MR Imaging of CNS Leiomyosarcoma in AIDS Patients

Sukalaya Lerdlum MD, MSc*, Siriporn Lalitanantpong MD**,
Numphung Numkarunarunrote MD**, Pattraporn Chaowanapanja MD**,
Chusana Suankratay MD***, Shanop Shuangshoti MD****

** Department of Radiology, Faculty of Medicine, Chulalongkorn University*
*** Department of Radiology, King Chulalongkorn Memorial Hospital*
**** Department of Medicine, Faculty of Medicine, Chulalongkorn University*
***** Department of Pathology, Faculty of Medicine, Chulalongkorn University*

Leiomyosarcomas of the central nervous system are extremely rare; however they are becoming more prevalent in immunocompromised patients. The authors present MRI (Magnetic Resonance Imaging) of six cases of pathological proved leiomyosarcomas of the central nervous system in patients infected with human immunodeficiency virus. MR images of 4 cases of intraspinal leiomyosarcoma showed lobulated masses expanding multilevel of neural foramina with extradural and intradural extension, giving dumbbell appearance which mimic neurofibroma. Two cases of intracranial leiomyosarcoma revealed a mass at the left cavernous sinus involving prepontine cistern in one case and two lesions in the other case showing masses with dural based appearance at the region of the planum sphenoidale and the posterior aspect of the falx cerebri which mimiced a meningioma. The leiomyosarcoma should be included in the differential diagnosis of extra-axial CNS lesions in HIV-infected patients.

Keywords : *MR imaging, CNS Leiomyosarcoma, AIDS*

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The spectrum of diseases in HIV-infected patients is changing with improved treatments and prolonged patient survival. An increased rate of neoplastic disease is a well-known phenomenon in HIV-infected patients [1,2]. Recently, there has been increasing incidence of malignant smooth muscle tumors in immunocompromised patients, predominantly in children [3,4]. The association of Epstein-Barr virus (EBV) with smooth-muscle tumors in HIV-infected patients had also described [3]. These malignant mesenchymal tumors with myogenic components presenting in the CNS remain exceptionally rare, and almost exclusively as metastasis [5,6]. However, the several reports of primary leiomyosarcoma in the central nervous system have been documented [7-11]. This study reports six cases of leiomyosarcoma in the central nervous system (CNS) in HIV-infected patients.

Material and Method

The present study was a retrospective review of all the medical and pathological records of patients with HIV infection from January 2001 to February 2004 in King Chulalongkorn Memorial Hospital, a total of 1,325 patients (male 887 and female 438). The HIV disease resulting in malignant neoplasm was diagnosed in 34 from 1,325 patients. There were 9 from 34 patients diagnosed as AIDS with leiomyosarcoma; six in the central nervous system, one involved the false vocal cord, one in the liver and one involved the right iris. The MR imaging of CNS leiomyosarcomas of the 6 patients were reviewed by two radiologists. All MR imagings were performed by using a 1.5 Tesla whole body MR imaging system (Signa Horizon Echospeed, General Electric Medical Systems). The signal characteristic, pattern of enhancement and location of the mass were observed. Clinical symptoms at presentation were obtained by reviewing the medical records.

Correspondence to : Lerdlum S. Department of Radiology, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

Results

Of the 6 patients diagnosed as CNS leiomyosarcoma with HIV infection, there were 5 female and 1 male. Mean age was 35.3 years, ranging from 25-49 years. CD_4 cell counts were available in 4 cases, ranging from 20-160 cell/mm^3. The patients presented with pain due to nerve root compression, hemiparesis and paraparesis due to cord compression and also opthalmoplegia with ptosis due to a lesion at the region of the cavernous sinus. Tumors were confined at the region of the spine and intracranial area. Multifocal lesions

were detected in each patients except one with only a mass at the left parasellar area. Intracranial lesions were detected in 2 cases and spinal lesions in 4 cases. Most of the spinal lesions showed lobulated contour with dumbbell appearance causing enlarged neural foramina and mass effect on the spinal cord and nerve roots. All of the spinal lesions showed low signal intensity on T1 weighted images, heterogeneous high signal intensity on T2 weighted images with inhomogeneous enhancement. The intracranial lesions in two cases were dural based lesions showing low signal intensity on T1 and slightly high signal intensity on T2 weighted images with intense enhancement. Clinical information, location of the lesions and details of operation are summarized in Table 1.

Case 1

History: A 34-year-old woman in whom HIV infection was diagnosed 3 years prior to her presentation, presented with progressive weakness of bilateral lower extremities for 2 months and acute urinary retention for 3 days.

