ELSEVIER

Seminars in
NUCLEAR
MEDICINE

CASE REPORT

Recurrence of Lymphoma Presenting as Asymmetrically Increased Testicular Activity on FDG-PET/CT

Phillip H. Kuo, MD, PhD,* Dennis L. Cooper, MD,† and David W. Cheng, MD, PhD*

A 65-year-old man with a history of recurrent lymphoma status-post matched sibling donor transplant presented with swelling of the right testicle. Four years earlier, he had presented with right leg swelling, night sweats, and pelvic pain. Computed tomography (CT) scan showed bulky right-sided pelvic adenopathy. Biopsy showed diffuse high-grade B-cell lymphoma. The remainder of the staging evaluation, including bone marrow biopsy, magnetic resonance imaging (MRI) of the brain, CT scans of the chest, abdomen and pelvis, and gallium scan, showed no evidence of disease outside the pelvis.

Chemotherapy and radiation achieved an initial complete response with resolution of the pelvic adenopathy, but the patient relapsed in the right maxillary region less than a year later. He then underwent intensive chemotherapy with autologous stem cell rescue and remained free of disease for nearly 2 years. However, he developed a mass over his left knee, and biopsy showed recurrent disease. Again, chemotherapy achieved a complete response. He then received a reduced-intensity matched sibling donor transplant from his sister.

Ten months after the transplant, he complained of swelling of the right testicle. Ultrasound showed a solid mass. A positron emission tomography (PET)/CT study showed very intense uptake of FDG in the right testicle and no other sites of abnormal activity (Figs. 1 and 2). He underwent right orchiectomy, and pathology confirmed malignant lymphoma (Burkitt's-like) with no evidence of spread outside the testicle.

Figure 1 Maximum intensity projection (MIP) image in the anterior view from a FDG-PET/CT scan showed asymmetrically increased activity in the right testicle and no other sites of abnormal FDG uptake.

Discussion

Most intravenous cytotoxic agents used in chemotherapy do not significantly cross the blood–brain and the blood–testis

*Department of Diagnostic Radiology, Yale University School of Medicine, New Haven, CT.
†Department of Medical Oncology, Yale University School of Medicine, New Haven, CT.
Address correspondence to Phillip H. Kuo, MD, PhD, Department of Diagnostic Radiology, Yale University School of Medicine, 333 Cedar Street, PO Box 20842, New Haven, CT 06520-8042. E-mail: phillip.kuo@yale.edu

