Angiosarcoma of the scalp in an elderly man with HIV infection: A case report

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ABSTRACT:

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Cutaneous angiosarcoma is a rare malignant tumor of vascular mesenchymal origin with a propensity for local recurrence and metastasis. It is associated with a poor prognosis unless diagnosed early. The most common type is angiosarcoma of the face and scalp, especially in elderly men. We reported a case of HIV infected elderly man with angiosarcoma of the scalp which treated by local wide excision followed by radiotherapy. To our knowledge, few studies have been reported about angiosarcoma in HIV infection which the pathogenesis is still controversial in the immunocompromised host.

Key words: Angiosarcoma, HIV infection

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The cutaneous angiosarcoma is a rare malignant tumor of vascular mesenchymal origin. It found less than 1% of all sarcomas with a propensity for local recurrence and metastasis associated with a generally poor prognosis[1]. The delay in diagnosis can lead to extensive and diffuse infiltration on the affected area, even metastasis. It is also one of the Non-AIDS-Defining Cancers (NADCs) in which the incidence has been increasing due to the introduction to highly active antiretroviral therapy (HAART) since the lifespan of people with HIV infection has been extended significantly and the risk factors for HIV-infected persons with NADC are multifactorial. It usually progresses more aggressively, detected at a later stage, and recurs more frequently in HIV patients. The potentially curative treatment in cutaneous angiosarcoma is wide local excision because positive margins predict the worst outcome. Systemic chemotherapy followed by adjuvant radiation therapy is recommended in metastatic disease.

Case report

Our 69-year-old Thai male presented with rapidly ulcerated violaceous to blackish plaques on vertex for 3 months. The lesions started with multiple erythematous to violaceous papules and patches then turned into violaceous to blackish plaques with contact bleeding. (Fig. 1) The other part of dermatological findings is unremarkable. There was no lymphadenopathy detected in this patient. He denied significant weight loss or loss of appetite. There was no history of previous radiotherapy or trauma to the scalp. He has an HIV infection since 2010, currently with a CD4 count of 311 cell/mm^3. His current antiretroviral drugs are tenofovir 300 mg, efavirenz 600 mg, and emtricitabine 200 mg once daily. He had no history of any opportunistic infection. He denied a drug allergy or smoking. There was no history of a similar skin lesion or any cancer in his family.

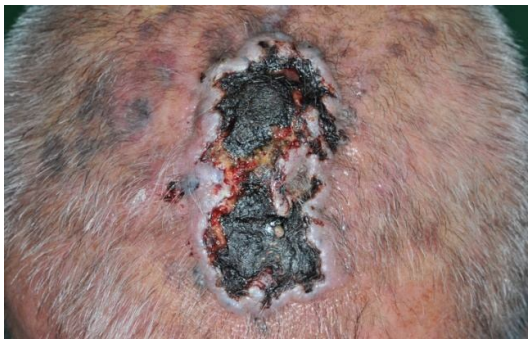

Figure 1 Patient developed localized well-defined ulcerated hyperkeratotic violaceous to blackish scale-crusted and hemorrhagic ulcerative plaque with hemorrhagic scale-crusts and, sized 7 cm by 4 cm with contact bleeding and surrounded by multiple discrete well-defined non-scaly bruise-like erythematous to violaceous patches on vertex scalp.

He went to a nearby hospital. The lesion was initially thought to be an abscess so he received oral antibiotics but showed no improvement. The lesion was subsequently ulcerated so he was

referred to the Institute of Dermatology in Bangkok, Thailand. The biopsy was done on the vertex scalp (Fig. 2A&2B) and showed unremarkable epidermis with hyperkeratosis. The dermis shows the proliferation of spindle cells forming irregular vascular channels. Pleomorphic and plump endothelial cells are occasionally observed. Mitosis is seemingly present. Some inflammatory cell infiltration is noted. The immunohistochemistry staining showed positive CD 31 (Fig. 3) and Ki-67 which confirmed the tumor's vascular origin. The HHV-8 (Fig. 4) is negative, so the Kaposi sarcoma is excluded.

The patient was sent to the oncologist and surgeon. He had wide-excision with approximately 5 cm margin with split-thickness skin grafting followed by 30 sessions of radiotherapy. He has also been continuing the HAART with closed follow up by the infectious disease doctor. Unfortunately, after 4 months of treatment, the lesion relapsed and recurrent angiosarcoma was confirmed by the biopsy. Now he is currently in the process of distant metastases investigation by the oncologist.

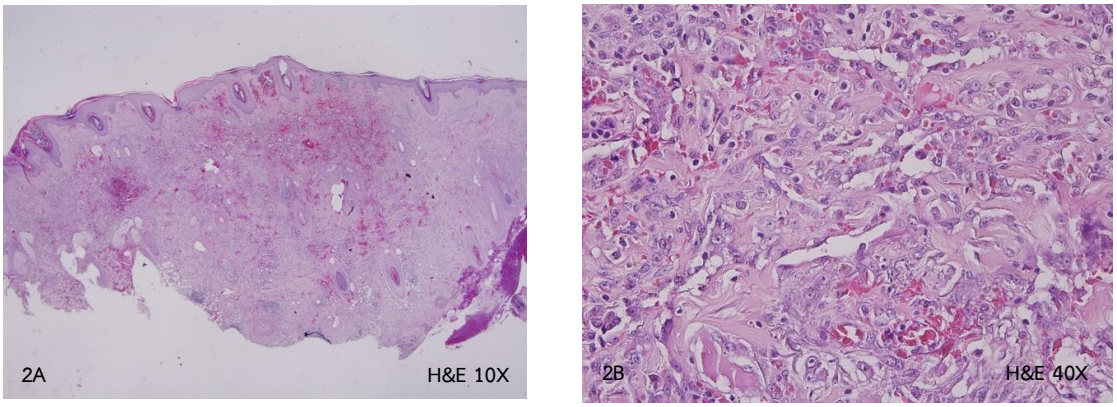

Figure 2 A) A scalp biopsy (vertical section), H&E 10X shows unremarkable epidermis with hyperkeratosis, proliferation of spindle cells forming irregular vascular channels in the dermis and some inflammatory cell infiltration.

B) A scalp biopsy (vertical section), H&E 40X shows some pleomorphic and plump endothelial cells with mitosis.

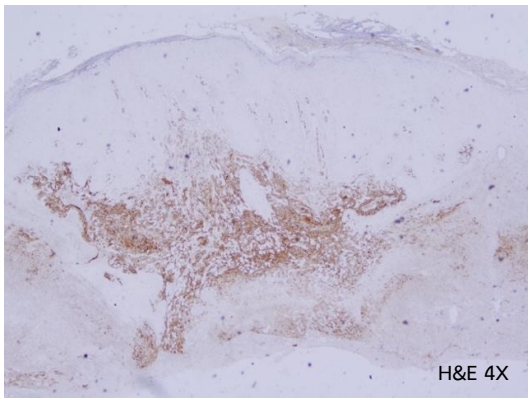

Figure 3. An immunohistochemistry of CD 31 is positive.

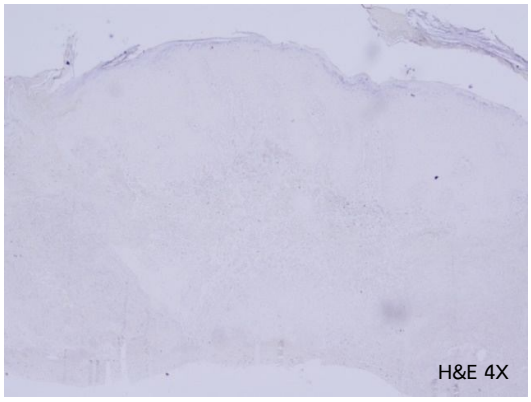

Figure 4. An immunohistochemistry of HHV-8 is negative.

Discussion

Most cutaneous angiosarcomas arise within the following clinical settings: 1) angiosarcoma of the face and scalp in elderly 2) angiosarcoma secondary to chronic lymphedema (Stewart-Treves syndrome) and 3) angiosarcoma as a complication of chronic radiodermatitis or arising from the consequences of severe skin trauma or ulceration. Other risk factors are exposure to vinyl chloride monomer or dioxin. Angiosarcoma is more common in older individuals, with a reported median age between 60 and 71 years[2]; there is generally no gender predilection apart from cutaneous lesions, which are more prevalent among males. The most common site of origin in cutaneous angiosarcoma is the head and neck region, especially the scalp of Caucasian men[1]. Cutaneous angiosarcoma of the head and neck is a distinct subtype which most ordinarily presents as an enlarging purple bruise-like lesion that develops over several months with a history of intermittent bleeding, edema, or ulceration. A delay in diagnosis is common within the early stage of the disease because it is likely to be an infection or traumatic bruise[3]. The differential diagnosis includes haemangioblastoma, Kaposi sarcoma, metastatic cancer from an unknown primary site, sinonasal squamous cell cancer, and Merkel cell carcinoma[4]. The dissemination of angiosarcoma is predominantly by hematogenous spreading. The lung is the most frequent site for metastasis. Other frequent sites include the liver, bone, and lymph nodes[5]. Angiosarcoma contains a greater tendency to involve lymph nodes than any other type of sarcoma that affect the head and neck region regardless of its site of origin[6].

This patient is an elderly male, had no risk factor of chronic lymphoedema or radiation

therapy, but he has been infected with HIV for almost 10 years, currently with a CD4 count of 311 cell/mm^3. People with HIV/AIDS have an increased risk of these following cancers: Kaposi sarcoma, non-Hodgkin lymphoma and cervical cancer, in which often called "AIDS-defining conditions" that means if a person with an HIV infection has one of these cancers, it means that AIDS has developed[7]. Angiosarcoma is also found in people with HIV/AIDS but less commonly than the three cancers aforementioned and it is defined as a Non-AIDS-Defining Cancers (NADCs). HIV infection has shown a statistically significant increase in the incidence and relative risk of many NADCs. In cancer development, decreasing of immune surveillance and increasing immune activation play an important role. In vitro studies, suggest that HIV may activate cellular oncogenes or proto-oncogenes and inhibit tumor suppressor genes[7]. The risk factors for HIV-infected persons with NADC are multifactorial, include lifestyle habits such as smoking and sun exposure), HIV itself, coinfection with oncogenic viruses, and possibly drugs or medications[8]. However, the role of immunosuppression in the pathogenesis of NADCs is controversial, based on some studies demonstrating that the increased risk of NADC is not associated with low CD4 T-lymphocyte cell counts or the onset of AIDS[9,10].

Angiosarcoma has a poor prognosis with reported 5-year survival rates ranging from 12 to 35%[11]. Recently found 5-year relative survival rate was 40.3% for those without prior primary cancer and 45.8% for those with[1]. Poor prognosis factors include age $\geq$ 70 years, tumor size greater than 5 cm, and distant disease[12]. Surgical excision with wide-margin is considered the mainstay of treatment even with a negative margin by histologic examination. The surgery usually requires additional radiotherapy, or adjuvant/neoadjuvant chemotherapy because negative surgical margins are achieved in only 21-47% of cases[13]. However, some studies showed no additional benefits of combining the surgery and radiotherapy in cutaneous angiosarcoma[1]. The only role of chemotherapy in angiosarcoma is as a palliative treatment. For chemotherapy in advanced angiosarcoma, Paclitaxel is the standard first-line treatment for advanced angiosarcoma. Second-line treatment options include pazopanib, eribulin mesylate, and trabectedin[14].

There was no specific regimen for an HIV patient but complications such as immunosuppression or drug interactions between HAART and chemotherapy should be closely observed[15]. T he spontaneous regression of angios arcoma is extremely rare[16]. The immune responses, elimination of carcinogens, increased level of cancer cell apoptosis, hormonal influences, and epigenetics are the proposed mechanisms. However, there was not enough evidence concerning the benefit of HAART in the

spontaneous regression of angiosarcoma in an HIV positive patient.

In conclusion, we present a case of angiosarcoma of the scalp in an elderly man with HIV infection, which the pathogenesis of angiosarcoma as a NADC is still controversial. Along with wide-excision, additional radiotherapy, or adjuvant/neoadjuvant chemotherapy have no significantly improve survival. Besides the continuing of HAART is beneficial by improving control of HIV replication and from the prevention of opportunistic infections but the spontaneous regression from the effective HAART is still skeptical.

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