Imaging: MRI of the cervical and thoracic spine revealed multiple lobulated masses along the left and right side of the spinal cord at the level of T3-T5 and T9-T11, respectively, with evidence of extension through the corresponding widened neural foramina. There were also other intraspinal masses which showed a similar appearance at both sides of T12-L1 level, right side of L1-L2 level and bilateral S1 neural foramina. Pressure effect to the adjacent spinal cord from these masses was detected. All of these masses showed mixed iso and low signal intensity to the spinal cord on T1-weighted image and heterogeneous high signal intensity on T2-weighted image with heterogeneous enhancement after contrast material was added.

Operation and pathological findings: Operative findings showed two well-defined, brownish extradural masses with firm consistency along the right and left side of the thoracic spinal cord at the level of T4 and T8-T9, respectively. Partial tumor removal with laminectomy of T4, T8 and T9 was performed. The

Table 1. Clinical information, location of the lesions and detail of operation

Case	Clinical information	Location of the lesions	Operation
1.	A 34-year-old female presented with progressive paraparesis for 2 months	Masses at multilevel of thoracic, lumbar and also sacral foramina showing lobulated contour and expanding neural foramina	Laminectomy of T4, T8 and T9 with partial tumor removal
2.	A 43-year-old female presented with back pain and cervical myelopathy	Extradural masses along left side of spinal cord from T3 to T6 level and right side of T6-T7 level with extension into the corresponding neural foramina	Laminectomy of T2-T5 with removal of the tumor
3.	A 40-year-old female presented with right hemiparesis	Multiple extradural dumbbell-shaped masses at the right side of C1-C7 and T12-L1 and left side of T2 expanding to the adjacent neural foramina	Laminectomy at C4-C5 level with tumor removal (Accidental findings of heterogeneous enhancing lesion at the bilateral suprarenal region, FNA positive for mycobacterium tuberculosis)
4.	A 30-year-old female presented with left ptosis and total opthalmoplegia of the left eye	Lobulated mass at the left cavernous sinus extending anteriorly to the region of the left optic canal and posteriorly to the prepontine cistern	Craniotomy with tumor biopsy at the left cavernous sinus
5.	A 31-year-old female presented with right subcostal pain and low back pain	Intraspinal extremedullary masses at the level of T11 and L4 with involvement of the adjacent bony structure	Laminectomy with tumor removal at level of T11 and L4 (Follow up study 5 months later by CT brain and MRI of spine revealed an extra-axial mass at the right cerebellopontine angle cistern and recurrent tumors at T7-8, 11, 12)
6.	A 35-year-old male with binocular diplopia and ptosis of the left eye	Lobulated extra-axial masses at planum the sphenoidale and posterior aspect of the falx cerebri	Craniotomy with tumor removal mass at right thigh proved to be leiomyosarcoma by incisional biopsy also detected during the post operative hospital course)

histopathology exhibited interlacing fascicles of spindle cells with some degree of nuclear atypia. There was less than 1 mitotic figure/10 HPF. Branching capillaries were occasionally observed within the tumor tissue. The tumor cells expressed smooth muscle actin. The S100-protein, EMA and CD99 were nonreactive. The pathologist assigned this tumor as a smooth muscle tumor of undetermined malignant potential. Radiotherapy was started after the operation.

Case 2

History: A 43-year-old woman presented with severe nausea and vomiting. She was admitted for supportive therapy. During the hospital course, she developed back pain with radiating to the left scapular region and cervical myelopathy. The patient had been diagnosed as HIV-infected 4 years prior to presentation. She had symptoms of CN IV & VI palsy for the prior 6 months, MRI of the brain revealed a 0.5x1 cm extra-axial mass at the left side of prepontine cistern. The patient was trial treated as chronic hypertrophic pachymeningitis from tuberculosis. The follow up clinical and imaging findings of the brain showed no improvement.

Imaging: MRI of the cervical and thoracic spine revealed a lobulated extradural mass along the left side of the spinal cord from T3 to T6 level and right side of T6-T7 level, with extension into the corresponding neural foramina. These lesions were characterized by isosignal intensity to the spinal cord on T1-weighted image and heterogeneous hypersignal intensity on T2-weighted image. After injection of contrast material, heterogeneous enhancement of this mass was demonstrated. (Fig. 1)

Operation and pathological findings: The patient underwent laminectomy of T2-T5 level with removal of the tumor. A lobulated extradural mass at the left side of T3-T5 level with compression of the adjacent dural sac was detected. The tumor cells were plump and some showed prominent nucleoli. Mitoses were scattered, approximately 4-12/10 HPF. Hematoxylin and eosinstained section demonstrated interlacing fascicles of spindle-shaped neoplastic cells. Immunohistochemistry study revealed strongly expressed smooth muscle actin. The final diagnosis was compatible with leiomyosarcoma. Some of the tumor nuclei were reactive with EBER in situ hybridization for EBV.

Case 3

History: A 49-year-old woman presented with progressive right hemiplegia and pain at right scapular region for 1 year. She also complained of blurring of vision for 1 month before the admission. She was diagnosed with HIV infection 3 years before this presentation.

