

Contamination of revision procedures in patients with adverse tissues reaction to metal on metal implant

F. FAVETTI¹, G. MAZZOTTA², M. PAPALIA², G. PANEGROSSI¹, F. CASELLA¹, F. FALEZ¹

¹Orthopaedic and Traumatology Department, Santo Spirito Hospital, Rome, Italy

²Orthopaedic and Traumatology Department, Nuova Itor Clinic, Rome, Italy

Abstract. – OBJECTIVE: The aim of this study is to evaluate the incidence of infections in MoM total hip replacement revisions and to propose a therapeutic algorithm that can reduce the onset of this complication.

Total hip arthroplasty is one of the most successful procedures performed annually in the world. As the population ages, the number of primary arthroplasty procedures performed each year is rising in conjunction with an increasing revision burden. Metal on Metal (MoM) total hip arthroplasties were reintroduced in over the last fifteen years to meet these needs, larger diameters, improved lubrication, better stability, increased ROM and wear properties of the bearing couple. These advantageous features have led to an exponential diffusion of MoM. Since over last decade, it has become evident that hip replacements with MoM bearing have significantly higher revision rates compared to those with Metal on Polyethylene. The common pathway for this failure mode appears to be increased wear or corrosion with excessive release of metal ions and nanoparticles. Complications such as elevated serum metal ion levels, aseptic lymphocyte-dominated vasculitis-associated lesion (ALVAL) and pseudotumours have all been well documented, but recent studies suggest increased risk of infection with MoM bearing surfaces.

PATIENTS AND METHODS: We collect data from a cohort of 44 patients who underwent revision of total hip arthroplasty between 2014 and 2017 for the complication of MoM bearing. Studied by radiological images, blood tests, and intraoperative clinical status, part of the population was treated with one stage revision, while the other was treated with a two-stage revision.

RESULTS: Results showed a difference in the occurrence of infections in the two populations.

CONCLUSIONS: We consider it appropriate to perform two-stage revision in all case of failure of MoM replacement so as to allow to minimize the likelihood of infection in patients with damaged tissues by ALVAL, pseudotumour, and necrosis that could create an ideal environment for bacterial development.

Key Words

Total hip arthroplasty, ALVAL, Metal on metal, Infections, Total hip arthroplasty revision.

Introduction

Total hip arthroplasty (THA) is one of the most successful procedures performed annually in the world. As the population ages, the number of primary arthroplasty procedures performed each year is rising in conjunction with an increasing revision burden. As patients live longer and place higher demands on their prosthesis, the choice of bearing surface is critical to the longevity of the implant. One of the common technologies utilized to optimize implant longevity has been the use of alternative bearings to decrease wear at the primary articulation. Metal on Metal (MoM) total hip arthroplasties were reintroduced in over the last fifteen years to meet these needs, larger diameters of these implants appeared to improve the lubrication and wear properties of the bearing couple. In addition, the promise of better stability and increased range of motion led to the widespread enthusiasm and early clinical adoption of this technology. These advantageous features have led to an exponential diffusion of MoM with over 1 million implants carried out between 1996 and 2007. Since 2008, it has become evident from national joint registry data that hip replacements and resurfacing with Metal on Metal bearing have significantly higher revision rates compared to those with Metal on Polyethylene (MoP)¹. Approximately 1 in 5 MoM hip replacements will need revision 10-13 years after they were implanted, with larger sizes (> 36 mm) ascribing higher risk. This is compared with MoP implants, which are revised in less than 4% of cases in 10 years after insertion^{1,2}. Af-

ter companies' recalls (Durom, Zimmer Biomet, Warsaw, IN, USA and ASR, DePuy Orthopaedics Johnson & Johnson, Warsaw, IN, USA) the number of MoM hip replacements has reduced dramatically. MoM now accounts for less than 1% of all hip arthroplasty procedures in Australia and UK¹. The increased revision rates of MoM hip replacements are related to adverse reactions to metal debris released from the bearing surface as the implant wears. The aim of the study is to evaluate the incidence of infections in MoM total hip replacement revisions and to propose a therapeutic algorithm that can reduce the onset of this complication.

