

Fast growing pseudotumour in a hairdresser after metal-on-metal hip resurfacing: a case report

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Abstract. – A 44-year-old female hairdresser who underwent metal-on-metal hip resurfacing (MOMHR) for hip osteoarthritis developed a benign pelvic pseudotumour. Elevated levels of chromium and cobalt ions were detected in the blood. Patch testing after pseudotumor formation, showed positive skin reactions to cobalt and nickel. Marked hypereosinophilia was noted, as well as the presence of eosinophils in the pseudotumor mass. A revision to a ceramic-on-ceramic implant was performed. Radiographs showed no implant loosening or bone resorption. We hypothesized that a steep cup positioning as well as hypersensitivity response to the metal nanoparticles and ion release may have induced pseudotumour development. Currently there is no evidence that negative patch testing reduces the probability to develop an adverse reaction to metal debris therefore we suggest to carefully investigate patient medical history regarding occupation exposure and daily contact with jewellery, beauty and cleaning products before implanting MOMHR. The main challenge is to identify a sensitive patient candidate to MOMHR never suspected to be.

Key Words:

Pseudotumour, Metal-on-metal hip resurfacing, Hypersensitivity response, Occupational pre-sensitisation.

Introduction

Over the last few years, there has been a revival in metal-on-metal hip resurfacing (MOMHR). Despite the encouraging results, concerns have been expressed about the potentially hazardous release of metal ions and nanoparticles from these implants¹. Several studies have documented osteolysis and implant loosening^{2,3}, the development of hypersensitivity⁴ and

the occurrence of abnormal soft tissue reactions, sometimes called pseudotumours, following MOMHR⁵⁻⁹. However, the exact biological pathway that leads to the local effects seen in MOMHR hips remains unclear¹⁰. We report a particular case of pseudotumour formation after MOMHR in a female who previously worked as a hairdresser. To investigate occupational exposure to metals prior to prosthetic surgery in order to limit pseudotumour risk is clinically relevant both for patients and surgeons. Moreover, clarifying the pseudotumour pathogenesis would increase the safety of metal-based implants.

Case Report

A 44-year-old female with no medical history of metal allergies underwent MOMHR (Birmingham Hip Resurfacing, Smith & Nephew, Birmingham, UK) after diagnosis of osteoarthritis of the left hip. On pre-operative radiographs, the head-neck ratio measured according to Grammatopoulos et al¹¹, was 1.57. We implanted a 42 mm femoral component and a 48mm acetabular component with an inclination of 65° measured on post-operative X rays as described by Beaulé et al¹². Twelve months after MOMHR surgery, the patient complained about pain and quadriceps weakness in her left thigh. Radiographs showed a stable implant (Figure 1a), but a solid, circumscribed heterogeneous lesion around the femoral neck and proximal femur, passing along the right hemi-pelvis at the sacral promontory (Figure 1b), was revealed by CT scan. Before revision surgery a more accurate recording of patient's medical history revealed that she had been working as a hairdresser for approximately 30 years, and she was routinely exposed to utensils and to chemicals of hair dyes and permanent wave solutions.

