DEKA IN MEDICINE

Case report

Exploring a rare oncologic complication: alveolar rhabdomyosarcoma in HIV patient

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Citation: Santoso DSB, Santoso B, Kristyana S, et al. Exploring a rare oncologic complication: alveolar rhabdomyosarcoma in HIV patient. Deka in Medicine. 2024; 1(2): e277

Received: July 30, 2024
Revised: August 12, 2024
Accepted: August 15, 2024
Published: August 18, 2024

ABSTRACT

BACKGROUND: Alveolar rhabdomyosarcoma is one of the rare oncological complications in Human Immunodeficiency Virus (HIV) patients, but it has a serious impact. Therefore, case report study discussing case of alveolar rhabdomyosarcoma in HIV patient is very important.

CASE: A 22-year-old man complained of pain and a growing lump behind his right knee for 9 months. The lump, initially small, became larger and more painful, affecting his ability to move his leg. The patient was diagnosed with HIV 3 years ago and also had leprosy. Additionally, the patient had a history of weight loss and a low body mass index (BMI). Physical examination revealed a 10x15x10 cm mass behind the right knee. Magnetic Resonance Imaging (MRI) of the right knee showed a complex cystic solid lesion involving several muscles and blood vessels. Fine Needle Aspiration Biopsy (FNAB) suggested a High-Grade Sarcoma. Open biopsy confirmed alveolar rhabdomyosarcoma with aggressive features and high mitotic activity.

CONCLUSION: In conclusion, our study reported the first case of alveolar rhabdomyosarcoma in an HIV patient. Our study emphasizes the importance of thorough diagnosis for suspected malignancies in HIV patients.

KEYWORDS: Human Immunodeficiency Virus; alveolar rhabdomyosarcoma; oncologic complication; HIV-related malignancies.

INTRODUCTION

The Human Immunodeficiency Virus (HIV) is a virus that targets the immune system. HIV infection gradually weakens the body's defenses against various infections and certain types of cancers.[1] Although there have been advancements in HIV treatment, HIV infection remains a serious global health issue.[2] By the end of 2020, prevalence data estimated that approximately 37.7 million people were living with HIV worldwide. This number includes 36 million adults and 1.7 million children aged 0-14 years.[3] Furthermore, in terms of mortality, around 680,000 people died due to HIV-related causes.[4] Additionally, it is estimated that approximately 1.5 million individuals were newly infected with HIV in 2020.[5] On the other hand, the clinical manifestations of HIV infection vary depending on the stage of the disease. In advanced stages, symptoms can include swollen lymph nodes, weight loss, persistent fever, diarrhea, tuberculosis, cryptococcal meningitis, severe bacterial infections, and malignancies.[6] Various types of cancers reported in HIV patients include lymphoma, Kaposi sarcoma, osteosarcoma, fibrous histiocytoma, leiomyosarcoma, angiosarcoma, and alveolar rhabdomyosarcoma.[7] Among these cancers, alveolar rhabdomyosarcoma is the rarest. Its occurrence in HIV patients is significantly less common compared to other types of cancer, making it an important but infrequent complication in HIV-infected individuals.[7]

Alveolar rhabdomyosarcoma is a subtype of rhabdomyosarcoma. Rhabdomyosarcoma is a soft tissue cancer that originates from mesenchymal cells, which are precursor cells to skeletal muscle tissue. This cancer is characterized by its aggressive nature and is typically found in the head and neck region, urogenital tracts,

torso, and extremities.[8] Additionally, the prevalence of alveolar rhabdomyosarcoma is approximately 20-30% of all rhabdomyosarcoma cases. This prevalence rate makes alveolar rhabdomyosarcoma the second most common type of rhabdomyosarcoma.[9] On the other hand, the clinical manifestations of alveolar rhabdomyosarcoma can vary depending on the location and extent of the tumor, including mass or swelling, pain, systemic symptoms, metastasis, bone marrow involvement, neurological symptoms, genitourinary symptoms, gastrointestinal symptoms, and respiratory symptoms.[10] Furthermore, the causes or etiology of alveolar rhabdomyosarcoma are primarily related to genetic factors, specifically chromosomal translocations that lead to the formation of oncogenic fusion proteins.[11] Alveolar rhabdomyosarcoma is a highly aggressive type of rhabdomyosarcoma, characterized by rapid growth and a high potential for metastasis.[8] Given the rarity of alveolar rhabdomyosarcoma in HIV patients and the serious complications it can cause, this study aimed to report a case of alveolar rhabdomyosarcoma in an HIV patient. This case report was expected to serve as an initial foundation for further research and to provide a reference for managing alveolar rhabdomyosarcoma in HIV patients.