Failure of Metal on Metal Replacement and Adverse Reaction to Metal Debris

The particles generated by the MoM bearing are significantly smaller (average size of 42 nm) than a metal-on-polyethylene bearing (average size of 0.21 μm)^{3,4}. Although the particle size is smaller, the number of particles generated is 13–500 times greater and they have been found to be more biologically active than other particles debris generated with conventional bearing⁴. Component design, component position, metal hypersensitivity, and female sex are risk factors for elevated metal ion levels. Higher metal ion levels in patients with cups positioned at greater abduction angles ($>55^\circ$) due to edge loading, and they also noted the influence of component design^{5,6}. Many monoblock MoM acetabular components were designed with less than 180° coverage. Since these components were designed to be less than a full hemisphere, cups placed with an abduction angle of 45° would behave as if they were in a more vertical position, leading to increased edge loading, wear and circulating metal ion levels. Additionally, early components with narrow clearance on the perimeter can be deformed with impaction causing failure of fluid film lubrication and increased wear. Furthermore, trunniosis (Figures 1, 2), defined as metal wear at the head-neck junction of the total hip implant, is an important contributor (along with wear to metal particle release in metal-on-metal total hip arthroplasty). Trunniosis occurs similarly in modular MoM and MoP total hip replacements as both head-neck junctions consist of metal on metal surfaces.

Soft tissue inflammatory reactions to metal debris are recognised complication of MoM hip arthroplasty. These reactions have been called inflammatory pseudotumour, aseptic lymphocytic



Figure 1. Metal wear due to Trunniosis.

vasculitis associated lesion (ALVAL) and metallosis⁷. Inflammatory pseudotumour is the clinical term given to an aseptic mass in the periprosthetic tissues that are either solid or cystic and is associated with clinical, radiological or histopathological signs of inflammation. It is thought to develop as a result of an adverse reaction to



Figure 2. Particular modular of Trunniosis.



Figure 3. Metallosis of periprosthetic tissue.

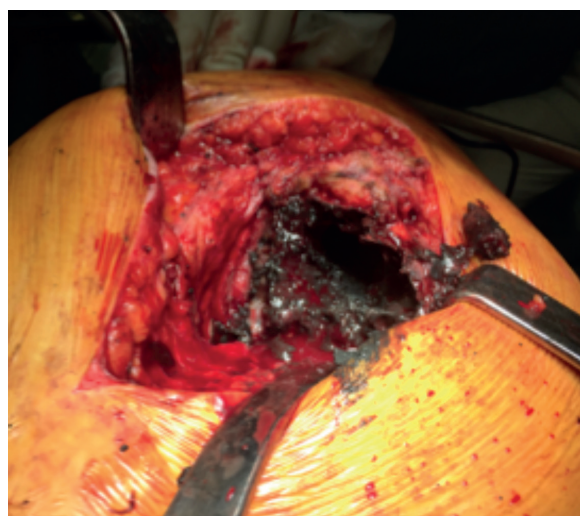


Figure 4. Muscle degeneration due metal debris.

the metal ions released from the wear of a metal articular bearing surface. ALVAL describes the cellular changes that occur periprosthetically in response to metal particles: cobalt and chromium ions. The presence of this reactions is thought to be proportional to the amount of wear debris released, but also be observed in patients with smaller amounts of wear debris⁸. Metallosis, defined as aseptic fibrosis, local necrosis or loosening of a device secondary to metallic corrosion and release of wear debris, is commonly found in tissue samples from joints exhibiting an adverse reaction to metal debris (Figures 3, 4). It has been suggested that pseudotumours are on the same pathological spectrum of disease as metallosis, and will develop if given enough time⁸. Recent research has suggested that all MoM bearing surfaces have a higher risk of developing infection compared to other bearing surfaces⁹⁻¹¹. It has been postulated that the combination of metal debris, ALVAL, pseudotumour formation, and necrotic tissue provides a unique environment for the bacterial proliferation in MoM implants¹².