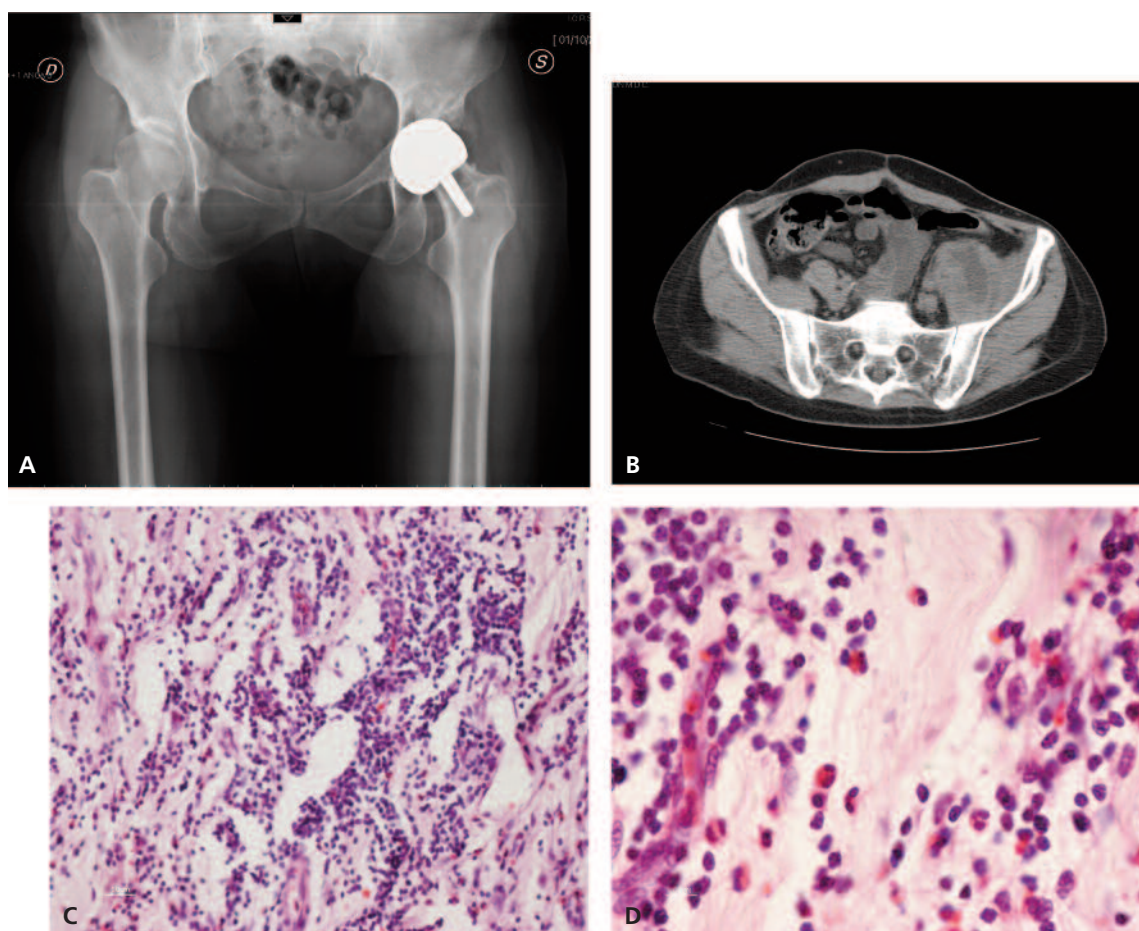


Figure 1. **A**, Radiograph of the left hip 12 months after MOMHR prosthesis implantation. **B**, CT scan showing pelvic mass. **C**, Histology of a portion of the iliopsoas mass. Areas of fibrous tissue with infiltration of lymphocytes, mainly arranged as follicles, giant cells and macrophages can be seen (H.E. $\times 20$). **D**, Histology of a portion of the iliopsoas mass showing large eosinophils and lymphoid follicles (H.E. $\times 60$).

A two-step revision surgery was planned. First, the mass was removed through a laparoscopic approach. The mass was necrotic, with some liquefaction around the left psoas and the iliac muscles, extending below the inguinal ligament and involving the femoral nerve. Histological examination showed areas of dense fibrous tissue with lymphocyte aggregates, necrotic muscle tissue and undefined necrosis. High levels of chromium (Cr) and cobalt (Co) ions were detected in the periprosthetic tissues by atomic absorption spectrophotometry (AAS) (141.18 $\mu\text{g/g}$ and 57.26 $\mu\text{g/g}$ of Cr and Co respectively; normal values: Cr 0.005-0.18 $\mu\text{g/g}$, Co 0.006-0.24 $\mu\text{g/g}$, based on wet weight). High Cr (8.11 ng/ml; normal values: < 0.5 ng/ml), and Co levels (4.15 ng/ml; normal values: < 0.5 ng/ml) were measured in the serum by AAS. Infection was excluded, no systemic toxic effects

were highlighted, and kidney and liver functions were normal. Inflammatory indices were all within the normal range.