0001-2998/06/$-see front matter
doi:10.1053/j.semnuclmed.2005.08.005

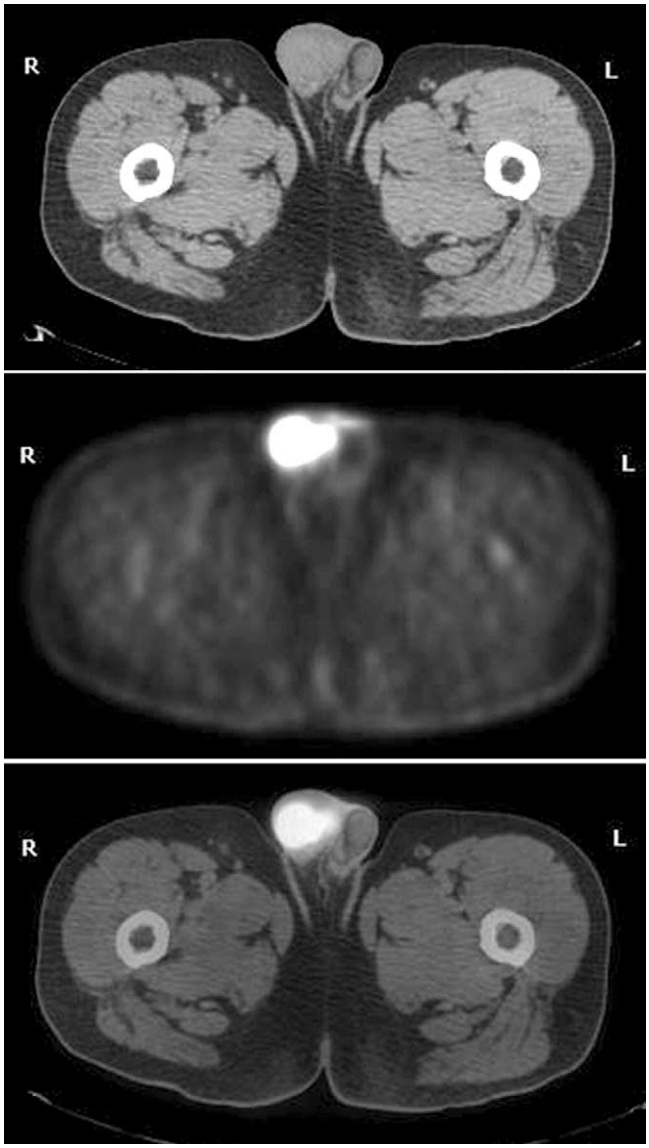

Figure 2 CT, PET, and fused PET/CT images (from top to bottom) demonstrated very intense uptake with a maximum standardized uptake value (SUVmax) of 17 in the right testicular mass.

barrier, resulting in possible tumor sanctuary sites in the central nervous system and testis.[1,2] The barrier has a physical component in the form of tight cellular junctions and a molecular component in the form of an efflux pump known as P-glycoprotein.[3,4] When there is a clinical suspicion for central nervous system involvement, treatment with intrathecal chemotherapy may be effective in preventing leptomeningeal recurrence, but there is no standard treatment that is known to reduce the possibility of parenchymal brain or testes spread.[5]

Growing evidence supports that successful allogeneic bone marrow transplant uses graft-versus-tumor (lymphoma) effect in which the immune cells from the transplant attack the disease.[6-9] In the body, however, there are immunologically privileged extramedullary sites at which the immune system is impaired, and these again include the central nervous system and testis.[10-17]

The physiologic uptake of FDG by the normal testis may complicate detection of disease.[18,19] Special attention is warranted for asymmetrical and intense activity in the testes, a potential site of disease recurrence after chemotherapy and transplant.

A search of the literature reveals few reports of asymmetric testicular activity on FDG-PET; therefore, many of the entities on this list of differential diagnoses are included on a logical basis rather than reports in the literature.

Differential for asymmetrical or increased testicular activity includes: (1) testicular germ cell tumor (seminoma and nonseminona)[20-22]; (2) primary testicular lymphoma[23]; (3) metastatic disease[24]; (4) unilateral orchiectomy with or without testicular prosthesis; (5) undescended testis[25,26]; (6) unilateral orchitis[27,28]; (7) testicular torsion[27,28]; (8) retractile testis[29]; (9) congenital monorchidism[30]; (10) testicular sarcoid[31]; (11) bladder hernia (mistaken as testicular activity)[32]; (12) unilateral hydrocele or varicocele; and (13) inguinoscrotal hernia.

References

1. Bart J, Groen HJ, van der Graaf WT, et al: An oncological view on the blood-testis barrier. Lancet Oncol 3:357-363, 2002
2. Begley DJ: Delivery of therapeutic agents to the central nervous system: The problems and the possibilities. Pharmacol Ther 104:29-45, 2004
3. Begley DJ: ABC transporters and the blood–brain barrier. Curr Pharm Des 10:1295-1312, 2004
4. Fromm MF: Importance of P-glycoprotein at blood-tissue barriers. Trends Pharmacol Sci 25:423-429, 2004
5. Rizzieri DA, Johnson JL, Niedzwiecki D, et al: Intensive chemotherapy with and without cranial radiation for Burkitt leukemia and lymphoma: Final results of Cancer and Leukemia Group B Study 9251. Cancer 100:1438-1448, 2004
6. van Besien KW, de Lima M, Giralt SA, et al: Management of lymphoma recurrence after allogeneic transplantation: The relevance of graft-versus-lymphoma effect. Bone Marrow Transplant 19:977-982, 1997
7. Bierman PJ, Sweetenham JW, Loberiza FR, et al: Syngeneic hematopoietic stem-cell transplantation for non-Hodgkin's lymphoma: A comparison with allogeneic and autologous transplantation. J Clin Oncol 21: 3744-3753, 2003
8. Jones RJ, Ambinder RF, Piantadosi S, et al: Evidence of a graft-versus-lymphoma effect associated with allogeneic bone marrow transplantation. Blood 77:649-653, 1991
9. Mandigers CM, Meijerink JP, Raemaekers JM, et al: Graft-versus-lymphoma effect of donor leucocyte infusion shown by real-time quantitative PCR analysis of t(14;18). Lancet 352:1522-1523, 1998
10. Choi SJ, Lee JH, Lee JH, et al: Treatment of relapsed acute myeloid leukemia after allogeneic bone marrow transplantation with chemotherapy followed by G-CSF-primed donor leukocyte infusion: A high incidence of isolated extramedullary relapse. Leukemia 18:1789-1797, 2004
11. Chong G, Byrnes G, Szer J, et al: Extramedullary relapse after allogeneic bone marrow transplantation for haematological malignancy. Bone Marrow Transplant 26:1011-1015, 2000
12. Lee KH, Lee JH, Kim S, et al: High frequency of extramedullary relapse of acute leukemia after allogeneic bone marrow transplantation. Bone Marrow Transplant 26:147-152, 2000
13. Au WY, Lie AK, Liang R, et al: Isolated extramedullary relapse of acute lymphoblastic leukaemia after allogeneic bone marrow transplantation. Bone Marrow Transplant 24:1137-1140, 1999
14. Forrest DL, Dalal BI, Naiman SC, et al: Testicular relapse of acute promyelocytic leukemia after allogeneic BMT. Bone Marrow Transplant 20:689-690, 1997