Patients and methods

Between 2014 and 2017 forty-four patients (29 male and 15 female, average age 64.7) with MoM total hip arthroplasty undergoing revision for persistent pain and dysfunction.

All patients were pre-operative studied with blood tests (ESR, CRP and metal ion concentration) (Table I) and radiological imaging (plain radiography, MRI with MARS technique and

bone scintigraphy) (Figures 5, 6).

All patients had preoperative findings of ALVAL, pseudotumour or metal debris reaction. Thirty-one patients had MoM bearing; thirteen patients had an adverse reaction to metal debris due to trunniosis.

Time from primary total hip arthroplasty to revision range from 4 to 8 years. At the time of revision surgery, periprosthetic tissue samples were always sent for microbiological and extemporaneous histological examination in order to confirm the cause of implant failure. Patients were treated with two different methods: from the beginning of 2014 to the first half of 2015 twenty-three patients undergoing to one-stage revision, from the second half of 2015 until 2017 twenty-one undergoing to two-stage revision. The patients were followed between 1, 3, 6 months and 1 year after revision. Pathological microbiology and laboratory markers for infection were assessed. Post-operative treatment courses were also reviewed.

Results

All samples sent for microbiological tests at the time of revision were sterile. The histological samples showed various conditions that included: perivascular infiltration of lymphocytes, the presence of plasma cells and macrophages containing metal particles and severe ulceration of tissue surfaces and evidence of fewer lymphocytes, but more macrophages and metal particles. All

Table I. Analyzed population.

Patient	Head size (mm)	ESR (2-12 mm/h)	CRP (0-3 mg/L)	Cr/Co (2-7 mcg/L)
1	44	14	9	6.5
2	40	7	2	4.8
3	32	10	2	7.2
4	40	15	6	5.3
5	38	14	4	6.9
6	44	2	2	8.1
7	42	18	12	4.1
8	32	14	7	3.7
9	44	13	4	5.2
10	46	18	5	6.3
11	40	22	7	5.4
12	36	6	2	9.3
13	42	2	0	7.2
14	44	6	1	8.7
15	40	2	0	7.5
16	36	13	5	7.3
17	32	4	2	5.7
18	42	11	2	8.3
19	38	16	4	5.6
20	46	3	1	7.3
21	48	12	3	5.1
22	46	13	7	6.7
23	42	8	2	8.4
24	38	14	6	5.5
25	44	26	16	4.9
26	44	14	7	3.9
27	36	8	0	7.6
28	46	20	10	3.8
29	44	18	8	4.5
30	32	10	3	5.8
31	32	16	6	4.1
32	42	32	8	7.3
33	40	18	7	6.1
34	46	20	5	7.5
35	32	24	10	8.1
36	38	22	12	7.2
37	46	8	2	4.4
38	38	14	5	6.1
39	36	15	7	9.7
40	32	18	6	5.2
41	46	16	6	4.3
42	36	4	2	6.3
43	32	18	5	4.8
44	38	20	15	7.9

patients treated with two-stage revision undergoing to a new total hip arthroplasty after a range from 4 to 8 weeks concurrently with a reduction of ESR and CRP values. In this series, no patients developed an infection during subsequent

controls. In the series of patients treated with one-stage revision, seven [patients 2, 5, 7, 11, 17, 18, and 23] (30%) developed an infection: four patients within the first 6 postoperative weeks, two patients after third postoperative month and

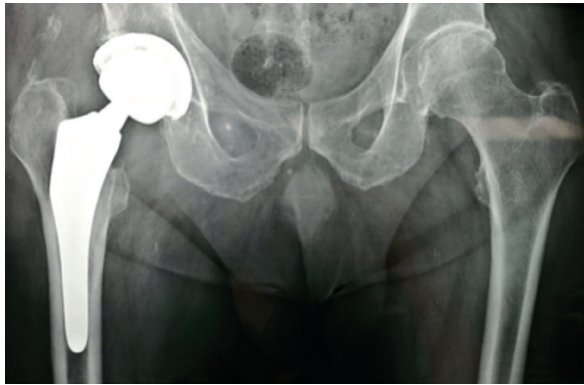


Figure 5. X-ray in a patient with metal debris disease showing no specific changes.