Nearly one month later, as soon as the patient recovered from previous surgery, the second-step was scheduled for MOMHR revision. The patient was still complaining about pain in her left thigh and no recovery of the partial femoral nerve palsy was observed. Positive skin reactions to Co and nickel (Ni) were recorded by patch testing. High serum Cr (11.53 ng/ml) and Co (7.09 ng/ml) levels and a normal Ni level (< 0.1 ng/ml) were recorded. A marked hypereosinophilia (about 1500 eosinophils/ μl = 18.6%) was also present. The implant was well fixed, as no radiolucencies were observed on X-rays. CT scan showed the presence of a new iliopsoas mass which was removed during MOMHR revision.

MOMHR was replaced by a ceramic-on-ceramic total hip arthroplasty. During the implant removal, some tissue samples from the periacetabular region and from the pseudotumor were collected. Histology of the periacetabular tissue showed a dense lymphocytic infiltrate, a large number of mast cells and several eosinophils (Figure 1c). Analysis of the periacetabular tissues detected 0.72 µg/g of Cr, 0.32 µg/g of Co and 1.09 µg/g of Ni. The biopsy taken from the mass was completely necrotic with 21.82 µg/g of Cr, 18.52 µg/g of Co and 1.36 µg/g of Ni.

Two biopsies from the iliopsoas mass and one from the reactive tissue between the acetabular component and the iliac bone were retrieved. Histological examination of a portion of the mass showed giant cells, macrophages and fibrous tissue with infiltration of lymphocytes mainly arranged in follicles (Figure 1d). In some areas, liquefaction and fat necrosis were observed. Another portion of the mass showed a fibrous-macrophage reaction, and it was characterized by large eosinophils and hemorrhagic areas, as well as by some lymphoid follicles (Figure 1d). Using AAS, 166.5 µg/g of Cr and 91.6 µg/g of Co were detected in the mass, while in the periprosthetic tissue 86.8 µg/g of Cr and 124.4 µg/g of Co were measured. Ni was undetectable. As before, no systemic toxic effects were observed and laboratory values were unaltered. Only by peripheral blood cell count an increased eosinophilia from 2.9% to 8.3% was observed. Infection was excluded once again.

Ten days after the implant removal the eosinophil percentage decreased to 7.7%, and returned to 2.1% after one month. Other laboratory parameters were unaltered. Pain subsided one month after revision surgery and CT imaging confirmed the disappearance of the mass; nevertheless femoral nerve palsy is still present and should be considered as permanent thus the patient walks with the aid of a knee brace.

Discussion

Although the occurrence of pseudotumours after hip arthroplasty is relatively uncommon, there are several reports about their development after MOMHR^{5,7,13,14}. The mechanism leading to pseudotumour formation is currently unclear. Pandit et al⁵, reported on 17 females who developed pseudotumours after MOMHR. The authors suggested that these bodies might be the result of

a toxic effect of a large amount of particulate wear debris on cells, or of an idiosyncratic response to a moderate release of Co-Cr particles. Furthermore, pre-operative sensitisation to metal might be a factor involved in this phenomenon, as all the affected patients in their series were female. Indeed, nickel allergy is a condition predominantly found in women, and it is related to wearing costume jewellery. Lymphocyte infiltrates seen in patients with pseudotumours are often similar to an aseptic lymphocyte-dominated vasculitis-associated lesion (ALVAL)⁶, thus suggesting a delayed-type metal hypersensitivity reaction related to previous exposure. Nevertheless, ALVAL-type response is not present in all pseudotumours, therefore other mechanisms are likely to be involved. In some cases a metal-induced cytotoxic effect has been postulated, due to the presence of metal nanoparticles, heavy macrophage recruitment and extensive tissue necrosis⁶. In this context, the role of nano-sized metallic wear debris and metal ions in the pathogenesis of pseudotumours should be further investigated.

