Case Report

Regression of A Cervical Spinal Mass following Highly Active Antiretroviral Therapy (HAART) in Child with Advanced Human Immunodeficiency Virus (HIV) Disease

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This report documents a case of infiltrating cervical spinal mass, most likely a spinal tumor, in a girl with HIV infection that regressed following HAART and without treatment of the tumor or any anti-infectives.

Keywords: *HIV, Spinal tumor, Spinal mass, ARV, HAART, Leiomyosarcoma, Cancer*

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HIV infection is associated with an increased risk of malignant neoplasm, both in adults and pediatric age groups[1,2], an estimated risk of ~10 times was recorded for HIV infected children compared to non-HIV infected children (0.6 per 1000 versus 0.07 per 1000 person-years)[2]. The commonest type of malignant neoplasm encountered in the pediatric age group is non-Hodgkin's lymphoma. The second is leiomyosarcoma and leiomyoma[3,4]. The introduction of HAART managed to prolong the life of children with HIV infection. With the longer lifespan, children may be more at risk for malignancy[1,5].

Case Report

A 7-year-old Thai girl was referred from a general hospital in the Northeast of Thailand, to King Chulalongkorn Memorial Hospital on the 15th of September 2003. She presented with left upper extremity weakness. One month prior, she complained of pain in her neck that radiated to the left shoulder. Following that, she was unable to lift her left arm to dress herself and weakness was noted in the left handgrip. She also developed fever at night during this period.

The patient's mother was diagnosed with HIV infection during pregnancy but neither she nor the patient received antiretroviral therapy (ARV) for prevention of maternal to child transmission. The patient was not breast fed. She had an elder sister, who passed away at the age of 8 years, due to cryptococcal meningitis. The presented patient was diagnosed with HIV infection at the age of 2 years. She has had many HIV-related illnesses including *Pneumocistis jiroveci* pneumonia at 5 month old, varicella infection at 2 years old, recurrent herpes zoster, chronic diarrhea, oral candidiasis, and wasting syndrome. Prior to admission, she was naive to ARV treatment.

At the initial visit, she was afebrile, cachetic, and pale. Her weight and height were 11.5 kg (-2SD) and 103 cm (-3SD) respectively. No significant finding was noted on examinations of the cardiovascular, respiratory, and gastrointestinal systems. There were multiple palpable lymph nodes in the cervical, axillary, and inguinal regions.

The patient showed good orientation and understood all commands ($E_4V_5M_6$). All the cranial nerves

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functions were normal. Examination of the both lower extremities showed grade 4 motor power, normal deep tendon reflexes, no Babinski sign and no fasciculation. The right upper extremity a motor power of grade 4 was found, however the proximal part of the left upper extremity had a motor power of grade 0 and the distal part of grade 2-3. Normal deep tendon reflex was noted on the right but was absent on the left upper extremity. No fasciculation was noted. Finding on the sensation as well as cerebellar system were inconclusive as patient was not cooperative.

Imaging studies included radiography of cervical and thoracic spines (anterior-posterior and lateral view) and magnetic resonance imaging (MRI) (cervical spine). The radiography of both cervical and thoracic spines did not reveal any abnormalities involving the spines; instead, it revealed that there was tracheal shift to the right at the cervical level and reticular opacities in the upper lobe of the right lung. The MRI (23rd Sep 2003) revealed three lesions: an infiltrating mass, a multiple cervical lymphadenopathy, and a pulmonary infiltration in the right upper lobe. The infiltrating mass was located at the left paravertebral space, extending from C3 to C6, encasing left vertebral artery, widening the neural foramina, and extending into the spinal canal. The left carotid artery and internal jugular vein were laterally displaced. The mass was isodense with muscle on T1WI (Fig. A), hyperintense on T2WI and homogenously enhanced after intravenous Gd injection (Fig. B). The lymphadenopathies involved the left lateral retropharyngeal node, bilateral jugular and spinal accessory nodes.

Laboratory examinations revealed hypochromic microcytic anemia [Hemoglobin (Hb) 7.4 gm%, mean corpuscular volume (MCV) 59, mean corpuscular hemoglobin (MCH) 17.8], normal white blood cell (WBC) count (8790 cells/mm^3), and normal platelet count (460,000/mm^3). CD4+ cell count and HIV RNA was not available. A leiomyosarcoma was suspected and an open biopsy of the spinal tumor was planned to confirm the diagnosis but it was postponed because the surgeons felt that she was too sick. She was discharged and put on close observation at her district hospital. She did not receive HAART as it was not available through the Thai Government Access to care Program at that time.

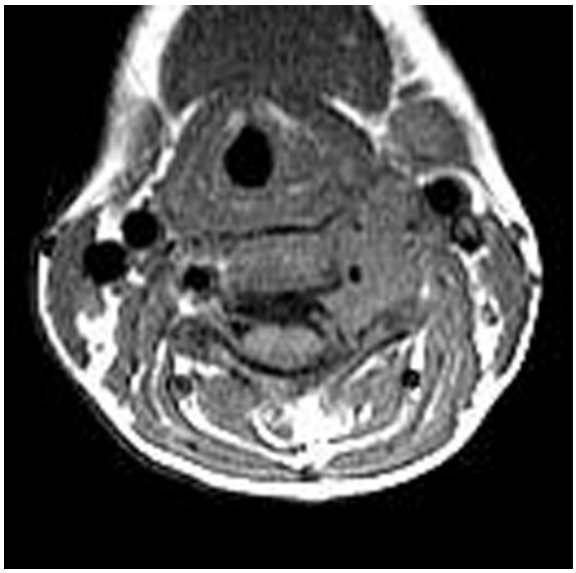
On 10th October 2003, patient was readmitted to King Chulalongkorn Memorial Hospital with an episode of seizure proceeded by high fever. A lumbar puncture was done and laboratory examination of the cerebrospinal fluid was found to be normal and negative for cryptococcal antigens. She was discharged subsequently with an appointment to follow up.

On 27th October 2003, she was electively admitted to King Chulalongkorn Memorial Hospital for open biopsy of her spinal tumor; however, the procedure was not done because the neurosurgeon felt that it would not help in her management due to her poor HIV disease prognosis and suspected cervical spinal malignancy. At this time, HAART was available at HIV-NAT, The HIV Netherlands Australia Thailand Research Collaboration, through the Thai Government Access to Care Program and she was started on HAART with generic stavudine, lamivudine, and nevirapine. Table 1 shows improvement of her clinical, CD4 and HIV RNA following HAART without any co-treatment with anti-infectives including antibacterial, anti-mycobacterial and antifungal medications.

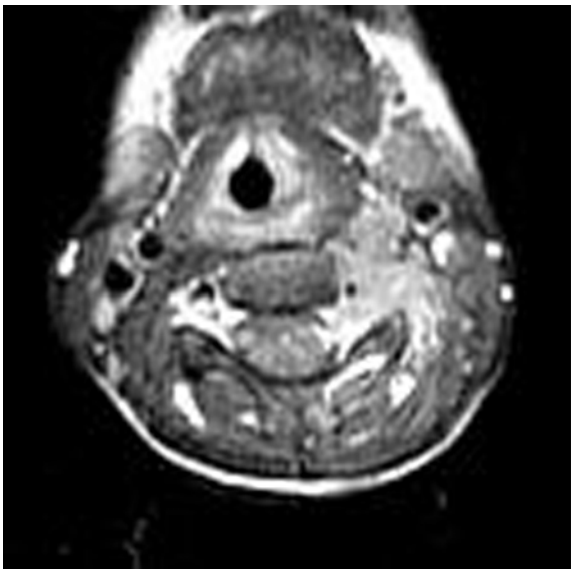
A follow-up MRI was done on 13th December 2005, 2 years after taking HAART. The lesion can still

Table 1. Treatment response before and after stavudine, lamivudine and nevirapine therapy

Week	CD4% (CD4 count cell/ml)	HIV RNA copies/ml (log)	Clinical picture
0	1 (13)	1540 (3.19)	Left arm – motor power grade 0, left hand – motor power grade 2-3
8	-	-	Improvement, left arm power grade 2-3
24	11 (321)	-	Left arm power grade 3, can lift left arm
36	12 (419)	< 50 (< 1.70)	Further improvement
60	19 (662)	-	Handgrip power grade 4
72	26 (819)	-	Minimal weakness
84	22 (748)	-	Good strength, power grade 5 for left arm and hand
96	26 (692)	-	Sustained grade 5 motor power
108	25 (689)	-	Sustained grade 5 motor power, follow up MRI performed

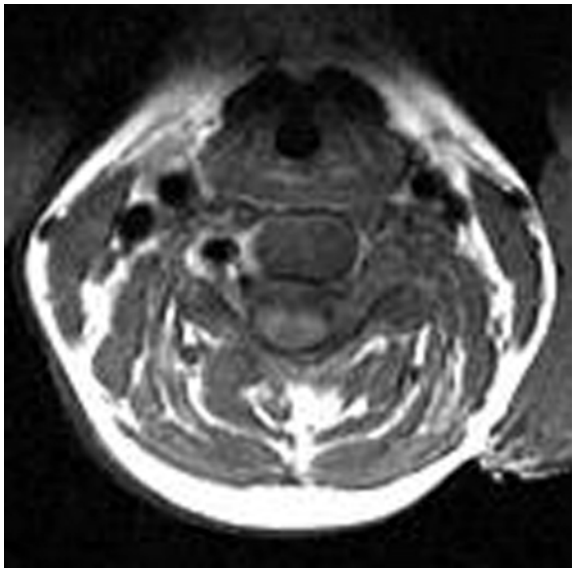


A - Axial T1WI

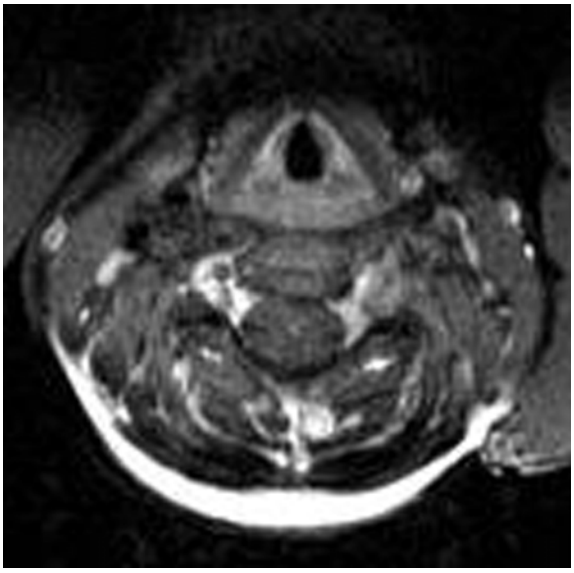


B - Axial T1WI fat sat + Gd

Fig. **A** and **B** were taken in 2003 before highly active antiretroviral therapy
At lower C4, showing the infiltrative homogenously enhanced mass at left paraspinal space extending into the spinal canal, widened left C4-5 intervertebral foramen and encasing left vertebral artery



C - Axial T1WI



D - Axial T2WI fat sat + Gd

Fig. **C** and **D** were taken in 2005 after 108 weeks of highly active antiretroviral therapy, at the same lower C4 level but slightly different angle showing significant regression of the mass

be visualized, it is still encroaching upon the cervical foramina, but it had regressed significantly (Fig. C). There is no new lesion. With contrast, the lesion showed mild homogenous enhancement (Fig. D). She is currently followed up in the authors' clinic every 3 months for clinical and CD4 monitoring. The physicians agreed that biopsy should be held off because of the patient's marked improvement, and the size and location of the

tumor would put the patient at significant risk for morbidity associated with biopsy. It is also felt that radiotherapy or chemotherapy would not help her significantly at this time considering her full clinical recovery. A periodic MRI is planned for follow up.

Discussion

The authors report a 7 year old Thai girl with vertically transmitted HIV infection who developed left upper extremity weakness. The MRI showed an infiltrating mass, located at the left paravertebral space, extending from C3-C6 encasing left vertebral artery, widening the neural foramina, and extending into the spinal canal. The mass was isodense with the surrounding muscle and homogenously enhanced with contrast. Due to the rapid onset of weakness, the location of the mass, the infiltrating nature and the appearance on MRI, a leiomyosarcoma was suspected[6,7]. Lymphoma would be one of the differential diagnoses but it is an uncommon presentation site of lymphoma in HIV patients and it does not have an infiltrating appearance on MRI. Infectious causes are always a consideration in HIV-infected patients. Bacterial, mycobacterial, and fungal infections can cause spinal mass. Spinal tuberculosis and transverse myelitis are the most frequent causes of spinal cord opportunistic infections[14,15]. Delay in establishing diagnosis and management cause spinal cord compression and spinal deformity[15]. It is unlikely that the mass would regress significantly without anti-infectives. However, without tissue diagnosis, the authors cannot prove the etiology of this mass.

Many studies have documented an increased risk of malignancy developing in HIV-infected adults and children[1-2, 8-10]. The pathogenesis of the tumor in the HIV positive patient is not well understood. CD8+ cytotoxic T cells can kill tumor cells by disrupting their cell membrane and nucleus. CD4+ T helper cells can interact with antigen presenting cells, and become activated, secretes lymphokines that will stimulate other effector cells[1]. Thus, HIV infection increases the risk of malignancy. Chadwick *et al*[11], 1990, reported the first case of pediatric HIV associated with leiomyosarcoma. Leiomyosarcoma are malignant neoplasm demonstrating smooth muscle differentiation that arises primarily in the uterus, gastrointestinal tract, skin, and blood vessels. Metastases are rare, but usually involve the bone, lung, and liver[7]. It is uncommon for the tumor to metastasize to the central nervous system. Thus, leiomyosarcoma that is detected in the central nervous system can be considered a primary lesion. Other sites of involvement are the bronchus, subcutaneous tissue, esophagus, liver, adrenal gland, kidney, and spleen. The development of leiomyosarcoma is poorly understood. Some studies postulate that smooth muscle tumors are stimulated by a humoral transforming growth factor that is elaborated during HIV infection[11]. The first noticeable symptom is usually a painless lump or swelling. As it enlarges further, it causes pain by compressing on the nearby nerves and muscles.

It is impossible for the authors to know the exact nature of the presented patient's spinal tumor without a tissue diagnosis; however, with all the reported spinal tumors, a direct intervention with surgery, chemotherapy, or radiation was needed. The authors felt strongly that the presented patient should have had a biopsy done when she first presented. With the reluctance of a surgeon willing to perform this procedure, the authors resorted to using HAART alone and were pleasantly surprised at the presented patient's remarkable clinical improvement following HAART. The authors have not seen a report of complete reversal of neurological symptoms and significant decrease in size of spinal tumors after HAART alone. From the latest MRI, the lesion, even though are still visible and encroaches upon the vertebral foramina, shows a significant reduction in size. Thus, the nerve roots are no longer affected. This might explain the clinical improvement. With HAART, children have an excellent capability of reconstituting their immune system. HAART improves CD4+ T cell count and function, decreases inappropriate immune activation, and improves CD8+ T cell and natural killer cell function[12,13]. The patient showed a rapid and sustainable CD4 rise with complete suppression of her HIV RNA. The authors suspect that the improvement of her immune system helped to control the spinal tumor. On the other hand, if the initial biopsy was done and leiomyosarcoma was indeed confirmed, the patient would receive the specific treatment such as surgery, chemotherapy, or radiation. However, the patient may get improvement from specific treatment or get worse from treatment side effects.

In conclusion, the authors have described a girl with severe immune suppression and clinical AIDS, whom infiltrating spinal mass, regressed significantly with complete resolution of neurological symptoms after excellent immune and virological responses to HAART without direct intervention to the tumor or any anti-infective therapy. This illustrates that even in children with advanced HIV manifestation and apparent poor prognosis, treatment including HAART and other

interventions should not be withheld. It is essential that a teaching hospital should try to do its best or as much as possible to secure antiretroviral and all the needed interventions to the HIV-infected patients.

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อาการแสดงและขนาดก้อนในไขสันหลังที่เล็กลงหลังเริ่มการรักษาด้วยยาต้านไวรัสในเด็กติดเชื้อเอชไอวี ที่มีระดับภูมิคุ้มกันต่ำมาก

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รายงานผู้ป่วยเด็กหญิงไทยติดเชื้อเอชไอวี อายุ 7 ปี มาด้วยแขนซ้ายอ่อนแรง มีก้อนในไขสันหลัง จาก MRI เข้าได้กับเนื้องอก และมีซีดีสี่ต่ำ หลังจากได้รับการรักษาด้วยยาต้านไวรัสโดยยังไม่ได้รับการรักษาเฉพาะทางอย่างอื่น เช่น การผ่าตัด ยาต้านมะเร็ง หรือยาปฏิชีวนะ พบว่าซีดีสี่ดีขึ้น อาการอ่อนแรงลดลง และตรวจพบก้อนยุบลงเอง