one after the fourth months. All of these had groin pain with occasional radiation to the greater trochanter, stiffness, reduced range of movement and muscles weakness. Three of these presented a panpipe with frank pus, the other four patients presented only an increase of ESR and CRP with swelling and reddening of the wound. Samples were taken by hip joint aspirate and swabs from panpipes and showed: three cases *Streptococcus hemolytic*, two cases *Staphylococcus epidermidis* and two MRSA *Staphylococcus*. Infections occurred into the first 6 weeks post-operative were treated with irrigation, debridement, bearing exchange and specific antibiotic therapy. Infection occurred at three and four postoperative months were treated with hip replacement removal, antibiotic-loaded spacer, and specific antibiotic therapy. When all inflammation values were negativized patients undergoing to new total hip arthroplasty.

Mann Whitney U test showed a statistically significant correlation between the values of ESR and CRP in the population treated with one-stage revision compared to that treated with two-stage revision (Figures 7, 8).

Discussion

The concern over adverse metal reactions and soft tissue pseudotumors in patients undergoing metal bearing hip arthroplasty continues to grow. Reports to date have been the mostly single case or case series, but Glyn-Jones et al¹³ presented a large series of patients undergoing revision of MoM total hip arthroplasty and found a 1.8% revision rate for pseudotumour alone. In their series, Kaplan Meier curves showing cumulative revision rate for pseudotumor increased with time, to as high as 4% at eight years.

It has also been found that infection in the face of adverse local tissue reaction after MoM total hip arthroplasty may be challenging to properly diagnose and treat given the overlap of symptoms, signs and laboratory values in both processes¹⁴. Despite the similarities in clinical presentation, the treatment strategies for these two clinical conditions are usually quite different. The accuracy of the diagnosis is important in optimizing patient outcome after revision. In general, the infection rate for the traditional (ceramic/polyethylene) bearing is around 1%. The overall infection rate for metal on metal THA has also been shown to have an incidence of 1% or less^{15,16}. Symptoms and signs of infection should be similar for both traditional bearings and metal bearings particularly in the

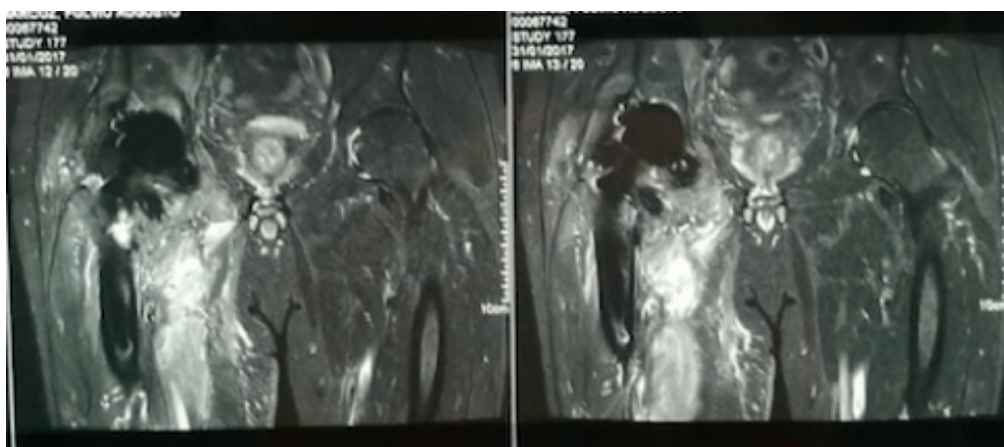


Figure 6. MRI with MARS technique showing a pseudotumour in the medial region of the leg.

