

Particle Disease on Fluoride-18 (NaF) PET/CT imaging

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ABSTRACT

Particle disease is a loss of bone that commonly occurs about five years after arthroplasty. The cause is secondary to microabrasive wear and shedding of any portion of the prosthesis, and the microscopic foreign bodies activate inflammation which can lead to pain. This report describes the imaging findings of an 80-year-old female with particle disease detected with 18F-fluoride PET/CT.

CASE REPORT

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An 80-year-old female had increasing back pain. Her past medical history is significant for stage IC carcinoma of the left breast (with no known recurrence), endometrial cancer status post total abdominal hysterectomy-bilateral salpingo-oophorectomy, lumbar facet arthropathy, sacroilitis, spinal stenosis and bilateral total hip arthroplasty. The pain was most severe in the left buttock, left anterior groin region, and radiated down the left leg laterally down to the knee. However, she recalled no inciting event. On physical exam, she had no signs of neuromuscular damage, but flexing the lumbar region or the left hip can reproduce the pain described above.

The lower back pain and radicular pain down the left leg can be attributed to her chronic arthropathy and stenosis. However cause of the buttock, lateral leg, and the left groin pain remained unclear. The primary team considered disc herniation or hip flexor strain as possible causes for this pain. Nevertheless, a computed tomographic (CT) scan without intravenous contrast of the pelvis was performed (Fig 1). Bilateral hybrid total hip arthroplasties with cemented femoral components all appeared intact with no significant lucency immediately around the hardware. Aseptic loosening is less likely the etiology of the patient's pain. However, at the left acetabular roof, there is an approximately 2.8 cm area of vertically extending lucency of uncertain etiology.

To characterize this lucency, an MRI was considered but the patient had a pacemaker. With a differential diagnosis

including infection, metastasis, and non-infectious etiology, a three phase bone scintigraphy of the whole body was performed with technetium 99m MDP (Fig 2-3). There was increased activity in the left acetabulum extending vertically into the iliac wing, corresponding to the lucency identified on CT scan. Normal flow and blood pool made infection quite unlikely (Fig 3). Metastasis is also unlikely given the size of the lytic lesion on CT in addition to the normal flow and blood pool. Hence, the diagnosis was thought to be most likely particle disease.

However, given the history of breast and endometrial cancer and the numerous areas of spine uptake, an 18F-Fluoride (NaF) PET/CT (Fig 4-5) was performed for better discrimination of metastases, which fortunately was negative. The spine uptake was confirmed to be facet arthropathy. We provide the first case of particle disease seen on 18F-Fluoride PET/CT and whole body bone scan (Fig 4).

DISCUSSION

Differential diagnosis for a left hip lytic CT finding include metastasis, infection, or non-infectious etiology. From observing the MDP and fluoride bone scan, the increased uptake in the lytic area means there is osteoblastic activity, which is present in metastasis, infection, or inflammatory conditions. However, infection and metastasis can be ruled out because in the 3-phase bone scan, there is no hyperemia during

the blood flow or pool phase. Furthermore, metastasis does not usually appear as a large single lesion. Non-infectious etiologies include insufficiency stress fracture or particle disease. However, there is no resemblance of an H-shaped "Honda sign" in the pelvic region which would be typical of insufficiency stress fracture. Thus, the most likely diagnosis is particle disease in the roof of the left acetabulum and extending vertically into the iliac wing, with no evidence of aseptic loosening.

Almost 1 million total hip replacements are done every year and 30% of these patients need revisions within a decade of initial surgery [1]. Because of this large and increasing number of surgeries, nuclear physicians will encounter many different complications of hip arthroplasties, of which particle disease is a rather common entity in this field.

Particle disease or osteolysis is an inflammatory response to micron or submicron particles from the wear and tear of hip arthroplasty. It is estimated that the typical polyethylene cup-metallic ball interface generates several hundreds of thousands of polyethylene particles during each gait cycle. As mononuclear phagocyte cells attempt in vain to eliminate these foreign particles by phagocytosis, they release numerous mediators and cytokines including Receptor Activator for Nuclear Factor κ B Ligand (RANKL). This key protein molecule causes an increase in osteoclasts activity eventually resulting in the formation of osteolytic granulomas that characterize particle disease [1, 2].