A combination of macrophage-induced necrosis and T lymphocyte-mediated hypersensitivity reaction may be suggested, with a variable balance between the two inflammatory/immune mechanisms. This variability possibly reflects a different toxicity threshold or immunological susceptibility¹⁰.

Our patient had some risk factors for pseudotumor development which only recently have been well defined: steep cup inclination, female sex, small components and more recently a pre-operative head-neck ratio > 1.3. When the patient came for the first time to our attention, she reported no medical history of metal allergies. Only when the pseudotumor developed we found out that she might have undergone occupational pre-sensitisation to Ni and Co during several years spent as a hairdresser. Indeed, Ni is found in scissors, hair clips and other tools, while Co is found in hair dyes and permanent wave solutions. There are many reports on the high rate of allergic contact dermatitis in hairdressers^{15,16}. To the best of our knowledge, if the steep cup orientation must be considered as the primary reason for pseudotumor formation the long term occupational exposure might have played a role in the pathogenesis of this huge to metal debris reaction.

The histological analysis of the pseudotumours and periprosthetic tissues seem to corroborate

orate this theory, as eosinophils are typically associated with allergies, as well as involved in tissue homeostasis, modulation of adaptive immune responses, and innate immunity. They secrete immunoregulatory cytokines and are actively involved in the regulation of Th2-type immune responses^{17,18}.

In our patient, patch test was performed later after MOMHR and found to be positive. This test has a high sensibility but low specificity therefore it is not suitable for an effective screening tool before joint replacement¹⁹. Moreover dermal response may not equally correspond to articular space since synovial tissue is particular reactive to immunogenic stimuli.

The outcome of revision for pseudotumor is poor and consideration should be given to early revision to limit the extent of the soft-tissue destruction²⁰. A negative patch test¹⁶ does not exclude a potential risk of hypersensitivity to metal implants, therefore prior to perform MOMHR we recommend to exhaustively collect patient medical history with an accurate risk assessment, paying particular attention to patient occupation.

Acknowledgements

This research was partially supported by the Italian Ministry of the Health, Financial Support for Scientific Research "5 per mille" 2009.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

References

- 1) URBAN RM, JACOBS JJ, TOMLINSON MJ, GAVRILOVIC J, BLACK J, PEOC'H M. Dissemination of wear particles to the liver, spleen and abdominal lymph nodes of patients with hip or knee displacement. *J Bone Joint Surg Am* 2000; 82-A: 457-477.
- 2) PARK Y-S, MOON Y-W, LIM S-J, YANG JM, AHN G, CHOI YL. Early osteolysis following second generation metal-on-metal hip replacement. *J Bone Joint Surg Am* 2005; 87: 1515-1521.
- 3) GLYN-JONES S, ROQUES A, TAYLOR A, KWON YM, McLARDY-SMITH P, GILL HS, WALTER W, TUKE M, MURRAY D. The in vivo linear and volumetric wear of hip resurfacing implants revised for pseudotumor. *J Bone Joint Surg Am* 2011; 93: 2180-2188.
- 4) WILLERT H-G, BUCHHORN GH, FAYYAZI A, FLURY R, WINDLER M, KÖSTER G, LOHMANN CH. Metal-on-metal bearings and hypersensitivity in patients with artificial hip joints. A clinical and histomorphological study. *J Bone Joint Surg Am* 2005; 87: 28-36.
- 5) PANDIT H, GLYN-JONES S, McLARDY-SMITH P, GUNDLE R, WHITWELL D, GIBBONS CL, OSTLER S, ATHANASOU N, GILL HS, MURRAY DW. Pseudotumours associated with metal-on-metal hip resurfacings. *J Bone Joint Surg Br* 2008; 90: 847-851.
- 6) 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: 2321-2327.
- 7) HART AJ, SATCHITHANANDA K, LIDDLE AD, SABAH SA, McROBBIE D, HENCKEL J, COBB JP, SKINNER JA, MITCHELL AW. Pseudotumors in association with well-functioning metal-on-metal hip prostheses: a case-control study using three-dimensional computed tomography and magnetic resonance imaging. *J Bone Joint Surg Am* 2012; 94(4): 317-325.
- 8) WILLIAMS DH, GREIDANUS NV, MASRI BA, DUNCAN CP, GARBUZ DS. Prevalence of pseudotumor in asymptomatic patients after metal-on-metal hip arthroplasty. *J Bone Joint Surg Am* 2011; 93: 2164-2171.
- 9) GRUBER FW, BÖCK A, TRATTNIG S, LINTNER F, RITSCHL P. Cystic lesion of the groin due to metallosis: a rare long-term complication of metal-on-metal total hip arthroplasty. *J Arthroplasty* 2007; 22: 923-927.
- 10) GILL HS, GRAMMATOPOULOS G, ADSHEAD S, TSIALOGIANIS E, TSIRIDIS E. Molecular and immune toxicity of CoCr nanoparticles in MoM hip arthroplasty. *Trends Mol Med* 2012; 18: 145-155.
- 11) GRAMMATOPOULOS G, PANDIT H; OXFORD HIP AND KNEE GROUP, MURRAY DW, GILL HS. The relationship between head-neck ratio and pseudotumour formation in metal-on-metal resurfacing arthroplasty of the hip. *J Bone Joint Surg Br* 2010; 92: 1527-1534.
- 12) BEAULÉ PE, DOREY FJ, LE DUFF M, GRUEN T, AMSTUTZ HC. Risk factors affecting outcome of metal-on-metal surface arthroplasty of the hip. *Clin Orthop* 2004; 418: 87-93.
- 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) BOARDMAN DR, MIDDLETON FR, KAVANAGH TG. A benign psoas mass following metal-on-metal resurfacing of the hip. *J Bone Joint Surg Br* 2006; 88: 402-404.
- 15) IORIZZO M, PARENTE G, VINCENZI C, PAZZAGLIA M, TOSTI A. Allergic contact dermatitis in hairdressers: frequency and source of sensitisation. *Eur J Dermatol* 2002; 12: 179-182.

- 16) O'CONNELL RL, WHITE IR, MC FADDEN JP, WHITE JM. Hairdressers with dermatitis should always be patch tested regardless of atopy status. *Contact Dermatitis* 2010; 62: 177-181.
- 17) KITA H. Eosinophils: multifaceted biological properties and roles in health and disease. *Immunol Rev* 2011; 242: 161-177.
- 18) PANDIT H, VLYCHOU M, WHITWELL D, CROOK D, LUOMANI R, OSTLERE S, MURRAY DW, ATHANASOU NA. Necrotic granulomatous pseudotumours in bilateral resurfacing hip arthroplasties: evidence for a type IV immune response. *Virchows Arch* 2008; 453: 529-534.
- 19) CARULLI C, VILLANO M, BUCCIARELLI G, MARTINI C, INNOCENTI M. Painfull knee arthroplasty: definition and overview. *Clin Cases Miner Bone Metab* 2011; 8: 26-28.
- 20) GRAMMATOPOULOS G, PANDIT H, KWON YM, GUNDLE R, McLARDY-SMITH P, BEARD DJ, MURRAY DW, GILL HS. Hip Resurfacings revised for inflammatory pseudotumor have a poor outcome. *J Bone Joint Surg* 2009; 91B: 1019-1024.