

Gynecomastia with microcalcifications in an HIV infected Hemophilia A patient

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Section: Breast imaging

Case Type: Clinical Cases

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Patient: 24 years, male

Clinical History:

A 24-year-old hemophilic man, who had been a HIV-positive for the past 22 years, presented with a bilateral breast enlargement with the presence of microcalcifications.

Imaging Findings:

A 24-year-old hemophilic man presented to our hospital with bilateral breast enlargement that had developed gradually over the past six months. The patient denied of having any pain or nipple discharge. There was no family history of breast cancer. The patient was HIV seropositive since 1982 and he had exhibited an HIV-related thrombocytopenia with frequent subcutaneous hematomas in 1988 that was responded to with antiretroviral therapy, started in 1990. He is currently on HAARTT (stavudine, lamivudine, and efavirenz for three years) and the stage according to CDC is B2. He was coinfectd with HCV and had not responded to combined therapy with interferon plus ribavirin. He denied having used alcohol, recreational drugs, methadone or medications other than antiretroviral therapy. A physical examination was done, which revealed a slightly tendered bilateral breast enlargement.

Laboratory examination showed a CD4+ cell count of 432 cells/?l and a HIV-RNA of 42000 copies/ml.

Endocrinologic investigations including prolactin, thyroid-stimulating hormone (TSH), follicular-stimulating hormone (FSH), luteal hormone (LH), free testosterone (FT), estradiol, and FT3, FT4 revealed values within the normal ranges. The results of chest X-rays and blood and urine cultures for Mycobacterium tuberculosis and avium were found to be negative. Mammography revealed enlargement of both the breasts. The presence of a glandular tissue was demonstrated in a pattern similar to that seen in the heterogeneously dense female breast. At the upper outer quadrant of both the breasts, round and punctuate, well-circumscribed, high density, round calcifications were also seen. No other abnormal lesion was present. Breast ultrasonography revealed the presence of a normal-appearing glandular tissue. No other abnormal lesion was present. In both axillaries, well-circumscribed enlarged lymph nodes were demonstrated. An abdominal CT revealed diffuse fatty liver infiltration and spleen enlargement.

Ultrasonography of the testis showed the presence of a small calcified lesion with characteristic acoustic shadow in the lower part of the scrotal sac. In order to investigate breast enlargement and to assess the best choice in managing this in our patient, an MR mammography was then performed. MR mammography with fat saturation sequence revealed the presence of an enlarged glandular tissue, which could be easily differentiated from an adipose tissue.

Discussion:

Breast enlargement in the human immunodeficiency virus (HIV)-infected population was first described in 1987. Since then there has been an increasing number of reports in the medical literature, suggesting that breast enlargement could present as a long-term adverse side effect of highly active antiretroviral therapy (HAART). Today