Not every prosthetic develops particle disease. A study on different prosthetics (metal-on-polyethylene, ceramic-on-ceramic, ceramic-on-polyethylene) causing particle disease found no statistically significant difference between all three. Furthermore, particle disease may be completely asymptomatic making it very difficult to detect, if there is no reason to order imaging [3]. In addition, physicians have noticed different rates of osteolysis in patients with the same prosthesis and wear rate. There may be other factors including hypersensitivity to prosthetic materials or polymorphism of genes [4]. Once it manifests within the 1 to 5 years after implantation, it relentlessly leads to aseptic loosening or fractures [5]. The inflammatory response from foreign body fragments causes up to 50% of hip implantations to develop loosening [6]. Therefore, imaging may become an important step to detect early evidence of its presence.

Cross-sectional imaging of osteolysis can help map bone loss for revision surgery. On CT, osteolysis is characterized by well-defined lobulated lucencies devoid of osseous trabeculae. They are continuous with the prosthesis and have a typical attenuation of about 30 HU. On MRI, there is low T1 signal with intermediate to increased T2 signal [7, 8]. Depending on the amount of bone loss, acetabular roof may require bone graft with mesh support or the patient may simply need a cementless cup [2].

Also known as cement disease, aggressive granulomatosis, and osteolysis, particle disease should not be confused with aseptic loosening [2, 4, 7]. Aseptic loosening is diagnosed only when there is migration of any component of the

prosthesis, fracture in the cement mantle, or osteolysis surrounding the majority of the cement [7, 8]. If a joint arthrography was done, there would be filling of areas of periprosthetic hyperlucency due to communication with the joint itself [8].

Infection must be differentiated from aseptic loosening because both clinical presentations, namely pain, and histopathologic changes are remarkably similar. Nonspecific markers such as ESR or CRP are elevated in both cases. Joint aspirations have variable success due to large numbers of false positive and false negative results [6]. Although infection accounts for only 1-3% of cases [6, 9, 10], the treatment is radically different from aseptic loosening. For aseptic loosening, the patient must have a single-stage revision arthroplasty which requires one hospital admission. On the other hand, infection requires excisional arthroplasty to remove the entire prosthesis followed by revision arthroplasty. Multiple-day admissions are therefore necessary [6]. On CT, infection is characterized by ill-defined margin with periostitis, indicated by periosteal new bone. There may be other soft tissue markers such as joint distention, or fluid in the soft tissues [7]. In MRI, some of the signs of infection include hypointense bone marrow on T1 and hyperintense hallow surrounding the cortex on T2 weighted images [11]. In a review article involving 209 patients, Zoccali found that FDG-PET has a sensitivity of 82% with a specificity of 87% for infected prostheses [12]. They recommend using the following method to differentiate infection from aseptic loosening in FDG-PET: An uptake in the bone-prosthesis interface and in periprosthetic soft tissue is indicative of infection. An uptake in the femoral neck and cup interface without compromising periprosthetic soft tissue is indicative of aseptic loosening [13]. However, FDG-PET is still inferior to WBC scintigraphy, and if physicians want to rule out infection, WBC scintigraphy would be the first choice and gold standard, because it can localize neutrophil activity, which is not present in aseptic loosening [11]. When combined with a complementary bone marrow imaging using Tc-99m sulfur colloid, diagnosis of osteomyelitis can be 90% accurate [14]. Thus, WBC-marrow imaging can help rule out infection in prosthetic joints, fractures, or neuropathic joints especially in the cases of bizarre WBC activity.

