The imaging spectrum of HTLV-1 related neurological disease: a pooled series and review - Supplementary material

eTable 1: Adapted from Castro-Costa et al. 2006 detailing a modified model of the WHO diagnostic criteria for HAM/TSP.

	Definite	Probable	Possible
Clinical	Non-remitting, progressive spastic paraparesis +/- urinary and bowel signs/symptoms	Monosymptomatic presentation: spasticity or hyperreflexia in the lower limbs or isolated Babinski sign or neurogenic bladder confirmed by urodynamic testing	Complete or incomplete clinical presentation
Serological	Presence of HTLV-1 antibodies in serum and CSF confirmed by Western blot and/or a positive PCR for HTLV-1 in blood and/or CSF	Presence of HTLV-1 antibodies in serum and/or CSF confirmed by Western blot and/or a positive PCR for HTLV-1 in blood and/or CSF	Presence of HTLV-1 antibodies in serum and/or CSF confirmed by Western blot and/or a positive PCR for HTLV-1 in blood and/or CSF
Exclusion	Exclusion of other disorders that can resemble TSP/HAM	Exclusion of other disorders that can resemble TSP/HAM	Disorders that can resemble HAM/TSP have not been excluded.

eTable 2 Summaries of acute and subacute cases of HTLV-1 myelopathy described to date.