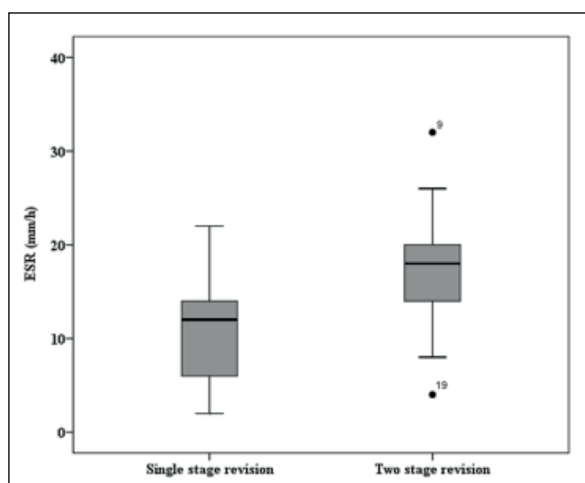


Figure 7. Relationship between ESR values and rate of infection in the two patients' populations.

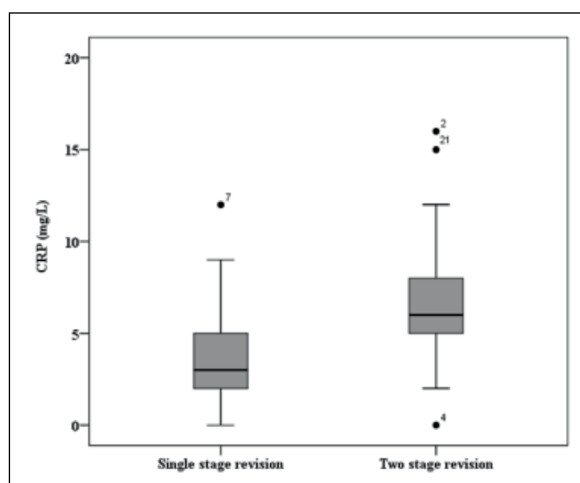


Figure 8. Relationship between CRP values and rate of infection in the two patients' populations.

absence of any adverse local soft tissue reactions. Patients presenting with an adverse soft tissue reaction and/or pseudotumor typically present with pain, usually located in the groin, with occasional radiation to the greater trochanter and down the thigh, stiffness, reduced range of movement, abductor weakness and even rash as reaction to metal ions. This pain will often cause patients to adopt an antalgic gait, over time, this may progress to instability with or without dislocation and patients may complain of clicking or clunking sensations in the hip along with radiographic findings of a cystic mass. This presentation may be difficult to differentiate from infection¹⁴. The standard evaluation to diagnose an infected arthroplasty includes serum ESR and CRP values, and if these are elevated or suspicion is high, a hip joint aspiration sent for white total nucleated cell count and differential (PMN percentage in particular), furthermore bacterial culture with sensitivity testing. Leukocyte scintigraphy and the improved version of the technique – combined leukocyte/bone marrow scintigraphy – have been proposed as the gold-standard technique for the diagnosis of infection. The technique is most useful for identifying neutrophil-mediated inflammatory processes, such as distinguishing between an infected prosthesis and an aseptically loosened prosthesis, in which neutrophils are generally absent^{17,18}. Although leukocyte scintigraphy and leukocyte/bone marrow scintigraphy demonstrate the outstanding capability for the diagnosis of PJI, there are definite limitations to these techniques. Radiolabeled leukocytes are less effective in non-neutrophilic processes, such as tuberculous infections^{17,18,19}. In

chronic, long-standing infections, the neutrophil recruitment is less evident. The bacterial biofilm retards the invasion of labeled leukocytes into the infected area and a longer time is needed for white cell accumulation. For this reason, a delayed imaging at 24 h is more preferable when using leukocyte imaging for the detection of prosthesis joint infection; finally, one major disadvantage of leukocyte scintigraphy is that leukocytes accumulate not only in the infected area but also in the bone marrow. Non-specific the ESR and CRP are good indicators of systemic inflammation when elevated. The joint aspiration is a more accurate test for the diagnosis, but false positives and negatives do occur, as well an inability to obtain fluid on occasion. Hip aspirates with a total nucleated cell count greater than 4200 cells/ml and greater than 80% PMN if taken in isolation or with a total nucleated cell count > 3000, if both ESR and CRP are elevated above 30 mm/hr and 10 mg/dl respectively, have a high probability of being infected. A positive culture from the hip aspirate is the gold standard for pre-operative diagnosis of infected THA, but it can take as long as 5-10 days to grow²⁰. Gross purulence and positive intra-operative tissue culture then become the final test used to confirm or refute infection.