Imaging: MRI of the spine revealed multiple extradural dumbbell-shaped lesions at the right side of C1-C7 and T12-L1 levels, and at the left side of T2 level involving the corresponding right nerve roots and expansion of the adjacent neural foramina. These lesions showed isosignal intensity on T1-weighted image and slightly hypersignal intensity on T2-weighted image. After contrast material (Gd-DTPA) was added, heterogeneous enhancement of these masses and dural tail sign were demonstrated. There were incidental findings of two 5x5 cm heterogeneous enhancing lesions, on each side of the suprarenal regions and another 4x5 cm lesion at the dome of the liver. The CT scan of the brain demonstrated bony destruction at the anterosuperior aspect of the clivus and inner table of the left frontal bone, associated with enhancing soft tissue masses at these regions. There were two enhancing soft tissue lesions in the left temporal lobe and posterior aspect of the right temporal lobe. Evidence of a 1x1.5 cm oval-shaped enhancing mass abutted the right optic nerve (Fig. 2).

Operation and pathological findings: The operative findings were extradural white color mass located on the right side from level C5-C7 with elevated adjacent nerve roots. Laminectomy at C4-C7 level with tumor removal was performed. The microscopic examination showed spindle-shaped tumor cells, forming fasicular arrangement. Tumor nuclei were moderately pleomorphic, but mitotic figures were rarely observed (0-1/10 HPF). The pathological diagnosis was smooth muscle neoplasm. Tissue diagnosis of those lesions in the brain was not performed. However, metastasis was the preferential diagnosis.

Fine needle aspiration tissue from the the right adrenal mass revealed mycobacterium or norcadia infection and positive for acid-fast stain. The tissue diagnosis of the lesion at the dome of the liver was not yielded.

Case 4

History: A 30-year-old woman presented with left ptosis, diplopia and left facial paresthesia for 2-3 months. These symptoms had progressed for three months. She was HIV-infected 5 years prior to this presentation.

Imaging: MRI revealed a lobulated mass at the left petrous tip and left parasellar region. This