In our case, we used 18F-Fluoride for PET/CT since bone metastases occur in up to 90% of breast or prostate cancer patients and is thought to be more sensitive and specific than planar bone scan [15]. This radiotracer has highly specific bone uptake, rapid clearance from the blood pool because of minimal protein binding, and dosimetry similar to that of Tc-99m MDP. These characteristics make 18F-Fluoride PET/CT superior over the planar imaging or SPECT with Tc-99m MDP for localizing and characterizing both malignant and benign bone lesions [15, 16]. Furthermore, imaging can be performed in less than 1 hour after 18F-Fluoride administration, which makes 18F-Fluoride PET a faster study and more convenient to the patient compared to Tc-99m MDP scintigraphy (3-4 hours). Thus, 18F-Fluoride PET can potentially replace Tc-99m MDP for many clinical indications except for in cases of acute infection [16]. Although no study has proven that 18F-Fluoride PET is useful in infection, we suspect the findings

would be similar to the Tc-99m MDP delayed image. 18F-Fluoride PET does not have flow or blood pool images like a traditional bone scan would. Furthermore, 18F-Fluoride is not known to accumulate in soft tissue. Quantitative 18F-Fluoride PET may prove useful for the assessment of metabolic bone disorders such as renal osteodystrophy, osteoporosis, or Paget's disease [16]. Because cancers have variable rates of glucose metabolism, a cocktail of 18F-Fluoride and 18F-FDG PET/CT has been used in a study that proved its feasibility for cancer detection [17]. The cocktail has the added advantage of producing skeletal landmarks which provide better anatomical localization. The 18F-Fluoride adds sensitivity for osteoblastic lesions while the 18F-FDG adds better detection of hypermetabolic, osteolytic lesions.

Despite the common presence of particle disease and its subsequent aseptic loosening, this disease is rarely mentioned in the radiographic or nuclear medicine journals. This may be because early particle disease is asymptomatic resulting in fewer studies. However, as the number of prosthetics increase especially for the aging population, it behooves imaging physicians to become more familiar with particle disease.

TEACHING POINT

Particle disease, an asymptomatic illness that will lead to aseptic loosening, can be differentiated from metastasis, infection, or non-infectious etiology by 3-phase bone scan and 18F-Fluoride PET/CT. On F-18 PET/CT, particle disease shows up as a well-defined, intense uptake surrounding an erosive lesion of bone with the lesion tracking along the screw. As the prevalence increases, proper recognition by CT, bone scintigraphy, or PET will dictate management of prosthetics.