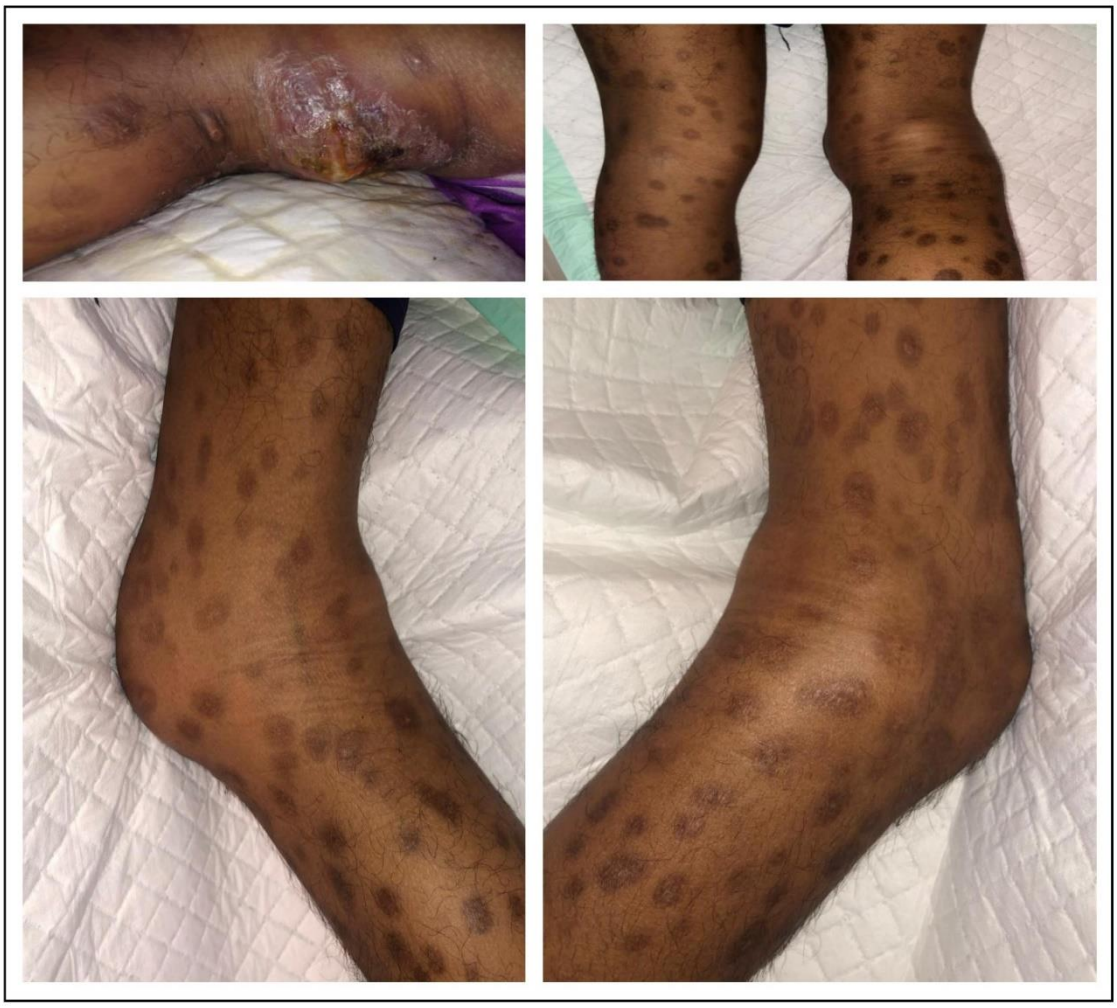

Figure 1. Clinical presentation of an HIV patient suspected to have a soft tissue tumor on the posterior side of the right knee. The figure showed the posterior view of the right knee of an HIV-positive patient with a suspected soft tissue tumor. The clinical presentation in this patient included swelling and localized erythema. The patient also reported pain and restricted movement in the affected area. Palpation of the tumor revealed a firm and non-mobile mass.