breast enlargement in male HIV patients is not a rare clinical condition. The incidence of gynecomastia in HIV male patients treated with HAART was 0.8/100 patients/year, with a prevalence of 2.8% in those treated for >2 years. After the use of highly active antiretroviral therapy (HAART), breast enlargement is emerging as a new problem among HIV-positive male population. These patients frequently center around cosmetic problems and sometimes have the fear of developing a breast malignancy. An evaluation of this condition helps to distinguish between true gynecomastia, pseudoangiomatous stromal hyperplasia, lipomastia, opportunistic infections, and malignancy. The cases described in the medical literature suggest that most cases of breast enlargement in HIV-positive men are caused by gynecomastia or lipomastia. True gynecomastia (proliferation of ducts and peripheral stroma) may have a hormonal cause, or it may be secondary to the use of medications other than those in HAART (including three to four antiretroviral drugs belonging to the nucleoside and nonnucleoside reverse transcriptase inhibitor categories and protease inhibitors), drugs for the treatment of cardiovascular conditions and antiulcer drugs or recreational use of marijuana, or it may reflect an underlying medical condition such as liver disease, renal failure, and the presence of certain neoplasms. The pathogenesis of gynecomastia is unclear; PI (protease inhibitors) and NNRTI (nonnucleoside reverse transcriptase inhibitors) may have an oestrogen-like effect on breast tissue, or may induce an elevation of the oestrogen-androgen reaction, or the breast tissue response to hormones may have been altered. Hypogonadism, which occurs in HIV-positive men, may be partly responsible for the occurrence of gynecomastia, in the form of many testicular tumors. True gynecomastia is nearly always unilateral with focal findings. When bilateral, it is usually asymmetric. It can develop rapidly and the breasts may be tender. Pseudoangiomatous stromal hyperplasia (PASH) is a proliferative process that appears to have a hormonal cause. Lipomastia (increased amounts of adipose, but not ductal, in the breast) is one of the body-shape changes that occurs due to the fat maldistribution (lipodystrophy) syndrome, associated to some extent with HAART. While the actual mechanisms underlying this abnormality are clearly unknown, HIV-1 protease inhibitors may be the causal agents in many cases. However, the observations of lipodystrophy in patients who did not receive protease inhibitors suggest other possible mechanism; the mitochondrial toxicity in patients treated with nucleoside reverse transcriptase inhibitors was also indicated in the pathogenesis of lipodystrophy. In this syndrome, there is a wasting (lipoatrophy) of the peripheral body fat in the face, limbs and buttocks and a deposition of fat (lipohypertrophy) centrally in the abdomen, the breasts and the cervicodorsal fat pad. Typically lipomastia is presented as bilateral, with more-generalized enlargement than gynecomastia. Opportunistic infections that occur in the breasts depend largely on the geography and degree of immune depression. Generally, the most common infection is tuberculosis (TB). Nonpuerperal periductal mastitis (duct ectasia) can be the result of impaired immunity secondary to HIV infection as well. Although most cases of breast enlargement in HIV-infected male patients have been presented as benign, there have been various reports in this population. A strong susceptibility to male breast cancer is seen in Klinefelter's syndrome, feminization, hypogonadism, gynecomastia and obesity. Breast adenocarcinoma in HIV-positive patients tends to occur at an early age. Kaposi's sarcoma (KS) can be localized to the breast in HIV-infected patients. Breast is also a recognized site of non-Hodgkin's lymphoma (NHL) in HIV-infected patients. In our case, infection and antiretroviral drugs could be the precipitating causes for the development of gynecomastia. In liver disease, gynecomastia is observed in advanced hepatic failure, which was not the case in our patient, as there were no signs of decompensated cirrhosis or even portal hypertension. In our patient, the presence of microcalcifications in mammography raised the possibility of either adenocarcinoma or KS. However, their diffuse appearance led us to attribute these findings to previous subcutaneous hematomas which had mainly occurred during the period with the HIV-related thrombocytopenia. A biopsy was postponed and a systematic follow-up was decided. On this follow-up, three and six months after diagnosis, the mammographic findings remained stable. Until today, little information exists, in the imaging literature, regarding breast enlargement in HIV-positive patients. HIV may directly and indirectly affect the glandular, mesenchymal, and intramammary lymphoid tissue in these patients. Breast imaging and therapeutic challenges have not been well addressed. Ultrasonography and MR mammography should be advised in HIV-infected patients with breast enlargement. Mammography must always be performed in order to evaluate the radiographic breast density, to reveal palpable or not palpable lesions and to identify the possible presence of microcalcifications. Ultrasonography is a useful modality to identify the abnormality of the breast, guiding further investigations. MR mammography would seem ideally suited to breast imaging in order to distinguish the adipose tissue from the glandular tissue. In conclusion, HIV-positive patients must have a careful evaluation, including the obtainment of a clinical history and the performance of a physical examination, breast imaging with all

the available modalities and biopsy if necessary.

Differential Diagnosis List: Bilateral gynecomastia in a HIV male patient.

Final Diagnosis: Bilateral gynecomastia in a HIV male patient.