REFERENCES

- Gallo J, Kamínek P, Tichá V, Riháková P, Ditmar R (2002) Particle disease. A comprehensive theory of periprosthetic osteolysis: a review. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub* 146(2):21-28. PMID: 12572890
- Cahir JG, Toms AP, Marshall TJ, Wimhurst J, Nolan J (2007) CT and MRI of hip arthroplasty. *Clinical Radiology* 62(12):1163-1171. PMID: 17981163
- Cooper HJ, Ranawat AS, Koob TB, Foo LF, Potter HG, Ranawat CS (2010) MRI in the detection of early particle disease in patients following total hip arthroplasty: a prospective study. *J Bone Joint Surg Br* 92-B(SUPP_1):88. http://proceedings.jbjs.org.uk/cgi/reprint/92-B/SUPP_1/88.pdf
- Gallo J, Raska M, Mrázek F, Petrek M (2008) Bone remodeling, particle disease and individual susceptibility to periprosthetic osteolysis. *Physiol Res* 57(3):339-349. PMID: 17465692
- Watt I, Boldrik S, Langelaan E. Hip - Total Hip Arthroplasty. Normal and abnormal imaging findings. *The Radiology Assistant*. (2006) <http://www.radiologyassistant.nl/en/431c8258e7ac3>
- Love C, Tomas MB, Marwin SE, Pugliese PV, Palestro CJ (2001) Role of Nuclear Medicine in Diagnosis of the Infected Joint Replacement. *Radiographics* 21(5):1229 - 1238. PMID: 11553828
- Agarwal S (2004) Osteolysis--basic science, incidence and diagnosis. *Current Orthopaedics* 18(3):220-231. doi:10.1016/j.cuor.2004.03.002
- White LM, Kim JK, Mehta M, Merchant N, Schweitzer ME, Morrison WB, Hutchison CR, Gross AE (2000) Complications of Total Hip Arthroplasty: MR Imaging-Initial Experience. *Radiology* 215(1):254 -262. PMID: 10751496
- Zhuang H, Duarte PS, Pourdehnad M, Maes A, Van Acker F, Shnier D, Garino JP, Fitzgerald RH, Alavi A (2001) The promising role of 18F-FDG PET in detecting infected lower limb prosthesis implants. *J. Nucl. Med* 42(1):44-48. PMID: 11197979
- Math KR, Zaidi SF, Petchprapa C, Harwin SF Imaging of total knee arthroplasty, in: *Seminars in Musculoskeletal Radiology*, 2006: p. 47. PMID: 16514580
- Love C, Marwin SE, Tomas MB, Krauss ES, Tronco GG, Bhargava KK, Nichols KJ, Palestro CJ (2004) Diagnosing Infection in the Failed Joint Replacement: A Comparison of Coincidence Detection 18F-FDG and 111In-Labeled Leukocyte/99mTc-Sulfur Colloid Marrow Imaging. *J Nucl Med* 45(11):1864-1871. PMID: 15534056
- Zoccali C, Teori G, Salducca N (2008) The role of FDG-PET in distinguishing between septic and aseptic loosening in hip prosthesis: a review of literature. *International Orthopaedics (SICO)* 33(1):1-5. PMID: 18594820
- Mumme T, Reinartz P, Alfer J, Müller-Rath R, Buell U, Wirtz DC (2005) Diagnostic values of positron emission tomography versus triple-phase bone scan in hip arthroplasty loosening. *Arch Orthop Trauma Surg* 125(5):322-329. PMID: 15821896
- Palestro CJ, Love C, Tronco GG, Tomas MB, Rini JN (2006) Combined Labeled Leukocyte and Technetium 99m Sulfur Colloid Bone Marrow Imaging for Diagnosing Musculoskeletal Infection. *Radiographics* 26(3):859 -870
- Langsteger W, Heinisch M, Fogelman I (2006) The role of fluorodeoxyglucose, 18F-dihydroxyphenylalanine, 18F-choline, and 18F-fluoride in bone imaging with emphasis on prostate and breast. *Semin Nucl Med* 36(1):73-92. PMID: 16356797

16. Grant FD, Fahey FH, Packard AB, Davis RT, Alavi A, Treves ST (2008) Skeletal PET with 18F-Fluoride: Applying New Technology to an Old Tracer. *J Nucl Med* 49(1):68-78. PMID: 18077529

17. Iagaru A, Mittra E, Yaghoubi SS, Dick DW, Quon A, Goris ML, Gambhir SS (2009) Novel Strategy for a Cocktail 18F-Fluoride and 18F-FDG PET/CT Scan for Evaluation of Malignancy: Results of the Pilot-Phase Study. *J Nucl Med* 50(4):501-505. PMID: 19289439