CASE PRESENTATION

A 22-year-old man complained of pain in the posterior right knee for the past 9 months. The pain was localized and very disruptive, causing difficulty in walking and performing daily activities. Additionally, the patient reported a lump behind and beside the right knee for the past 3 months. The lump, which initially started small, grew larger over the past 3 months and was accompanied by pain that made it difficult for the patient to bend and straighten his leg (Figure 1). The patient was diagnosed with HIV 3 years ago and was

treated with Evafirenz 600 mg, Tenofovir 300 mg, and Lamivudin 300 mg. Additionally, the patient was diagnosed with leprosy in 2018 and underwent a year of treatment before being declared cured. Three years ago, the patient experienced weight loss from 60 kg to 45 kg, but his weight initially increased after HIV treatment before decreasing again with the development of the knee lump. The patient is a student with a history of injectable drug use. His nutritional status indicated low body weight with a BMI of 13.84 kg/m². Physical examination revealed a mass in the posterior right knee measuring 10x15x10 cm, with minimal tenderness and a pain scale of 3/10.

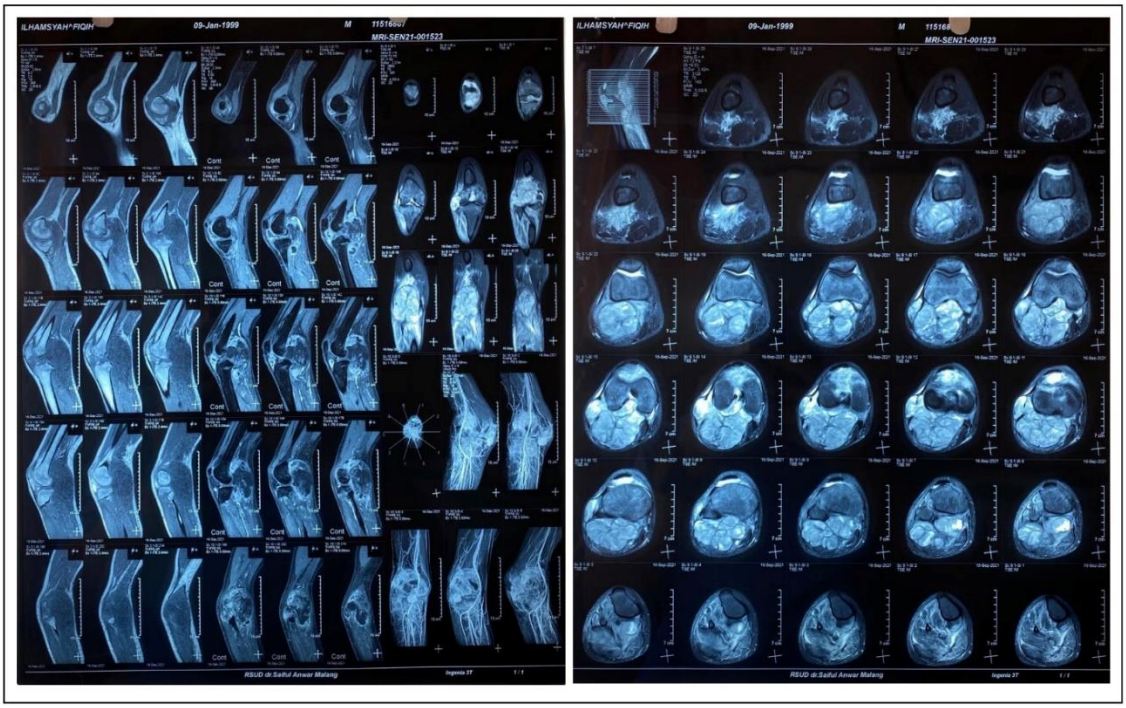

Figure 2. MRI of the right knee. The MRI showed a multiloculated cystic solid lesion located in the posterior region of the right knee. The lesion involved the posterior compartment of the femur region, including the Plantaris muscle, Gastrocnemius muscle, Soleus muscle, and Peroneus muscle. The lesion extended to both the suprapatellar and infrapatellar recesses and encompassed the right popliteal vessels, suggesting the presence of an abscess. No bone changes were observed in the right femur, right tibia, right fibula, or right patella.

