



Case report

Retroperitoneal lymphadenopathy secondary to joint replacement wear and debris, a case report

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ABSTRACT

We present a case of a 63-year-old female who initially presented with complaints of vulvar swelling and was subsequently found to have isolated retroperitoneal lymphadenopathy on imaging. Biopsy was performed and was indicative of weakly polarizable material that raised the consideration of joint prosthesis wear debris. Due to the patient's concern for an underlying malignancy of gynecologic origin, a laparoscopic lymphadenectomy was ultimately performed and final pathology was consistent with reactive changes due to joint wear and debris from the patient's bilateral total knee arthroplasties placed approximately 16 years prior. While this is a rare presentation, it is important to consider this in the differential of retroperitoneal lymphadenopathy as these patients are often referred to a gynecologic oncologist for further workup.

1. Introduction

The differential diagnosis of retroperitoneal lymphadenopathy is broad and includes both benign and malignant etiologies. We report an unusual case of pelvic retroperitoneal lymphadenopathy due to debris from total knee arthroplasty.

2. Case

A 63-year-old female presented to her gynecologist with swelling of the right side of her vulva. She had a history significant for diabetes, hypertension, stroke, and bilateral total knee arthroplasties 16 years prior to presentation. On exam, the patient's right labia majora was swollen, without a lesion or palpable mass. Initially, it was thought she may have a hernia and pelvic MRI was ordered.

Pelvic MRI demonstrated skin thickening and subcutaneous fat infiltration involving bilateral labia majora with a more pronounced effect on the right as well as moderate pelvic lymphadenopathy (see Fig. 1). This led to CT scan which again demonstrated pelvic lymphadenopathy with enlarged lymph nodes visualized along the pelvic sidewalls, the largest measuring 1.4 × 3.0 cm along the left pelvic sidewall. Enlarged lymph nodes were also noted adjacent to the external iliac vessels as well as the left common iliac vessels. No inguinal lymphadenopathy was noted on imaging. No other abnormalities were noted in the abdomen or pelvis, including no mass within the right vulva.

A CT-guided lymph node biopsy of an enlarged right pelvic lymph node demonstrated benign lymph node tissue with scattered clusters of epithelioid histiocytes. The epithelioid histiocytes contained scant, weakly polarizable material that raised the consideration of joint prosthesis wear debris (see Fig. 2).

In order to further evaluate for malignancy, excisional biopsy was recommended and the patient was referred to gynecologic oncology for further evaluation. On exam in the office the right labia was approximately twice the size of the left labia majora with no obvious lesion. No inguinal lymphadenopathy was palpable. A vulvar biopsy was performed in the office which demonstrated edema, chronic inflammatory infiltrate and mildly dilated lymphatic channels in the dermis with no evidence of malignancy. After discussion with the gynecologic oncologist, the patient opted for a definitive diagnosis and decided to proceed with diagnostic laparoscopy with lymph node excision and bilateral salpingo-oophorectomy to evaluate for an underlying malignancy.

Two representative right-sided lymph nodes and one left-sided lymph node were removed and sent for frozen section. The frozen section was benign and no further lymph node dissection was performed. Final pathology of sampled pelvic lymph nodes again demonstrated a patchy infiltrate of pale epithelioid histiocytes positive for PAS with diastase resistance as well as rare non-necrotizing granulomas which were negative for fungi and acid-fast bacteria on PAS and AFB stains (see Fig. 3). Non-necrotizing granulomas with giant cells were also noted. The sample was sent to Mayo Clinic for PCR studies for

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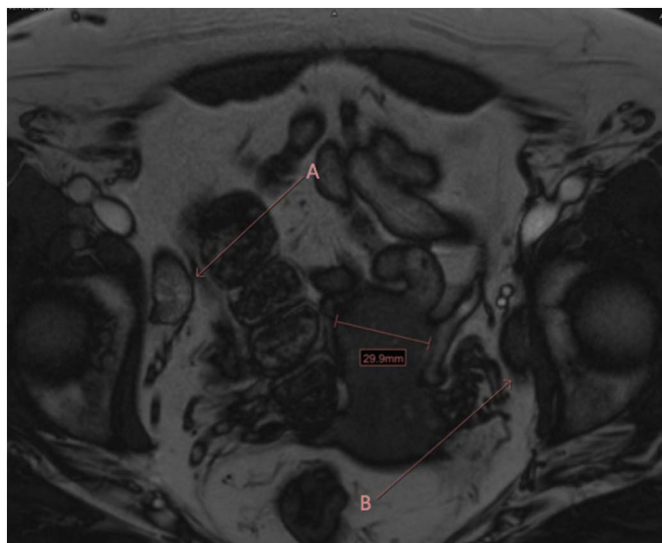


Fig. 1. MRI of the pelvis demonstrating enlarged right external iliac lymph node measuring 1.7×1.5 cm and left external iliac node measuring 2.5×1.3 cm.