Publication	Age, sex, ethnicity	Presentation	Likely route of transmission	HTLV-1 status	Imaging	Treatment and Outcome
Gero et al. 1991[1] (n=1)	34 M, Afro-Caribbean	Progressive quadriparesis	Unknown.	Tested in CSF no further detail	Longitudinally extensive cervical transverse myelitis. Associated with diffuse intramedullary high T2w signal and swelling with peripheral enhancement.	Lost to follow up
Lima et al. 2007[2] (n = 7)	Mean age 49.5y All female	Lower limb weakness (5/7) Arthralgia (1/7) Lumbar pain (1/7)	Sexual contact (5/7) Blood transfusion (1/7) Vertical (1/7)	8.5 copies/ 100 cells	Oedematous cord lesion (1/7) Normal spine MRI (2/7) Not imaged (4/7)	Mean time from onset to wheelchair bound (8.5 months) (range 1 – 23 months)
Yoshida et al. 2002[3] (n = 1)	66 F, Japanese	3 week history of rapidly progressive lower limb sensory loss and paraplegia.	9 months post blood transfusion.	CSF:Blood ratio 128:1	Normal MRI thoracic spine.	Not documented
Nakagawa et al. 1994[4] (n = 14)	Mean age 62.6y Japanese Sex not documented	All had acute lower limb spasticity	Unknown. No prior blood transfusion or transplantation.	CSF:Blood ratio 512:1	Higher proportion of abnormalities in brain MRI study compared to slow progressors (86 vs 67%) Spine MRIs not consistently performed	Higher eventual disability grade in acute progressors (30% over grade 7 compared to 15% in chronic progressors)
Hayashi et al. 2008[5] (n = 1)	56 F Japanese	3 week history of progressive spastic paraplegia with sphincter dysfunction.	Unknown. No prior blood transfusion or transplantation.	129/10^4 PBMC and 1355/10^4 in CSF. CSF:Blood ratio 10.5	Longitudinally extensive cervical transverse myelitis with high T2w signal in the dorsal spinal cord.	Combination of pulsed methylprednisolone followed by pulsed cyclophosphamide Reduction in CSF proviral loads however had repeat exacerbations when therapy removed.
Olindo et al. 2010[6] (n = 1)	61 M Afro-Caribbean	2 week history of rapidly progressive paraplegia with co-existent sialadenitis and necrotic myositis. Bilateral optic neuritis 5 years previously.	Unknown. No prior blood transfusion or transplantation.	218,000/106 PBMC and 400,000/106 in CSF. CSF:Blood ratio 1.8.	Longitudinally extensive, cervical predominant, transverse myelitis with diffuse intramedullary high T2w signal and swelling spanning C2 to T1. No pathological contrast enhancement. Evidence of bilateral chronic optic neuropathy with atrophy. Normal intracranial appearances.	Pulsed IV methylprednisolone followed by 6/12 of oral corticosteroids. Significant improvement in clinical condition and resolution of imaging abnormalities
Kashata et al. 2013 (n = 1)	52 M Japanese	Acute gait disturbance followed by rapidly progressive spastic paraparesis and bladder dysfunction.	Unknown. No prior blood transfusion or transplantation.	High antibody titre (1:1024)	MRI not performed. Swollen thoracic spinal cord on CT myelography.	Treated with multivitamins including vitamin B12 and Interferon alpha. Patient deteriorated rapidly over 2 months and died. Post-mortem showed diffuse thoracic spinal cord swelling with peri vascular lymphocyte infiltration in the lateral columns and myelin pallor in the lateral and deep dorsal columns.
Cucca et al. 2016[7] (n = 1)	21 F Dominican	10 day history of rapidly progressive paraplegia and back pain. Co-infection with HIV blood and CSF (2700 copies/milliliter and 320 copies/milliliter)	Unknown. No prior blood transfusion or transplantation.	6.1 × 10e4 copies/milliliter PMBC 1.4 × 10e3 copies/milliliter CSF. High antibody titre	Longitudinally extensive cervical transverse myelitis with high T2w signal and pathological enhancement noted in the anterior horns. No intracranial lesions.	Abnormal spinal cord signal resolved on 2 month follow up scan but clinical symptoms persisted.
Crawshaw et al. 2018[8] (n = 1)	52 F Caucasian	New encephalopathy, left 6th and 3rd cranial nerve palsies and rapidly worsening lower limb weakness on a background of chronic HAM/TSP. Presented several months after trial of infliximab..	Unknown. No prior blood transfusion or transplantation.	120% in CSF 17.9% in PBMCs	Longitudinally extensive cervical transverse myelitis with dorsal diffuse high T2w signal and cord swelling without enhancement. Concomitant abnormal cerebral white matter lesions involving the corticospinal tracts and dorsal brainstem (see "Encephalopathy" section).	Symptoms improved and abnormal spinal cord signal resolved following course of pulsed methylprednisolone.
Caswell et al. 2019[9] (n = 1)	Age not stated, F Caribbean	Influenza-like symptoms followed by subacute, rapidly progressive paraplegia with wheelchair dependence at 5 months from symptom onset. Dual sphincter involvement and sensory impairment.	Sexual transmission with rapid onset of symptoms following transmission.	16.2% in CSF 0.3% in PMBCs	Longitudinally extensive cervicothoracic transverse myelitis spanning C2 to T10 associated with swelling and patchy enhancement.	High dose corticosteroids. Clinical outcome not stated.
Roc et al. 2019[10] (n = 1)	54 F, Caucasian	(1) Subacute lower limb spasticity 8 months after transplant	Post solid organ transplantation (kidney)	High CSF pVL 2340 HTLV-1 DNA copies per 10,000 mononuclear cells/ml).	Not documented	Not documented
Local case (not previously published)	54 F Caucasian	Subacute progressive paraplegia and bladder dysfunction developing over a one month period	Unknown No prior blood transfusion or transplantation.	CSF 16% , 1% in PMBCs	Longitudinally extensive transverse myelitis spanning lower cervical and upper thoracic spinal cord. Central intramedullary high T2w signal with central and peripheral enhancement along the dorsal and lateral spinal cord. Associated with diffuse swelling involving the entire spinal cord extending beyond the segment of abnormal signal.	Treated with corticosteroids with intermittent improvement. Waxing and waning course over next 5 years with gradual loss of bladder function and development of a sensory level at T10 over this timeframe
Local case (not previously published)	55 F	Rapidly progressive paraplegia and bladder dysfunction developing over two month period	Unknown. No prior blood transfusion or transplantation.	CSF 20% , 4.3% in PMBCs	Longitudinally extensive thoracic transverse myelitis. Central intramedullary high T2w signal without enhancement. Associated with diffuse swelling involving the entire spinal cord extending beyond the segment of abnormal signal. Additional white matter lesion along the left trigeminal root entry zone.	Symptoms and abnormal spinal cord signal improved following course of pulsed methylprednisolone.
Local case (not previously published)	45 F, Afro-Caribbean	Subacute progressive paraplegia with increased stiffness in left lower limb.	Unknown. No prior blood transfusion or transplantation.	19.1% PMBCs	Moderately longitudinally extensive transverse myelitis spanning three vertebral segments involving the upper thoracic spinal cord. Associated with diffuse central intramedullary high T2w signal and swelling. Bilateral trigeminal root entry zone lesions.	Symptoms improved following course of pulsed methylprednisolone.
Local case (not previously published)	54 M, Afro-Caribbean	Rapidly progressive paraplegia with leg and back pain over 1 year.	Unknown. No prior blood transfusion or transplantation.	CSF 34%, 15.9% in PMBCs	Longitudinally extensive thoracic transverse myelitis. Central intramedullary high T2w signal without enhancement. Associated with diffuse swelling involving the entire spinal cord extending beyond the segment of abnormal signal.	Partial improvement in weakness following treatment with methylprednisolone and methotrexate.
Local case (not previously published)	69 M, Afro-Caribbean	Subacute progressive low back pain, paraplegia, urinary incontinence and weight loss.	Unknown. No prior blood transfusion or transplantation.	CSF 17%, 0.6% in PMBCs	Spine: Subtle diffuse swelling of the entire spinal cord and abnormal signal in the upper thoracic spinal cord in the region of both lateral corticospinal tracts. Brain: Bilateral high T2w signal in the deep precentral white matter along the path of both corticospinal tracts.	Symptoms improved following course of pulsed methylprednisolone.

eTable 3 Pooled cases of HTLV-1-related encephalopathy confirmed with serological evidence and excluding other causes.