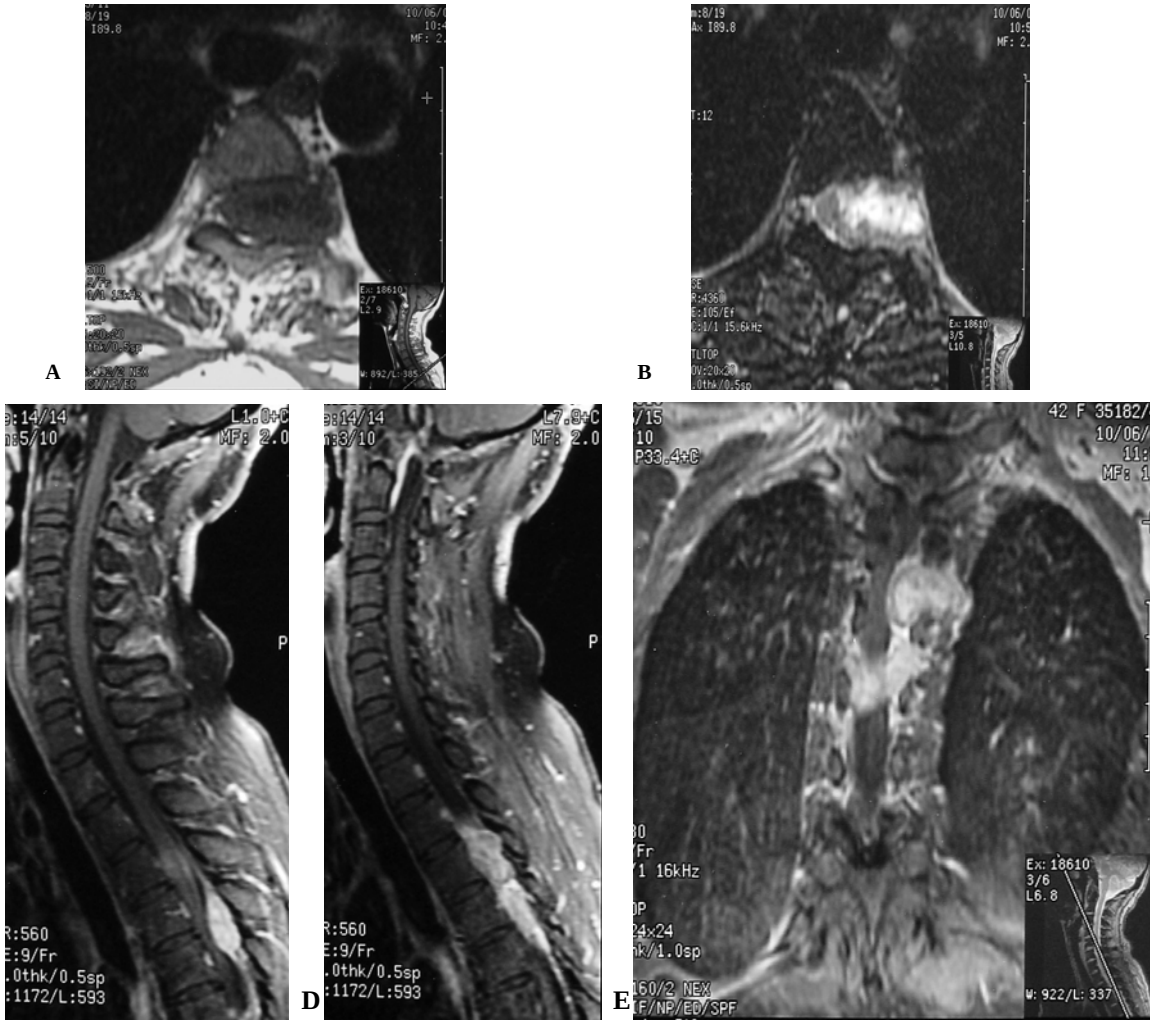

Fig. 1 Case II : A 43-year-old female presented with back pain and cervical myelopathy. Axial MR image reveals lobulated mass in the widening left neural foramen with intraspinal extension. This lesion shows mixed isosignal intensity at the peripheral portion and low signal intensity in the central portion on T1-weighted image (A) and turn to bright signal intensity on T2-weighted (B). Post contrast sagittal (C,D) and coronal (E) T1-weighted images with fat suppression demonstrates multilevel involvement at T3-T6 on the left side and T6-T7 on the right side

lesion showed isosignal intensity to gray matter on T1-weighted image and slight hypersignal intensity on T2-weighted image. After intravenous injection of contrast material, heterogeneous enhancement of this lesion was demonstrated. The mass extended anteriorly involving the left optic canal and extended posteriorly involving prepontine cistern, causing pressure effect to the left side of the pons. Encasement of the adjacent vessels including carvernous portion of left internal carotid artery, basilar artery and left posterior cerebral artery were demonstrated (Fig. 3).

Operation and pathological findings: The patient underwent a pterional craniotomy. The sylvian fissure was split and a yellowish-white solid mass at the left carvernous sinus was visualized. Tumor biopsy was performed. The specimen consisted of multiple pieces of small grayish white tissue, measuring together 1.5 x 1 x 0.3 cm. Microscopic examination showed spindle shaped cells, arranged in fascicular pattern. Mitoses were occasionally observed. Further complete immunohistochemical study demonstrated strongly expressed smooth muscle actin, consistent with leiomyosarcoma. Finally, the patient underwent postoperative radiotherapy.

Case 5

History: A 31-year-old woman presented with progressive abdominal pain at the right subcostal

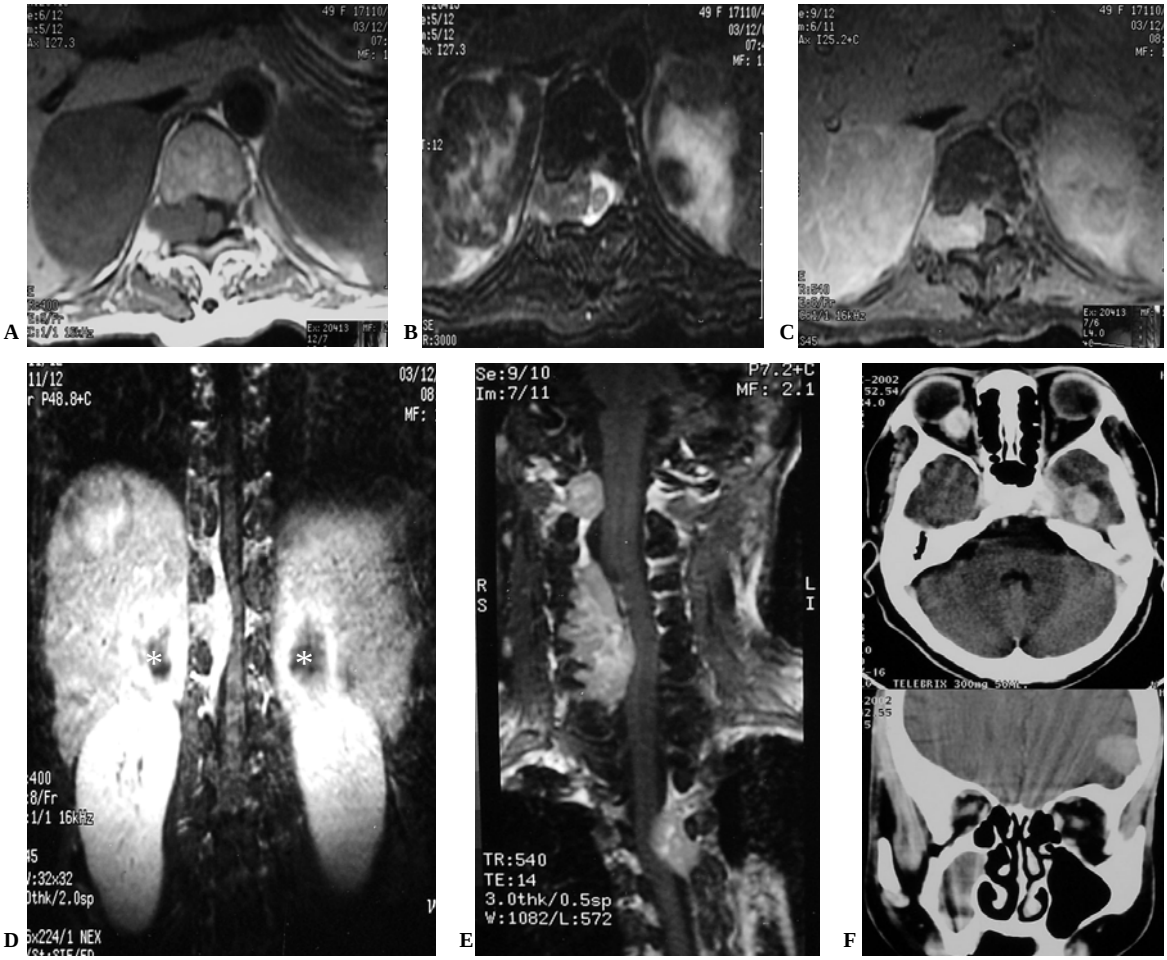

Fig. 2 Case III : A 40-year-old female presented with right hemiparesis. Axial image reveals a lobulated lesion expanding right neural foramen. This lesion shows inhomogeneous isosignal intensity to the spinal cord on T1-weighted image (A), slightly high signal intensity on T2-weighted (B) and heterogeneous enhancement after injection of contrast material (C). Post contrast coronal T1-weighted images at level of cervical (E) and thoracolumbar (D) spines demonstrate multilevel involvement at C1-C7, T12-L1 on the right side and T2 on the left side. Accidental findings of heterogeneous enhancing lesions at the bilateral suprarenal regions (*) and dome of the liver are noted. Post contrast axial and coronal CT images of the brain show two enhancing lesions in the left temporal lobe and left frontal lobe. The lesion in the left frontal lobe abuts the inner table of the left frontal bone which shows bony destruction. The other oval-shaped dense enhancing mass is also seen at the retrobulbar area

area for 3 months and low back pain for 1 month. She knew of HIV infection 1 year ago and did not receive any antiretroviral medications.

Imaging: MRI showed two irregular intraspinal-extramedullary masses at the level of T11 and L4 with local invasion to the adjacent bony structure. The masses showed hypointensity on T1 weighted image inhomogeneous hyperintensity on T2 weighted image with intense enhancement. Some areas of internal cystic or necrotic and also hemorrhagic, non-enhancing portions were noted. The lesions caused pressure effect and displacement of the adjacent spinal cord. Compromised exiting nerve roots in the corresponding neural foramina were also seen (Fig. 4).

The patient underwent laminectomy with tumor removal and palliative radiotherapy. Follow up CT brain and MRI of thoracic spine 5 months later disclosed intense enhancing, extra-axial masses at the right cerebellopontine angle cistern. Multiple residual and new tumors were noted at T7-8, 11 and 12 levels.

Operation and pathological findings: The specimen from tumor removal revealed densely-packed plump spindle cells, with hemangiopericytic vascular pattern. These tumor cells bore moderately pleomorphic