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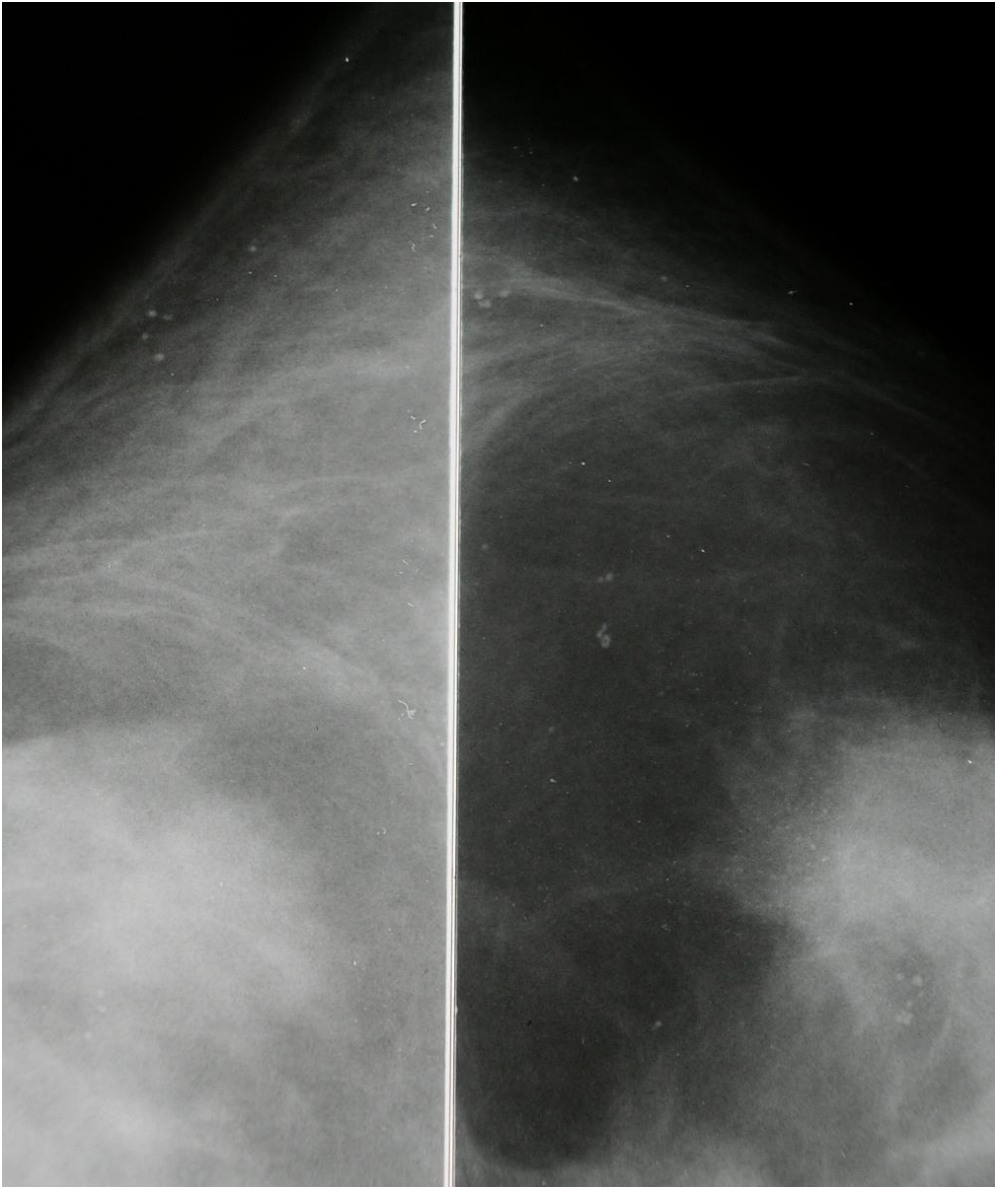
Figure 1

a



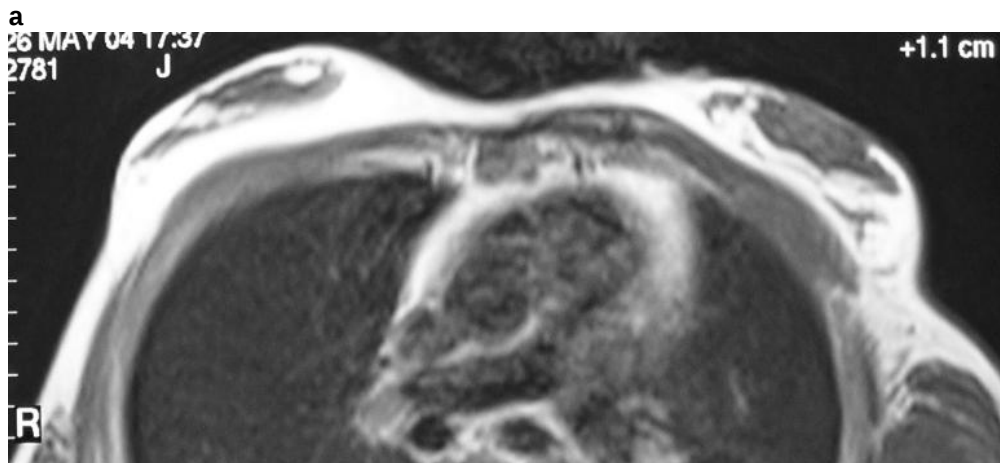
Description: A mammogram showing the enlargement of both breasts. The glandular tissue is demonstrated in a pattern similar to that seen in the heterogeneously dense female breast. At the upper outer quadrant of both breasts, round and punctuate, well-circumscribed, high density, round calcifications are also seen. **Origin:**