It is now being recognized, however, that many of these preoperative laboratory values may also be abnormal in MoM hips with local tissue relations but without infection. In our population, ESR and CRP were elevated in twenty-six patients (59%) without infection, and the total nucleated cell count was highly elevated in all uninfected hips. This considerable overlap can make obtain-

ing an accurate diagnosis and choosing the optimal treatment quite challenging. Differentiating the two processes as being separate or concomitant is critical since isolated local soft tissue reactions can often be treated with revision of the bearing surface only to a non-metal alternative; but for infection, irrigation and debridement with specific antibiotics or more commonly two-stage revision of the entire prosthesis may be necessary.

In the current series, 30% (7/23) of patients treated with one stage revision developed a post-operative infection between 6 weeks and 4 months. This ratio is much higher than that reported for either traditional bearing or MoM bearings without evidence of a local soft tissue reaction. Prior to this series, concomitant infection and local soft tissue reaction had been described in a single case report by Watters et al¹⁰. In this case, the presentation and treatment of a patient with concomitant local soft tissue reaction and local infection is described. This rate of coinfection is also presumably higher than those patients found to be infected at the time of revision for polyethylene wear.

The intraoperative observational evaluation also has the potential to be reliable in distinguishing infection from isolated local soft tissue reactions. Common are the findings of metal staining of soft tissue, cystic masses, large exudates, and tissue necrosis. In the current series, the pathological evaluation is consistent with previous descriptions of pseudotumour and local metal reactions²¹. In our infected patients, a pathology reading of the intraoperative frozen section of "acute inflammation" (>5 WBC per hpf in multiple fields) seemed to be the most predictive descriptor of infection as five of the seven patients had this present.

Finally, the prevalence of uncommon infective agents in our series was also felt to be unusual. *Streptococcus* has occasionally been implicated in concomitant infection in local metal reaction, but it is not among the more common agent isolated from infected total hip arthroplasties. This finding may certainly be due to the small number of patients but the predilection for infection with atypical agents in the face of soft tissue metal reaction cannot be excluded.

Conclusions

It's important to consider clinical examination findings, blood test results, and radiologic investigations when determining the likelihood

of failing prosthesis. Revision should be considered when symptoms become persistent, unmanageable, and progressive. Furthermore, any patient exhibiting progressive osteolysis, large or expanding pseudotumours or excessively high metal ion concentrations should also be considered for revision surgery. We consider it appropriate to perform two-stage revision in all case of failure of MoM replacement so as to allow to minimize the likelihood of infection in patients with damaged tissues by ALVAL, pseudotumour, and necrosis that could create an ideal environment for bacterial development.

Conflict of Interests

The authors declare that they have no conflict of interest.

References

- 1) AUSTRALIAN ORTHOPAEDIC ASSOCIATION. Metal non metal bearing surface total conventional hip arthroplasty. Supplement Report 2014. National Joint Replacement Registry.
- 2) NATIONAL REGISTRY FOR ENGLAND, WALES AND NORTHERN IRELAND. 11th annual report 2014.
- 3) DOORN PF, CAMPBELL PA, WORRALL J, BENVA PD, McKELLOP HA, AMSTUZ HC. Metal wear particle characterization from metal on metal total hip replacements: transmission electron microscopy study of periprosthetic tissues and isolated particles. *J Biomed Mater Res* 1998; 42: 103-111.
- 4) TOPOLOVEC M, COR A, MILOSEV I. Metal-on-metal vs metal-on-polyethylene total hip arthroplasty tribological evaluation of retrieved components and periprosthetic tissue. *J Mech Behav Biomed Mater* 2014; 34: 243-252.
- 5) DE HAAN R, PATTYN C, GILL HS, MURRAY DW, CAMPBELL PA, DE SMET K. 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.
- 6) DE HAAN R, CAMPBELL PA, SU EP, DE SMET KA. 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.
- 7) SCIENTIFIC COMMITTEE ON EMERGING NEWLY IDENTIFIED HEALTH RISKS. Opinion on: the safety of metal on metal joint replacement with particular focus on hip implants, 2014.
- 8) LANGTON DJ, JOYCE TJ, JAMESON SS, LORD J, VAN ORSOUW M, HOLLAND JP, NARGOL AV, DE SMET KA. Adverse reaction to metal debris following hip resurfacing: the influence of component type, orientation and volumetric wear. *J Bone Joint Surg Br* 2011; 93: 164-171.
- 9) JUDD K, NOISEUX N. Concomitant infection and local metal reaction in patients undergoing revision of metal on metal total hip arthroplasty. *Iowa Orthop J* 2011; 31: 59-63.