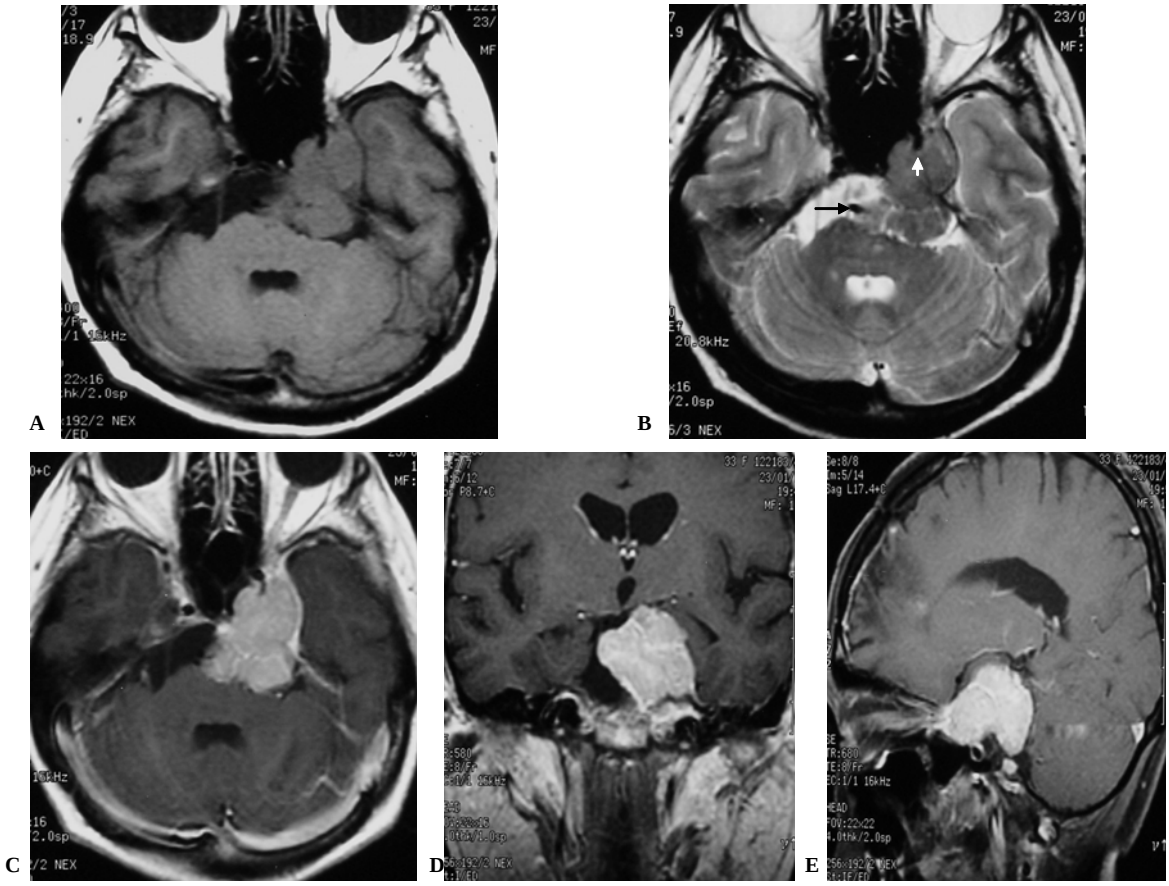

Fig. 3 Case IV: A 30-year-old female presented with left ptosis and total opthalmoplegia of the left eye. Axial T1-weighted (A) and T2-weighted (B) images show a 3x4 cm well-circumscribed extra-axial mass on the left side of the cavernous sinus and prepontine cistern, causing pressure effect on the pons and displaced basilar artery to the right side (black arrow). Encasement of the left internal carotid artery (white arrow) is noted.This lesion shows isosignal intensity to gray matter on T1-weighted image and minimally low intensity on T2-weighted image. Heterogeneous enhancement is observed after administration of contrast material (C,D and E)

nuclei with coarsely granular nuclear chromatin. The mitotic figures were rarely seen.

Case 6

History: A 35-year-old man presented with binocular diplopia and ptosis of the left eye for 1 month. There was no previous history of HIV infection before this illness. His serology for anti-HIV was positive.

Imaging: MRI of the brain showed two irregular, about 3-4 cm, extra-axial masses at the planum sphenoidale and posterior interhemispheric fissures. The massed appeared hypointense on T1 weighted image slightly hyperintense on T2 weighted image with intense enhancement.

Operation and pathological findings: Two settings of craniotomy with tumor removal were performed. The tumors were whitish, firm and hypervascularized. The tumor at the planum sphenoidale involved anterior clinoid processes and compressed on the optic chiasm. The posterior interhemispheric mass adhered to both-sides of the falx cerebri.

The microscopic features revealed interlacing fascicles of spindle-shaped tumor cells, with vesicular nuclei and small nucleoli. Although mitoses were rarely observed (0-1/10 HPF), approximately 4% of the tumor cells were reactive with Ki-67 (MIB-1). The tumor cells expressed smooth muscle actin and desmin, but were non-reactive with epithelial membrane antigen and S-100 protein.