Laboratory tests revealed normochromic normocytic anemia. Additionally, other tests showed reactive Venereal Disease Research Laboratory (VDRL) and Treponema pallidum Hemagglutination Assay (TPHA) results, positive Immunoglobulin M Cytomegalovirus (IgM CMV), low CD4 counts, and hypoalbuminemia. Chest X-ray results were normal. Magnetic Resonance Imaging (MRI) of the right knee revealed a multiloculated cystic solid lesion in the posterior region of the right knee, involving the posterior compartment of the femur, Plantaris muscle, Gastrocnemius muscle, Soleus muscle, and Peroneus muscle, extending to both the suprapatellar and infrapatellar recesses, and encompassing the right popliteal vessels, suggesting an abscess. No bone changes were observed in the right femur, right tibia, right fibula, or right patella (Figure 2). Fine Needle Aspiration Biopsy (FNAB) (Figure 3) showed a hypercellular smear with spindle-shaped and oval cells, pleomorphic nuclei, coarse chromatin, and an increased nuclear-to-cytoplasmic ratio. Faint acinar structures were observed, along with bizarre cells showing significant pleomorphism, coarse chromatin, and an increased N/C ratio, accompanied by fibrous tissue fragments. The background contained erythrocytes. The FNAB results concluded a High-Grade Sarcoma, likely Synovial Sarcoma or Malignant Peripheral Nerve Sheath Tumor (MPNST). An open biopsy further identified alveolar rhabdomyosarcoma, characterized by tumor tissue sections consisting of round proliferations resembling rhabdomyoblasts with eccentric nuclei and eosinophilic cytoplasm. Binucleated cells were also present, with tumor cells forming partially solid alveolar structures. Mitosis was observed at 27/10 HPF, with atypical mitoses easily found.

DISCUSSION

This study reported a case of alveolar rhabdomyosarcoma in the right knee of an HIV-positive patient. Our current study is the first case report documenting the occurrence of this type of sarcoma in an HIV-infected individual. Due to the uniqueness and rarity of this case, direct comparison with other studies in terms of diagnosis, management, and prognosis proved challenging. Nevertheless, there have been reports of several other types of sarcomas occurring in HIV patients, such as Kaposi's sarcoma,[12] malignant fibrohisticytoma of the knee,[13] and osteosarcoma.[14] Among these sarcomas, Kaposi's sarcoma is the most commonly found in HIV patients.[12] In contrast, non-Kaposi sarcomas are much rarer and require special attention.[15] Additionally, previous study has revealed that, in the context of non-Kaposi sarcomas, leiomyosarcomas are the most frequently reported type in HIV patients, followed by angiosarcomas and fibrohistiocytic tumors.[7] This context highlights the importance of the findings from this study, as it contributes to the knowledge of the sarcoma spectrum in HIV patients. By documenting this rare case of alveolar rhabdomyosarcoma, our results provide valuable insights into the less common manifestations of sarcoma in the HIV population. Furthermore, these findings may contribute to a more comprehensive understanding of the various types of sarcomas that can affect individuals with HIV.

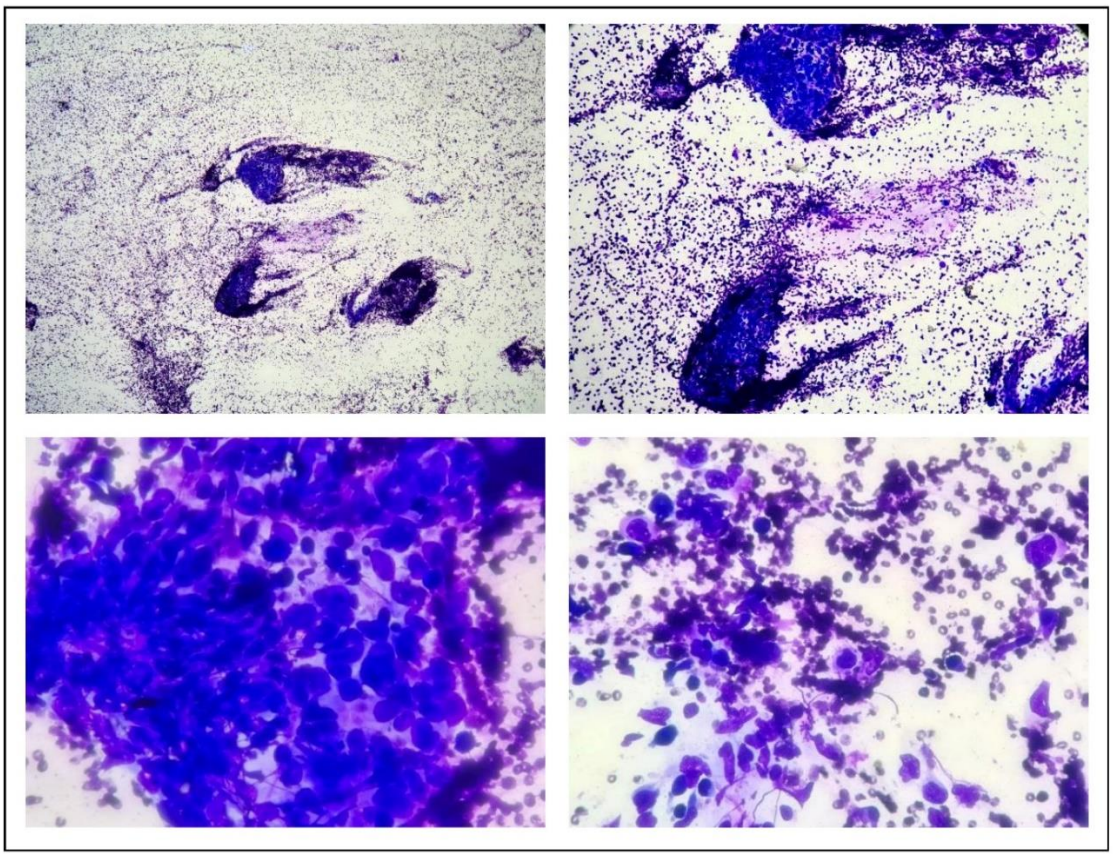

Figure 3. Fine needle aspiration biopsy of the mass in the right knee. FNAB was performed twice with a 25 G needle on a 15 cm solid-cystic mass in the right knee. The procedure yielded 10 Diff-Quick slides. Microscopic examination of the hypercellular smear revealed spindle-shaped and oval cells with pleomorphic nuclei, coarse chromatin, and an increased nuclear-to-cytoplasmic ratio. Additionally, faint acinar structures were observed along with bizarre cells showing significant pleomorphism and coarse chromatin. The background also contained fibrous tissue fragments and erythrocytes. These findings suggest a high-grade sarcoma, with differential diagnoses including Synovial Sarcoma and Malignant Peripheral Nerve Sheath Tumor (MPNST).

The mechanism underlying the development of alveolar rhabdomyosarcoma in the HIV-positive patient we reported remains unclear. However, several theories may provide a basis for understanding this case. Generally, the pathogenesis of Non-AIDS Defining Cancers (NADCs), including alveolar rhabdomyosarcoma in HIV patients, is not well understood. Studies suggest a correlation indicating that HIV may facilitate oncogenic transformation. For instance, in Kaposi’s sarcoma cases, interleukin-6 (IL-6),