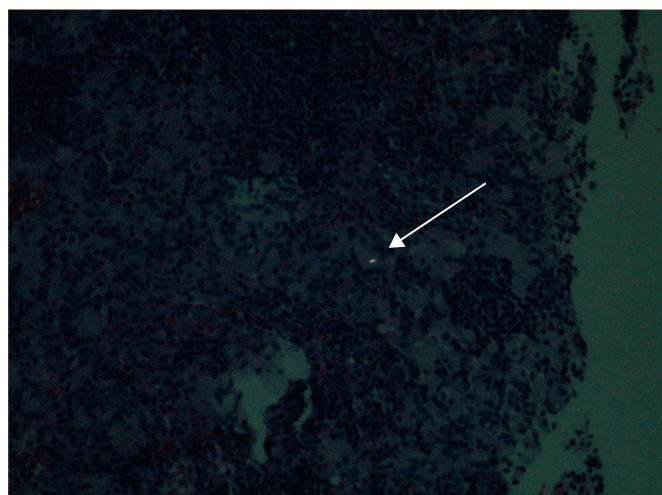


Fig. 2. Polarizable foreign body (arrow).

Tropheryma whipplei DNA which were negative. The patient underwent evaluation by consulting orthopedic surgeon. She had no complaints of pain or limited range of motion in her bilateral prostheses. X-rays taken of bilateral knees showed her prostheses to be well aligned without

radiographic evidence of loosening. It was concluded that the patient's lymphadenopathy was secondary to wear and debris from her bilateral total knee replacements sixteen years prior.

3. Discussion

When approaching the finding of incidental retroperitoneal and pelvic lymphadenopathy, it is important to include a broad differential and also understand the anatomic distribution and drainage of the pelvic lymphatics. The external iliac lymph nodes receive lymphatic flow from the legs via the inguinal nodes.

It is unclear why the patient developed asymmetric vulvar lymphedema as the pelvic lymph nodes were enlarged bilaterally. It does not appear that the vulvar swelling was directly related to the joint wear and debris as the histology was not consistent with the histology from the biopsy and subsequent retroperitoneal lymphadenectomy specimens. It is postulated that inadequate drainage of the vulva was secondary to the enlargement of the pelvic lymph nodes with poor drainage that was functionally worse on the right than the left. The presence of vulvar lymphedema, therefore, was thought to be due to poor drainage through groin channels as the inguinal lymph nodes were not enlarged on exam or imaging.

It is also unlikely that the patient's vulvar edema was related to other primary vulvar disease processes (lichen simplex chronicus, lichen sclerosis, lichen planus, atopic dermatitis, etc.) as the histopathology was not consistent with these vulvar lesions and a unilateral/asymmetric presentation would be unusual in any of these disease processes.

The differential for pelvic lymphadenopathy is very broad, and includes both benign and malignant etiologies. Aside from nodal metastases from an underlying malignancy (transitional cell carcinoma of the bladder, renal cell carcinoma, or gynecologic malignancies), the differential includes several disease processes such as autoimmune lymphoproliferative disorders, granulomatous disease, sporadic lymphangioleiomyomatosis, lymphoma, leukemia, retroperitoneal fibrosis, several infectious etiologies (toxoplasmosis, lyme disease, tuberculosis, CMV and HIV) and several travel-related infections (coccidiomycosis, histoplasmosis, African trypanosomiasis, Chagas disease and Typhoid fever).

Joint wear debris appears to be a rare cause of lymphadenopathy, but one that is important to be aware of as total knee arthroplasty rates continue to increase. The number of primary total knee replacements has doubled from 1991 to 2010 and is expected to increase by approximately 673% from 2005 to 2030 (Cram et al., 2012; Kurtz et al., 2007).

It has been well-documented that joint arthroplasties cause a significant local tissue inflammatory response. Most articular prostheses contain a metallic core composed of titanium, cobalt-chromium alloys,

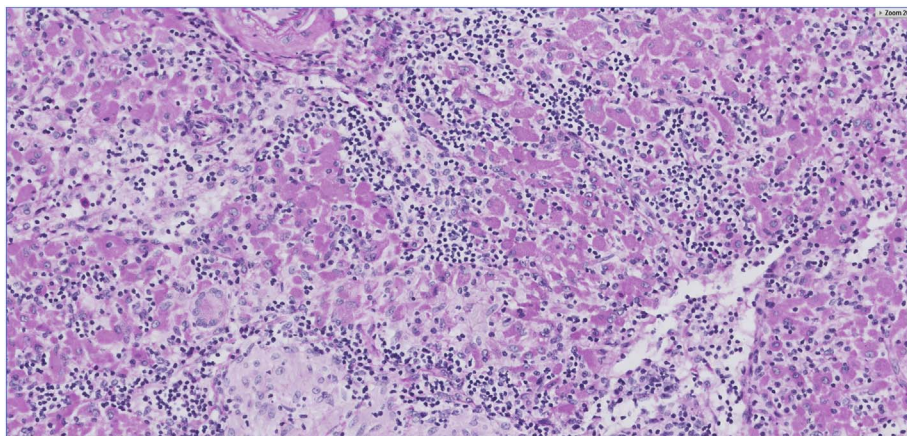


Fig. 3. PAS stain of lymph node.

and stainless steel as well as an articular surface composed of polymeric compounds such as polyethylene. Both the metallic and polyethylene particles have been shown to cause a histiocytic inflammatory response (Albores-Saavedra et al., 1994; Gray et al., 1989; O'Connell and Rosenberg, 1993).

The concept of “particle disease” was first introduced by Dr. William Harris in 1994 and stressed that the host inflammatory response was a reaction to micro particles produced by the prosthesis itself (Harris, 1994). Over time with prosthetic wear and generation of more particles this peri-prosthetic local inflammatory response can lead to osteolysis with aseptic loosening of the prosthesis (Willert and Semlitsch, 1977). While the joint wear of a prosthesis may only be in the order of tenths of millimeters, this wear produces a significant number of particles in the order of hundreds of trillions. In addition, an interval change in particle size of 0–1 μm can change the final number of particles by five orders of magnitude (Gallo et al., 2012). These wear particles have been found in the surrounding tissues of joint prostheses (Rae, 1986). In the presence of larger particles the inflammatory response generates monocytes and fibroblasts which create a granulomatous reaction surrounding the foreign particle (Anderson et al., 2008). This granulomatous reaction was evident on histopathology of this particular case.

These particles have been described to migrate to regional lymph nodes and tissues (Langkamer et al., 1992). Bae et al. reported a case of enlarged inguinal lymph nodes approximately fifteen years after total bilateral knee replacements. The histopathology demonstrated foreign body granulomas with abundant foreign body giant cells and sheets of sinus histiocytes, similar to the case described in this publication (Bae et al., 1996). There are several other reports of consistent histopathology with sinus histiocytosis of lymph nodes distant from the site of prostheses (Albores-Saavedra et al., 1994; Gray et al., 1989; O'Connell and Rosenberg, 1993). A small case series performed by Baslé et al. demonstrated nine cases of histiocytosis in regional lymph nodes with the presence of both metallic and polyethylene particles (Baslé et al., 1996).

Another case reported in the rheumatologic literature of lymphadenopathy approximately 15 years after bilateral knee replacement causing a granulomatous reaction with sheets of sinus histiocytes and multinucleate giant cells (Bae et al., 1996).

Reports of reactive lymphadenopathy caused by wear and debris from total joint replacement is limited in the gynecologic literature, but is an important etiology to consider in the differential. Uterine lymph flow drains along the round ligament and subsequently drains into the superficial inguinal lymph nodes. Due to various anastomoses it is possible for uterine and cervical cancer to spread to the superficial inguinal lymph nodes, as well as to the external iliac lymph nodes (Rock and Jone, 2003). The external iliac lymph nodes are a common lymphatic system for both the gynecologic organs as well as the lower extremities. Therefore, wear and debris of total joint replacements is important for Gynecologists and Gynecologic Oncologists to include in the differential of retroperitoneal lymphadenopathy.

Another important consideration during the evaluation of retroperitoneal lymphadenopathy is the removal of only representative lymph nodes. During this surgery two representative lymph nodes were removed on the right and one representative lymph node on the left. After the frozen section was confirmed to be benign, no further lymphadenectomy was performed. By obtaining only representative lymph nodes it is possible to limit the significant associated morbidity of full pelvic lymphadenectomy as well as to avoid further disrupting an already limited lymphatic drainage system.

Preliminary treatment strategies have focused on attenuating the local inflammatory response, specifically by deactivation of various pro-inflammatory cells such as macrophages (Valledor et al., 2010).

Treatment options focusing on the systemic response to particles and subsequent development of lymphadenopathy, however, are limited and currently there is no recommended treatment. There is some data in the palliative literature to support management of lymphedema with both manual lymphatic drainage and complete decongestive therapy. While there are no studies that specifically address vulvar and pelvic/retroperitoneal lymphadenopathy this would be a reasonable consideration when it comes to treatment options. Similar to the limited treatment options, there are currently no recommendations regarding monitoring of lymphadenopathy caused by joint arthroplasty.

4. Summary/conclusion

Joint prostheses are not biologically inert materials. A local inflammatory can occur with an aseptic loosening of the joint prosthesis or polyethylene wear and lead to the need for revision. These particles can travel to regional lymph nodes and cause lymphadenopathy, and, in our case, lymphedema of dependent portions of the body. It is unclear what detrimental effects remote migration of these foreign particles to regional lymph nodes might cause. We describe a case referred to Gynecology and Gynecologic Oncology of a woman with bilateral knee replacements presenting with vulvar lymphedema and pelvic lymphadenopathy due to joint wear debris. It is important, therefore, for Gynecologists, among other specialists, to consider this etiology of regional lymphadenopathy in their differential diagnosis.

Conflicts of interest

The authors have no conflicts of interest to disclose.

References

- Albores-Saavedra, J., Vuitch, F., Delgado, R., Wiley, E., Hagler, H., 1994. Sinus histiocytosis of pelvic lymph nodes after hip replacement. *Am. J. Surg. Pathol.* 18, 83–90.
- Anderson, J.M., Rodriguez, A., Chang, D.T., 2008. Foreign body reaction to biomaterials. *Semin. Immunol.* 20, 86–100.
- Bae, S.C., Park, C.K., Jun, J.B., Kim, S.Y., Bae, D.K., 1996. Multiple lymphadenopathy induced by wear debris after total knee replacement. *Scand. J. Rheumatol.* 25, 388–390.
- Baslé, M.F., Bertrand, G., Guyetant, S., Chappard, D., Lesourd, M., 1996. Migration of metal and polyethylene particles from articular prostheses may generate lymphadenopathy with histiocytosis. *J. Biomed. Mater. Res.* 30, 157–164.
- Cram, P., Lu, X., Kates, S.L., Singh, J.A., Li, Y., Wolf, B.R., 2012. Total knee arthroplasty volume, utilization and outcomes among medicare beneficiaries, 1991–2010. *J. Am. Med. Assoc.* 308, 1227–1236 (Sept.).
- Gallo, J., Slouf, M., Goodman, S.B., 2012. The relationship of polyethylene wear to particle size, distribution and number: a possible factor explaining the risk of osteolysis after hip arthroplasty. *J. Biomed. Mater. Res B Appl. Biomater.* 94, 171–177.
- Gray, M.H., Talbert, M.L., Talbert, W.M., Bausal, M., Hsu, A., 1989. Changes seen in lymph nodes draining sites of large joint prosthesis. *Am. J. Surg. Pathol.* 13, 1050–1056.
- Harris, W.H., 1994. Osteolysis and particle disease in hip replacement. A review. *Acta Orthop. Scand.* 65, 113–123.
- Kurtz, S., Ong, K., Lau, E., Mowat, F., Halpern, M., Apr 2007. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J. Bone Joint Surg. Am.* 89 (4), L780–5.
- Langkamer, V., Case, C., Heap, P., 1992. Systemic distribution of wear debris after hip replacement. A cause for concern? *J. Bone Jt. Surg.* 74B, 831–839.
- O'Connell, J.X., Rosenberg, A., 1993. Histiocytic lymphadenitis with a large joint prosthesis. *J. Clin. Pathol.* 99, 314–316.
- Rae, T., 1986. The biological response to titanium and titanium-aluminum-vanadium particles. *Biomaterials* 7, 30–36.
- Rock, J.A., Jone, H.W., 2003. *Te Linde's Operative Gynecology*, 9th ed. Lippincott, Philadelphia.
- Valledor, A.F., Comalada, M., Santamaria-Babi, L.F., Lloberas, J.A., Celada, A., 2010. Macrophage proinflammatory activation and deactivation: a question of balance. *Adv. Immunol.* 108, 1–20.
- Willert, H.G., Semlitsch, M., 1977. Reactions of the articular capsule to wear products of artificial joint prostheses. *J. Biomed. Mater. Res.* 11, 157–164.