During the post operative hospital course, the patient felt much pain at his right thigh with increased swelling of the tender area. MRI of the right thigh revealed an infiltrative mass with suspicion of neurovascular bundle involvement. The patient under-

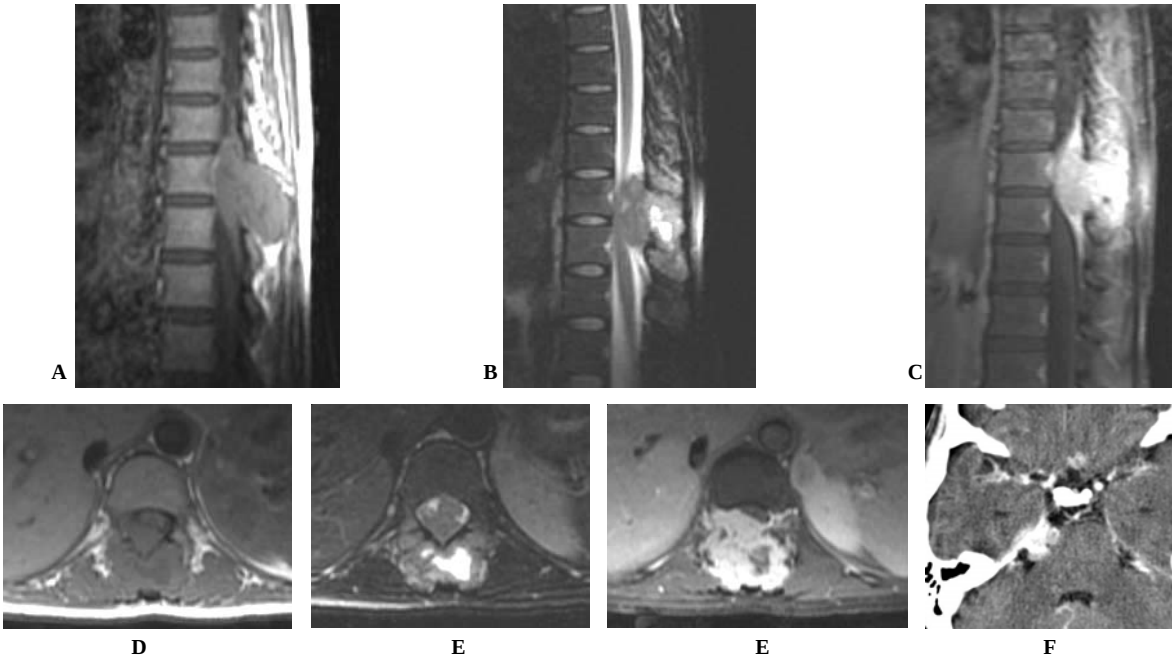

Fig. 4 Case V: A 31-year-old woman, presented with right subcostal pain and low back pain. Sagittal and axial T1WI (A,D), T2WI with fat suppression (B,E) and post contrast T1WI with fat suppression (C,F) reveal irregular intraspinal-extramedullary, 5 cm-mass at the level of T11, infiltrated posterior element and T11 body, showing hypointensity on T1WI, inhomogeneous hyperintensity on T2WI with intense enhancement. Some areas of internal cystic or necrotic component is seen. The mass causes pressure effect and displacement of the adjacent spinal cord. Another mass with the same characteristics is observed at L4 level (not shown here). Follow up CT brain later discloses dense enhancing, extra-axial masses at the right cerebellopontine angle cistern

went incisional biopsy of the mass and the specimen also showed the presence of leiomyosarcoma.

Discussion

Leiomyosarcomas are malignant neoplasms of smooth-muscle origin and are most commonly found in the genitourinary and gastrointestinal tracts, skin and blood vessels. The principle site of metastases include lung, bone and liver. The central nervous system is rarely involved[12]. Primary leiomyosarcoma of the CNS is exceedingly rare. However, there are seven reports in the literatures with 9 cases of primary CNS leiomyosarcoma in HIV-infected patients[13-19]. Two possibilities have been considered as the origin of leiomyosarcomas in the CNS. Such tumors may arise from the smooth muscle cells of the vasculature, as in the vascular leiomyosarcomas in other areas of the body. The pleuripotential mesenchymal cells are other possible source.

Both CT and MRI were extremely useful in preoperative study in the present cases. Site and extension of the lesion, and extrathecal nature of spinal cord compression were clearly defined by these non-invasive tests.

In the present study, intraspinal leiomyosarcomas from 4 patients are detected at multiple levels, the mostly in the level of thoracic spine. These masses mainly occupy the enlarged neural foramina with extradural and intradural extension, giving dumbbell appearance which mimic neurofibroma. An intraspinal leiomyosarcoma in an HIV-infected patient has been reported by Ann M. Ritter et al, occurring in a 35-year-old woman with AIDS who presented with weakness of the lower extremities. Her MR image demonstrated a tumor that appeared to originate in the vertebral body and pedicle with expansion into the epidural space, which resembled the appearance of the first case in the present study[19]. There are two reported cases of spinal dural leiomyosarcoma[10,13]. In one of these cases, an homogeneously enhanced extradural mass at T5 level was demonstrated in a 64-year-old female. In another case, a discrete subdural mass at C6 level was revealed in a 35-year-old male with HIV infection. Both of them demonstrated the dural attachment and, thus, grossly and radiographic, resembling a meningioma. All four cases of intraspinal leiomyosarcoma in the present study are radiological interesting, because the

appearance looks like neurofibroma showing tumor extension into the neural foramen. Dural-based appearance of these lesions are also detected on enhanced images. It seems likely that this tumor also arose from blood vessel elements, either from within the spinal dura or from epidural vessels creating a mass within the epidural space and neural foramen.

