2154-2163.
26. Suksomboon N, Poolsup N, Yuwanakorn A. Systematic review and meta-analysis of the efficacy and safety of chromium supplementation in diabetes. J Clin Pharm Ther 2014;39(3):292-306.
27. Trace elements in human nutrition. Report of a WHO expert committee. Report No. 532, World Health Organization, Geneva, 1973
28. Merritt K, Brown SA. Release of chromium with a valence of 6 from corrosion of stainless steel and cobalt-chromium alloys. J Biomed Mater Res 1995;29:627-33
29. Curtis JR, Goode GC, Herrington J, Urdaneta LE. Possible cobalt toxicity in maintenance hemodialysis patients after treatment with cobaltous chloride: a study of blood and tissue cobalt concentrations in normal subjects and patients with terminal and renal failure. Clin Nephrol. 1976; 5:61-5
30. Pehrsson K, Lins L-E. Cobalt in uræmic cardiomyopathy. Lancet 1978;312:51-2.
31. Ikeda T, Takahashi K, Kabata T, Sakagoshi D, Tomita K, Yamada M. Polyneuropathy caused by cobalt-chromium metallosis after total hip replacement. Muscle Nerve 2010;42(1):140-3.
32. Tower SS. Arthroprosthetic cobaltism: neurological and cardiac manifestations in two patients with metal-on-metal arthroplasty: a case report. J Bone Joint Surg Am 2010;92(17):2847-51.
33. Pelclova D, Sklensky M, Janicek P, Lach K. Severe cobalt intoxication following hip replacement revision: clinical features and outcome. Clin Toxicol 2012;50(4):262-5.
34. Bradberry SM, Wilkinson JM, Ferner RE. Systemic toxicity related to metal hip prostheses. Clin Toxicol (Phila) 2014;52(8):837-47.
35. Tower S . Cobalt toxicity in two hip replacement patients. State Alaska Epidemiol Bull 2010;14:1.
36. Günther KP, Schmitt J, Campbell P, Delaunay CP, Drexler H, Ettema HB, García-Cimbrelo E, Hannemann F, Hartmann A, Huberti H, Knahr K, Kunze J, Langton DJ, Lauer W, Learmonth I, Lohmann CH, Lützner J, Morlock M, Seidler A, Wimmer MA, Zagra L. Consensus statement "Current evidence on the management of metal-on-metal bearings". Hip Int 2013;23(1):2-5.
37. Matharu GS, Mellon SJ, Murray DW, Pandit HG. Follow-Up of Metal-on-Metal Hip Arthroplasty Patients Is Currently Not Evidence Based or Cost Effective. The Journal of Arthroplasty 2015;30:1317-1323.
38. Ebreo D, Khan A, El-Meligy M, Armstrong C, Peter V. Metal ion levels decrease after revision for metallosis arising from large-diameter metal-on-metal hip arthroplasty.Acta Orthop Belg 2011;77(6):777-81.