Publication	Case	Age, sex, ethnicity	Presentation	Likely route of transmission	Pre-existing HAM/TSP	HTLV-1 status	Imaging	Treatment and Outcome
Araga et al. 1989[11]	1	52, F Japanese	Meningo-encephalitis	Unknown No prior blood transfusion or transplantation.	No	CSF antibody 1:128	Cortical swelling and mild hydrocephalus on CT	Treated with prednisolone and antibiotics. Died from pneumonia.
Iwata et al. 1991[12]	2	49, M Japanese	Encephalopathy and ataxia	Unknown	No	CSF antibody 1:1	-	IV corticosteroids Marked improvement
Smith et al. 1992[13]	3	73, F African-American	Encephalopathy with seizures	Unknown	Yes (24 years prior)	CSF pVL = 52/100 CSF cells	Normal MRI	Phenytoin Died of pneumonia
Tachi et al. 1992[14]	4	13, F Japanese	Encephalo-myelopathy with myoclonic seizures	Blood transfusion	Yes (Several months prior)	Antibody 1:8192	Extensive confluent, poorly defined high T2w lesions in the parieto-occipital white matter which was felt ADEM-like.	IV corticosteroids and alpha-interferon. Died
Tateyama et al. 1999[15]	5	65, F Japanese	Encephalo-myelo-neuropathy	Blood transfusion	Yes (1 month prior)	Antibody present (Not quantified)	Patchy signal abnormality in cerebral white matter.	IV corticosteroids Ongoing myelopathy and neuropathy. Resolution of cognitive symptoms
Puccioni-Sohler et al. 2003[16]	6	41, F Brazilian	Myelopathy then encephalopathy with seizures	Previous blood transfusion and partner IVDU.	Yes (1 month prior)	CSF pVL = 26/100 CSF cells	Normal CT	IV corticosteroids Died of pneumonia
Mendes et al. 2014[17]	7	54, F Brazilian	Multisystem involvement presenting acutely with worsening spastic gait and cognitive impairment.	Blood transfusion	Yes	CSF 45% PMBCs 12.2%	Extensive symmetrical high T2w signal throughout the deep and subcortical temporal and frontoparietal white matter. Additional involvement of the external capsular white matter and pons.	Supportive treatment Persistence of cerebral white matter abnormalities with no clinical progression.
Local cases and previously reported by: Crawshaw et al. 2018[8]	8	35, F Caucasian	Fever, spastic paraparesis, seizures	Unknown	Yes	Case predated pVL measurements	No abnormality.	Spontaneous improvement 4 days later with mild residual amnesia.
	9	52, F Caucasian	3rd and 6th nerve palsies, blurred vision and marked cerebellar signs.	Unknown. No prior blood transfusion or transplantation.	Yes	CSF 120%, 17.9% in PMBCs	Symmetrical high T2w signal along both cortical spinal tracts from the precentral white matter to the brainstem. Splenial and bilateral middle cerebellar peduncle lesions and diffuse high T2w signal in the brain stem – most severely affecting the dorsal pons and medulla. Bilateral trigeminal root entry zone lesions. Subtle pathological enhancement related to the splenial lesion and lining the 4th ventricle. Synchronous acute myelopathy (see Table 2).	IV corticosteroids associated with improvement in clinical condition and partial resolution of MRI changes. Complicated by relapse with more extensive abnormal signal along both corticospinal tracts.
	10	43, F Afro-Caribbean	Hypothermia, global aphasia and reduced consciousness.	Unknown	Yes	CSF 130%	Ill-defined T2w pontine hyperintensities.	Recurrent episodes treated with repeated doses of cyclosporin and corticosteroids. Thermal dysregulation never resolved (likely due to hypothalamic damage). Imaging findings resolved.
Local case and previously reported by: King-Robson et al. 2021[18]	11	53, F Afro-Caribbean	3-week history of upper limb weakness and sensory change, with head tremor, diplopia and ataxia.	Sexual	Yes	CSF 72%, 36% in PMBCs	Patchy T2w hyperintensities in the deep and subcortical white matter of both frontoparietal regions. Further abnormal signal in both superior and middle cerebellar peduncles. Leptomeningeal enhancement along cerebellar folia, bilateral trigeminal nerve root enhancement and multifocal punctate deep cerebral white matter	IV corticosteroids followed by prednisolone and methotrexate. Symptoms improved and gained functional independence following therapy. Complicated by further relapses associated with new frontoparietal periventricular and perirolandic white matter lesions.

							enhancement in an apparent perivascular distribution. Abnormal signal along the left trigeminal root entry zone. Previous resolved lesions in the median precentral white matter bilaterally along the corticospinal tract.	
Local case not previously published.	12	50, F Caribbean	Subacute neurological swallowing difficulties. Increased dizziness and somnolence. Poor memory. Worsening increased tone.		Yes – rapidly progressive HAM over 10 months	CSF 30% PMBCs 5%	Partially confluent, bilateral frontoparietal and precentral predominant, poorly defined white matter lesions. Symmetrical high T2w signal along the CSTs of the pons and medulla. Progressive brainstem and spinal cord volume loss.	IV corticosteroids associated with improvement in tone.

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