- 10) WATTERS T, EDWARD WC, HALLOWS RK, DODD LG, WELLMAN SS, BOLOGNESI MP. Pseudotumour with superimposed periprosthetic infection following metal on metal total hip arthroplasty. *J Bone Joint Surg Am* 2010; 92: 1666-1669.
- 11) WYLES C, VAN DENMARK RE, SIERRA RJ, TROUSDALE RT. High rate of infection after aseptic revision of failed metal on metal total hip arthroplasty. *Clin Orthop Relat Res* 2014; 472: 509-516.
- 12) DONALDSON JR, MILES J, SRI-RAM K, POUILLIS C, MUIR-HEAD-ALLWOOD S, SKINNER J. The relationship between the presence of metallosis and massive infection in metal on metal hip replacements. *Hip Int* 2010; 20: 242-247.
- 13) GLYN-JONES S, PANDIT H, KWON YM, DOLL H, GILL HS, MURRAY DW. Risk factors for inflammatory pseudotumour formation following hip resurfacing. *J Bone Joint Surg Br* 2009; 91: 1566-1574.
- 14) MIKHAEL MM, HANSEEN AD, SIERRA RJ. Failure of metal on metal total hip arthroplasty mimicking hip infection. A report of two cases. *J Bone Joint Surg Am* 2009; 91: 443-446.
- 15) MILOSEV I, TREBSE R, KOVAC S, COR A, PISOT V. Survivorship and retrieval analysis of sikomet metal on metal total hip replacements at mean of seven years. *J Bone Joint Surg Am* 2006; 88: 1173-1182.
- 16) KIM SY, KYUNG HS, IHN JC, CHO MR, KOO KH, KIM CY. Cementless Metasul metal on metal total hip arthroplasty in patients less than fifty years old. *J Bone Joint Surg Am* 2004; 86: 2475-2481.
- 17) LOVE C, TOMAS MB, MARWIN SE, PUGLIESE PV, PALESTRO CJ. Role of nuclear medicine in diagnosis of the infected joint replacement. *Radiographics* 2001; 21: 1229-1238.
- 18) PALESTRO CJ, LOVE C. Radionuclide imaging of musculoskeletal infection: conventional agents. *Semin Musculoskelet Radiol* 2007; 11: 335-352.
- 19) BUNYAVIROCH T, AGGARWAL A, OATES ME. Optimized scintigraphic evaluation of infection and inflammation: role of single-photon emission computed tomography/computed tomography fusion imaging. *Semin Nucl Med* 2006; 36: 295-311.
- 20) SCHINSKY MF, DELLA VALLE CJ, SPORER SM, PAPROSKY WG. Perioperative testing for joint infection in patients undergoing revision total hip arthroplasty. *J Bone Joint Surg Am* 2008; 90: 1869-1875.
- 21) CADOSI M, CHIARELLO E, SAVARINO L, MAZZOTTI A, TEDESCO G, GRECO M, GIANNINI S. Fast growing pseudotumour in a hairdresser after metal-on-metal hip resurfacing: a case report. *Eur Rev Med Pharmacol Sci* 2014; 18(1 Suppl): 29-33.