FIGURES

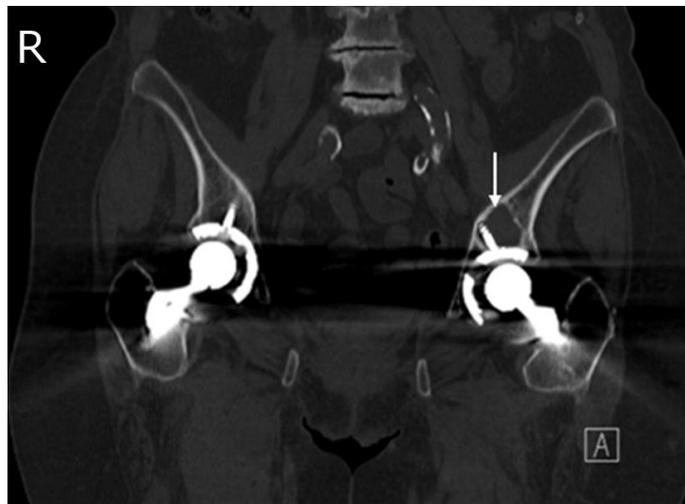


Figure 1 (left): An 80-year-old female with particle disease. Prosthetic hardware appears intact bilaterally on this coronal CT. A well-defined lucency tracking superiorly from the left acetabulum along the vertical aspect of the left iliac bone is noted (arrow). On another slice, this was seen to extend superiorly up well into the left iliac wing. Particle disease has a tendency to track along the screw. There is no lucency in the right iliac bone. [2.0 mm coronal CT reconstruction acquired at 140 kVp and 162 mAs on a GE 16-slice scanner, no contrast]