In the present study, there are two cases of intracranial involvement with pathological confirmation of leiomyosarcoma. The tumor involved left cavernous sinus and pontine cistern which demonstrated isointense to the gray matter on T1-weighted, slightly hyperintense on T2-weighted image with heterogeneous enhancement in one case. However, the lesion does not appear definitely dural-based. The preoperative differential diagnosis include meningioma and lymphoma. In the other case, dural-based appearance of the masses were demonstrated at the region of planum sphenoidale and at the posterior aspect of the falx cerebri. In another case of leiomyosarcoma involving multiple levels of the whole spine, multiple intracranial lesions were detected by CT but not pathologically proved. After reviewing the literature, the authors found six previously reported cases of intracranial primary leiomyosarcoma in HIV-infected patients. Three cases involved the cavernous sinus [15,17,19], two cases involved the right temporal dura [18] and the left dural transverse sinus [15] and the other one was located adjacent to the right occipital cortical surface [14]. Imaging characteristics of these six cases were suggestive of meningioma. Only one case of intracranial leiomyosarcoma was documented at the left side of the pontine cistern, mimicking schwannoma [16].

Multiple recent literatures document the association between the occurrence of EBV and leiomyosarcoma in patients with HIV infection. In situ hybridization and quantitative polymerase chain reaction (PCR) have been used to identify the EBV in malignant smooth-muscle cells tumor in patients with HIV infection, but not in human immunodeficiency negative patients. It may contribute to the pathogenesis of leiomyosarcoma in patients with HIV infection [19-21]. In the second case of the present study, the authors also demonstrated EBV infection in tumor cells by in situ hybridization. However, the tissue specimens of the remaining three cases were not study for EBV infection. Multifocal or multicentric locations are very rare in immunocompetent host [22]. In the present series the authors found multifocal lesions in 4 cases, this may suggest an EBV-associated leiomyosarcoma.

Conclusion

There is an increasing number of leiomyosarcoma involving the CNS in HIV-infected patients. They can mimic meningioma or neurofibroma on preoperative MR images. Further cases and further investigation of the pathogenesis of leiomyosarcoma will be necessary. Leiomyosarcoma should be included in the differential diagnosis of the CNS lesions in HIV-infected patients, because they may derive a similar benefit from aggressive antitumor therapy as immunocompetent individuals.

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การศึกษาลักษณะผิดปกติของภาพ MRI ที่ตรวจพบในเนื้องอกของกล้ามเนื้อเรียบที่เกิดขึ้นในบริเวณระบบประสาทส่วนกลางในผู้ป่วยเอดส์

สุกัลยา เลิศล้ำ, ศิริพร ลลิตอนันต์พงศ์, น้ำผึ้ง นำการุณอรุณโรจน์, ภัทราภรณ์ เชาวนะปัญจะ, ชุษณา สวนกระต่าย, ชนพ ช่วงโชติ

เนื้องอกของกล้ามเนื้อเรียบ (Leiomyosarcoma) ที่เกิดขึ้นบริเวณระบบประสาทส่วนกลางมีโอกาสพบได้ยาก แต่มีรายงานของโรคดังกล่าวเพิ่มมากขึ้นในผู้ป่วยที่มีภาวะภูมิคุ้มกันบกพร่อง รายงานนี้นำเสนอลักษณะผิดปกติของเนื้องอกดังกล่าวที่ตรวจพบจากการตรวจด้วยคลื่นสะท้อนในสนามแม่เหล็ก (Magnetic Resonance Imaging) ในผู้ป่วยเอดส์ 6 ราย ซึ่งได้รับการวินิจฉัยโดยการผ่าตัดพร้อมผลการตรวจทางพยาธิวิทยา การศึกษาแสดงลักษณะของโรคที่เกิดบริเวณตำแหน่งของช่องไขสันหลัง (spinal canal) ในผู้ป่วย 4 ราย ซึ่งแสดงลักษณะคล้ายเนื้องอกของเส้นประสาท (Neurofibroma) และเนื้องอกภายในกะโหลกศีรษะ 2 ราย ซึ่งแสดงลักษณะคล้ายเนื้องอกที่เกิดจากเยื่อหุ้มสมอง (Meningioma) ดังนั้นในกลุ่มผู้ป่วยเอดส์ที่ตรวจพบพยาธิสภาพแสดงลักษณะของก้อนในบริเวณระบบประสาทที่อยู่ในตำแหน่งของช่องไขสันหลังหรือตำแหน่งของเยื่อหุ้มสมอง จึงควรคำนึงถึง Leiomyosarcoma ในการวินิจฉัยแยกโรค