IL-1β, Tumor Necrosis Factors (TNF), and oncostatin-M have been shown to promote the growth of spindle cell derivatives of Kaposi's sarcoma, which are suspected precursors of tumor cells. Additionally, elevated levels of IL-6, IL-1, and TNF have been observed in HIV patients, with HIV-infected T cells and macrophages contributing to the increased production of these cytokines.[16] On the other hand, it is known that HIV patients face a higher risk of malignancies. This was evident even before the advent of effective antiretroviral therapy, with the occurrence of "AIDS-defining malignancies" (ADMs) such as Kaposi's sarcoma (associated with human herpesvirus 8), cervical cancer (associated with human papillomavirus), and Non-Hodgkin lymphoma (associated with Epstein-Barr virus).[17] These neoplasias are thought to be related to immune system damage and low CD4 T cell counts.[18] Although HIV itself is not considered a direct etiological pathogen for malignancy, it is believed to facilitate malignancy transformation through various mechanisms, primarily its immunosuppressive effects.[19] Moreover, the patient in this case did not exhibit other risk factors for alveolar rhabdomyosarcoma, such as in utero radiation exposure, accelerated in utero growth, low socioeconomic status, or parental drug use during pregnancy.[20] Therefore, the patient's HIV history may have influenced the development of alveolar rhabdomyosarcoma. Furthermore, the response to HIV therapy in this patient was suboptimal, as indicated by a CD4 count of 218 cells/μL. Studies have reported a consistent relationship between low CD4 counts (<350-500 cells/μL) and a higher risk of ADMs and/or NADCs.[21] The patient's CD4 count of 218 cells/μL, despite routine ARV therapy, may be associated with an increased risk of NADCs, including the occurrence of alveolar rhabdomyosarcoma.

This study had several clinical implications. First, our present study was the first case report to document the occurrence of alveolar rhabdomyosarcoma in an HIV patient. Therefore, this study might have served as a foundation for more complex future studies on the occurrence of alveolar rhabdomyosarcoma in HIV patients. Second, as is well known, the occurrence of alveolar rhabdomyosarcoma in HIV patients is very rare.[9] Therefore, this study highlighted the importance of suspecting alveolar rhabdomyosarcoma in any HIV patient presenting with a lump. This was crucial for planning the next diagnostic steps. Third, the study emphasized that individuals with weakened immune systems might be at a higher risk for rare and aggressive cancers. Therefore, this study underscored the importance of monitoring for secondary malignancies in HIV-infected patients. Fourth, the study emphasized the importance of comprehensive clinical monitoring, including diagnostic imaging, to identify such rare tumors at an early stage.

The study had several limitations. First, information regarding previous treatment history, adherence to treatment, and prior examinations was not obtained. Therefore, this limitation might have affected our ability to estimate specific factors that could have triggered the occurrence of alveolar rhabdomyosarcoma in the HIV patient. Second, the study was based on only one case report, which limited the generalizability of our findings. To obtain more robust data and deeper insights into the incidence, prognosis, and treatment outcomes of alveolar rhabdomyosarcoma in HIV-positive patients, further studies with larger sample sizes were needed. Third, the study did not evaluate the impact of antiretroviral therapy on the incidence, progression, or treatment outcomes of alveolar rhabdomyosarcoma in HIV-positive patients. This was an important aspect to address, given the role of antiretroviral therapy in managing HIV and its potential influence on cancer risk.[22]

CONCLUSION

In conclusion, our study reported the first case of alveolar rhabdomyosarcoma in an HIV patient. The study emphasizes the importance of a comprehensive approach in determining the differential diagnosis for HIV patients presenting with suspected malignancy. By considering various factors comprehensively, it is hoped that early detection and more accurate treatment planning for managing alveolar rhabdomyosarcoma can be improved.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Patient has provided consent for the writing of this article.

CONFLICTS OF INTEREST

We have no conflict of interest

FUNDING SOURCES
We have no source of funding

ACKNOWLEDGMENTS
None

AUTHOR CONTRIBUTION
Conceptualization: DSBS; Data Curation: DSBS; Formal Analysis: DSBS; Investigation: DSBS, BS, SK, DC; Project Administration: DSBS; Resources: DSBS; Methodology: DSBS, BS, SK, DC; Software: DSBS; Visualization: DSBS, BS, SK, DC; Supervision: DC; Validation: DSBS, BS, SK, DC; Writing – Original Draft Preparation: DSBS, BS, SK, DC, SMDN, AE; Writing – Review & Editing: BS, DC. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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