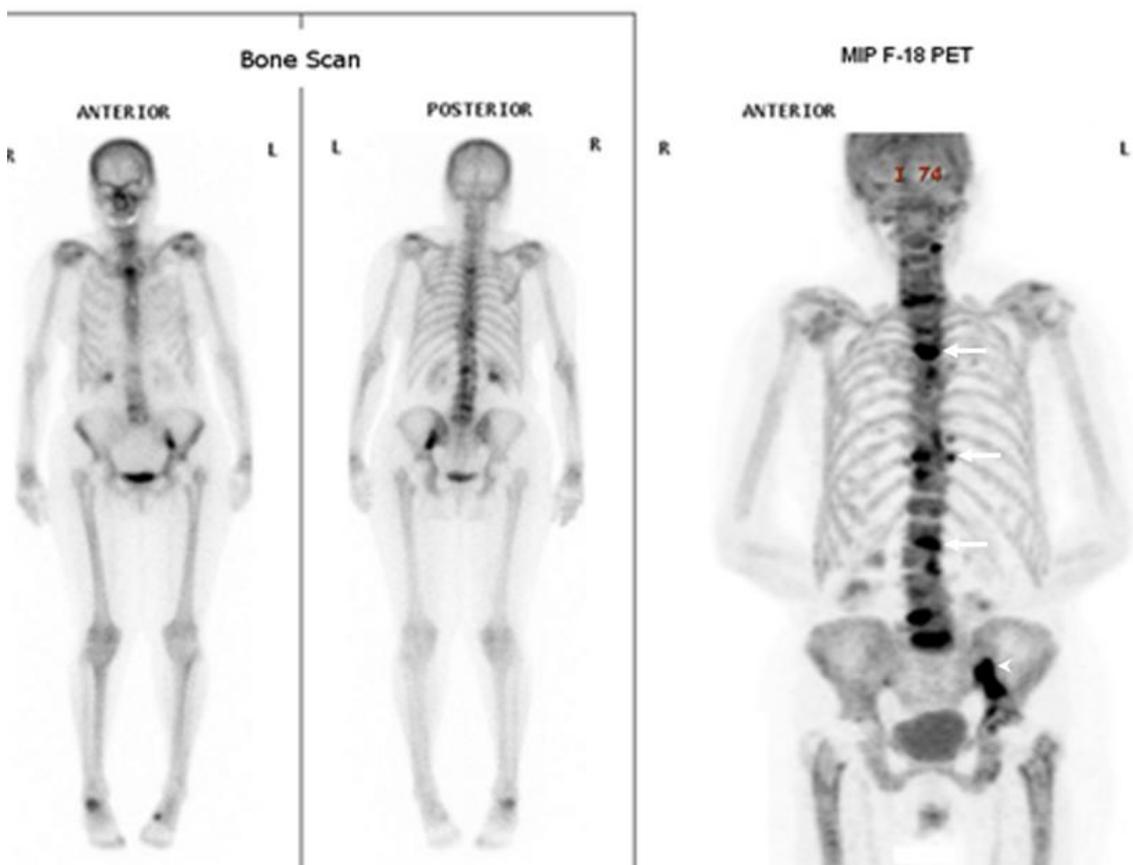


Figure 2: An 80-year-old female with particle disease. The Tc-99m MDP scan above reveals increased activity in the left iliac bone as does the coronal presentation of the MIP F-18 PET (arrowhead). There is no abnormal activity in the right iliac bone, and no abnormal activity inside the acetabular joints bilaterally. There is decreased activity in the femurs consistent with the total hip arthroplasties. Multiple foci of increased activity throughout the spine at the endplates and osteophytes are compatible with facet arthropathy and degenerative changes (arrows). Because of the multiple foci of activity in the spine, metastatic disease could not be ruled out and thus an F-18 PET/CT was justified. The F-18 PET/CT confirmed that the spine uptake was secondary to diffuse arthropathic disease. [Hawkeye Bone Scintigraphy with 20 mCi Technetium-99m MDP injected in left antecubital. Coronal plane. Bone scan was acquired 3 hours after injection with a 25 minute scan time.]

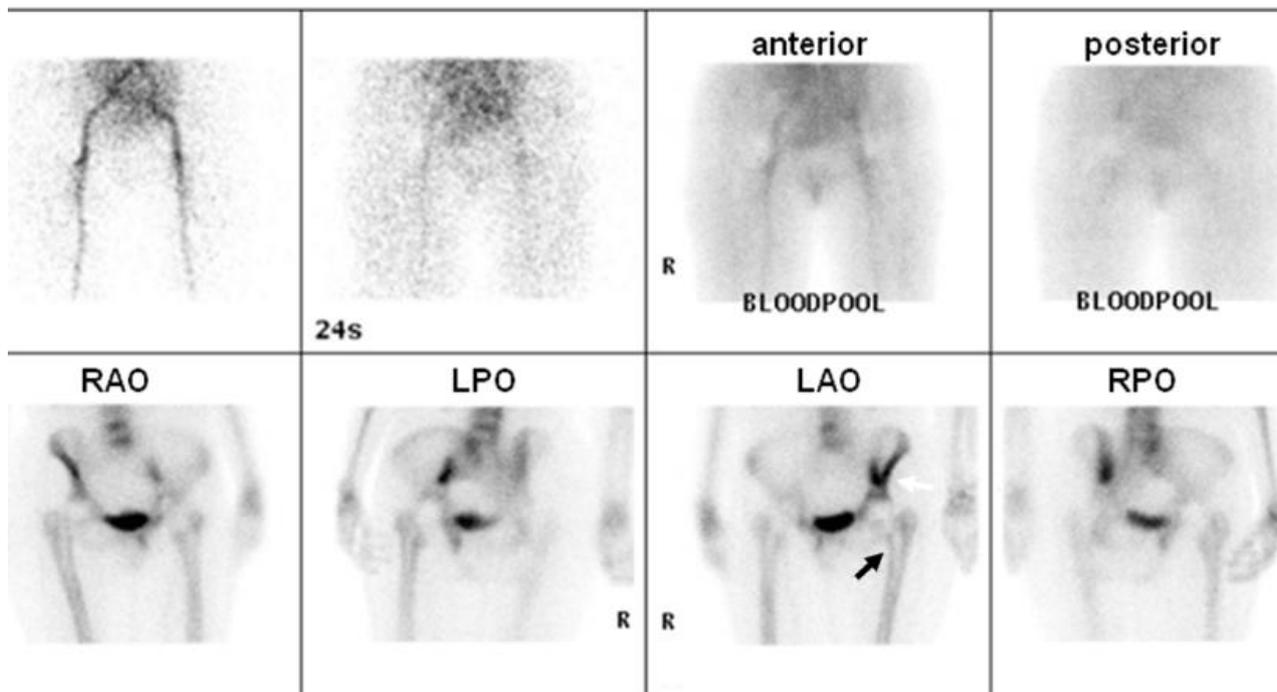


Figure 3: An 80-year-old female with particle disease. Bone scintigraphy images show normal flow and normal blood pool which essentially rules out active osteomyelitis. Increased activity seen above the left acetabulum extending superiorly toward the iliac wing (white arrow) which is consistent with particle disease. There is no activity around the prosthetic device (black arrow). [Hawkeye Bone Scintigraphy with 20 mCi Technetium-99m MDP injected in left antecubital, coronal plane. The blood flow images were acquired immediately after injection. Blood pool was acquired 2 minutes after injection. The spot films are done 3.5 hours after injection, each scanned for 5 minutes.]

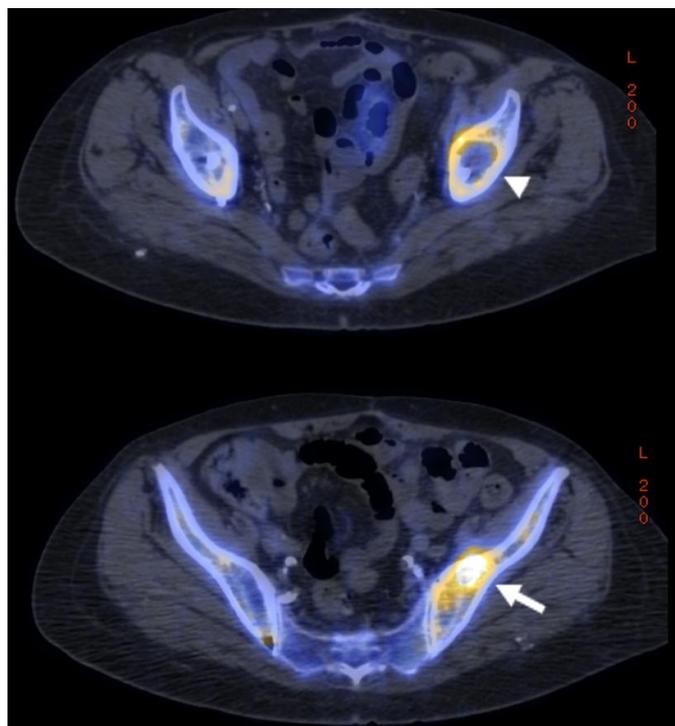


Figure 4: An 80-year-old female with particle disease. These axial images result from fusion of colorized F-18 PET with the axial CT images. (a) PET/CT shows a lucency (arrowhead) superior to the left acetabulum with peripheral uptake of F-18. (b) Moving superiorly, the particle disease extends well above the acetabular joint and is quite intense (arrow). [Helical CT set at 120 kVp and auto mAs on a 16-slice scanner, axial plane, no IV contrast. Acquired for 35 minutes after waiting 1 hour post IV injection of 15.5 mCi F-18 sodium fluoride via a right antecubital vein]

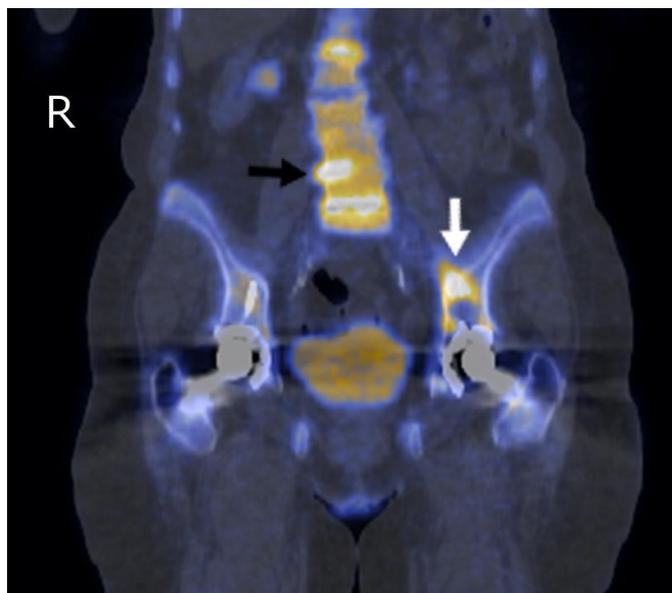


Figure 5: An 80-year-old female with particle disease. This coronal view of a fusion 18F-Fluoride PET/CT demonstrates the particle disease superior (white arrow) to the left acetabular joint. No activity is seen in the erosive lesion in which the screw of the prosthetic lies. Infection might appear similar on PET/CT but was better ruled out with the 3-phase bone scan. Arthropathic changes and uptake (black arrow) are noted in the spine. We noted that activity is only localized to the joint spaces which is uncharacteristic of metastases. [Helical CT set at 120 kVp and auto mAs on a 16-slice scanner, axial plane, no IV contrast. Acquired for 35 minutes after waiting 1 hour post IV injection of 15.5 mCi F-18 sodium fluoride via a right antecubital vein]

	CT	MDP Bone scan	NaF PET/CT	FDG PET/CT
Infection	<ul style="list-style-type: none"> • Periosteal new bone • Marrow density increased relative to healthy marrow • Inflammatory changes in adjacent soft tissue 	<ul style="list-style-type: none"> • Hyperemia in the blood pool phase • Intense focal uptake in the delayed phase 	<ul style="list-style-type: none"> • May have increased uptake in chronic states due to increased bone turnover • Unexpected distribution 	<ul style="list-style-type: none"> • Increased uptake of lesion • Abnormal uptake along prosthesis bone interface in middle portion of shaft • Uptake in the surrounding soft tissue
Metastasis	<ul style="list-style-type: none"> • Soft tissue attenuation • Low attenuation in necrotic bone • High attenuation in mineralized matrix • Mixed lytic and sclerotic lesions 	<ul style="list-style-type: none"> • Multiple lesions of varying size and shape • Irregular distribution throughout the axial skeleton • Increased blood flow, blood pool, delayed images 	<ul style="list-style-type: none"> • Multiple lesions of varying size and shape • Increased accumulation around primary or secondary bone malignancy 	<ul style="list-style-type: none"> • Multiple lesions of varying size and shape • Irregular distribution throughout the axial skeleton
Degeneration	<ul style="list-style-type: none"> • Subchondral sclerosis, joint space narrowing, osteophytosis 	<ul style="list-style-type: none"> • Uptake restricted to joint spaces • Low uptake in blood flow or blood pool 	<ul style="list-style-type: none"> • Increased uptake around the inflamed joint 	<ul style="list-style-type: none"> • Uptake restricted to joint spaces
Insufficiency fracture of sacrum	<ul style="list-style-type: none"> • “Honda” sign • Linear fracture line with cortical disruption • Bone marrow edema 	<ul style="list-style-type: none"> • Butterfly or “Honda sign” asymmetric incomplete pattern of sacral uptake 	<ul style="list-style-type: none"> • “Honda sign” 	<ul style="list-style-type: none"> • “Honda sign”
Particle Disease	<ul style="list-style-type: none"> • Erosive lesion. Loss of bone matrix 	<ul style="list-style-type: none"> • Uptake localized near the prosthetic joint 	<ul style="list-style-type: none"> • Activity around the borders of an osteolytic lesion • Probably no activity within the osteolytic lesion. • Lucency will track along the screw. 	<ul style="list-style-type: none"> • Nonspecific activity around the neck portion of prosthesis

Table 1. Differential diagnosis table of single lucent bone lesion around a hip prosthesis

Etiology	Breakdown of prosthetic releasing microscopic foreign bodies leading to inflammation and osteolysis.
Incidence	0-19% for cemented prosthesis. 0-22% for cementless prosthetics. Of 1 million total hip arthroplasties, 30% of cases need revisions.
Gender ratio	None
Age predilection	None
Risk factors	<ul style="list-style-type: none"> • Hypersensitivity to prosthetic material • Genetic • Use of screw for fixation of acetabular cup
Treatment	Hardware revision
Prognosis	Poor – particle disease will lead to aseptic loosening or fractures

Table 2. Summary table for particle disease

ABBREVIATIONS

CT = Computed tomography
 PET = Positron Emission Tomography
 NaF = Sodium Fluoride

KEYWORDS

particle disease; osteolysis; aseptic loosening; arthroplasty; 18F-Fluoride PET/CT

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