b



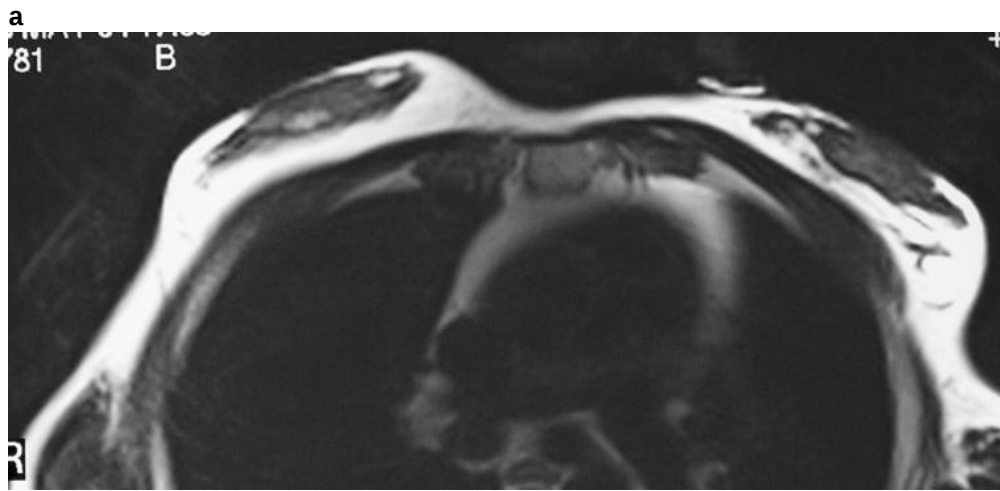
Description: A mammogram showing round and punctuate, well-circumscribed, high density, round calcifications at the upper outer quadrant of both the breasts (magnified views). **Origin:**

Figure 2



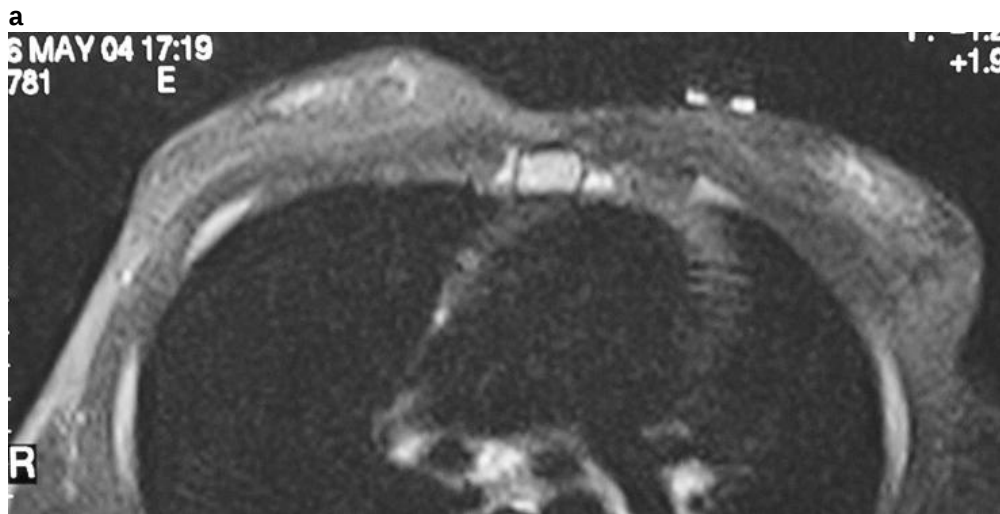
Description: An MRI T1WI (TE: 10.0, TR: 377) showing the breast parenchyma having a low signal intensity due to the presence of a glandular tissue, outlined by high signal intensity of the surrounding fat. **Origin:**