15. Tringali S, Vasta S, Scime R, et al: Testicular relapse of AML during chronic graft-versus-host disease induced by donor leukocyte infusion. Haematologica 81:339-342, 1996
16. Stewart PS, Buckner CD, Clift RA, et al: Allogeneic marrow grafting for acute leukemia: A follow-up of long-term survivors. Exp Hematol 7:509-518, 1979
17. Dai Z, Nasr IW, Reel M, et al: Impaired recall of CD8 memory T cells in immunologically privileged tissue. J Immunol 174:1165-1170, 2005
18. Kosuda S, Fisher S, Kison PV, et al: Uptake of 2-deoxy-2-[18F]fluoro-D-glucose in the normal testis: Retrospective PET study and animal experiment. Ann Nucl Med 11:195-199, 1997
19. Czernin J, Dahlbom M, Ratib O, et al: Atlas of PET/CT Imaging in Oncology. New York, Springer, 2004, pp 290–291
20. Kumar R, Zhuang H, Alavi A: PET in the management of urologic malignancies. Radiol Clin North Am 42:1141-1153, 2004
21. De Santis M, Pont J: The role of positron emission tomography in germ cell cancer. World J Urol 22:41-46, 2004
22. Hain SF, O'Doherty MJ, Timothy AR, et al: Fluorodeoxyglucose PET in the initial staging of germ cell tumours. Eur J Nucl Med 27:590-594, 2000
23. Lagrange JL, Ramaioli A, Theodore CH, et al: Non-Hodgkin's lymphoma of the testis: A retrospective study of 84 patients treated in the French anticancer centres. Ann Oncol 12:1313-1319, 2001
24. Weng LJ, Schoder H: Melanoma metastasis to the testis demonstrated with FDG PET/CT. Clin Nucl Med 29:811-812, 2004
25. Muttarak M, Peh WC, Chaiwun B: Malignant germ cell tumours of undescended testes: Imaging features with pathological correlation. Clin Radiol 59:198-204, 2004
26. Harris BH, Webb HW, Wilkinson AH Jr, et al: Protection of the solitary testis. J Pediatr Surg. 17:950-952, 1982
27. Wu HC, Sun SS, Kao A, et al: Comparison of radionuclide imaging and ultrasonography in the differentiation of acute testicular torsion and inflammatory testicular disease. Clin Nucl Med 27:490-493, 2002
28. Dogra V, Bhatt S: Acute painful scrotum. Radiol Clin North Am 42: 349-363, 2004
29. Fujii H, Yasuda S, Ide M, et al: Fluorine-18 fluorodeoxyglucose uptake in the retractile testis. Clin Nucl Med 24:323-325, 1999
30. Lamesch AJ: Monorchidism or unilateral anorchidism. Langenbecks Arch Chir 379:105-108, 1994
31. Czernin J, Dahlbom M, Ratib O, et al: Atlas of PET/CT Imaging in Oncology. New York, Springer, 2004, pp 308–309
32. Pirson AS, Krug B, Lacrosse M, et al: Bladder hernia simulating metastatic lesion on FDG PET study. Clin Nucl Med 29:767, 2004