Figure 3



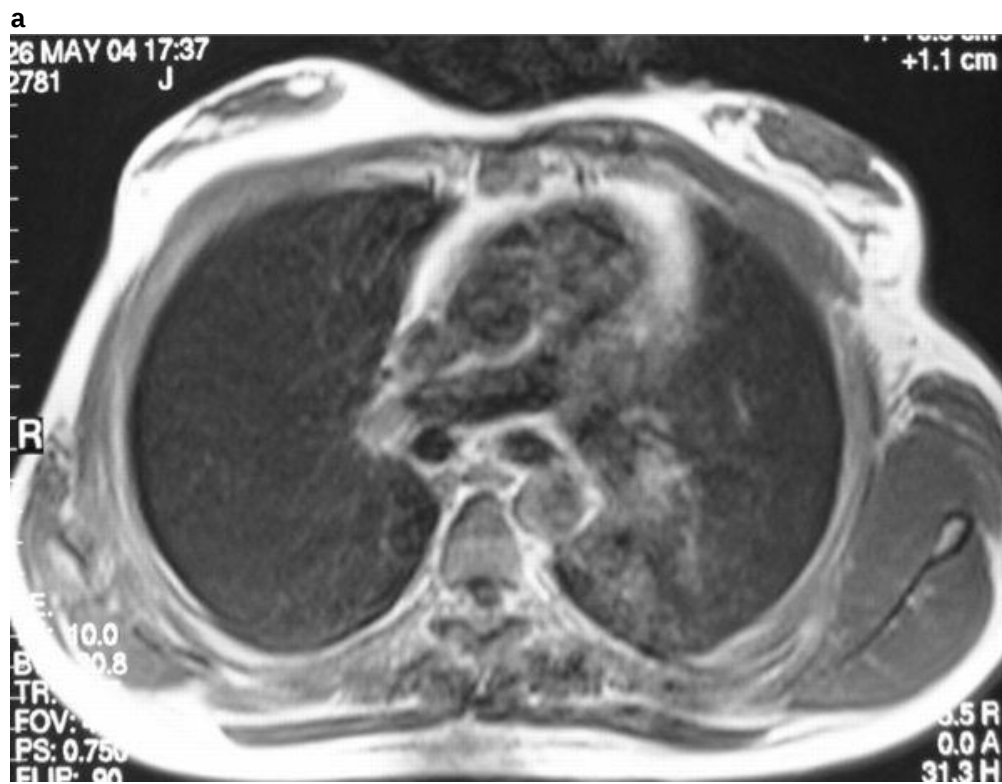
Description: An MRI T2WI (TE: 126.0, TR: 3581) showing the glandular tissue that produces low signal intensity. **Origin:**

Figure 4



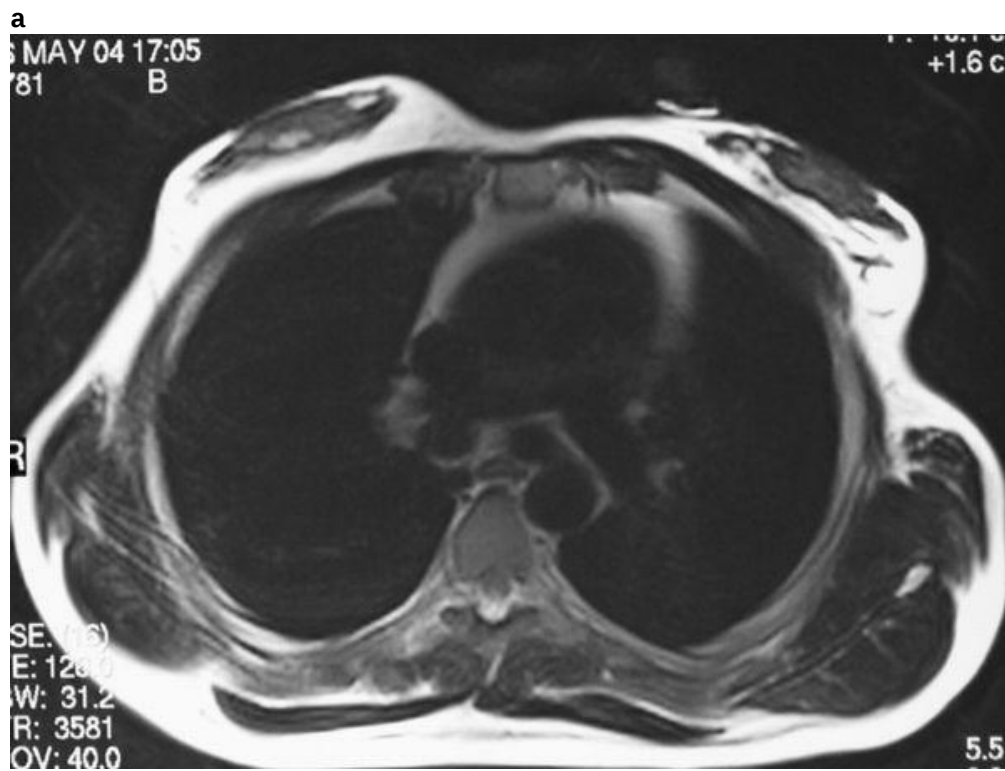
Description: MRI SPIR (TE: 110.0, TR: 4399) **Origin:**

Figure 5



Description: An MRI T1WI (TE: 10.0, TR: 377) showing the breast parenchyma with a low signal intensity due to the presence of a glandular tissue, outlined by a high signal intensity of the surrounding fat. **Origin:**

Figure 6



Description: An MRI T2WI (TE: 126.0, TR: 3581) showing the glandular tissue producing a low signal intensity. **Origin:**

Figure 7



Description: MRI SPIR (TE: 110.0, TR: 4399). Origin: