






Neuroimaging Pearls from the MDS Congress Video Challenge. Part 2: Acquired Disorders

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ABSTRACT: The MDS Video Challenge continues to be the one of most widely attended sessions at the International Congress. Although the primary focus of this event is the presentation of complex and challenging cases through videos, a number of cases over the years have also presented an unusual or important neuroimaging finding related to the case. We reviewed the previous Video Challenge cases and present here a selection of those cases which incorporated such imaging findings. We have compiled these “imaging pearls” into two anthologies. The first focuses on pearls where the underlying diagnosis was a genetic condition. This second anthology focuses on imaging pearls in cases where the underlying condition was acquired. For each case we present brief clinical details along with neuroimaging findings, the characteristic imaging findings of that disorder and, finally, the differential diagnosis for the imaging findings seen.

Since the inaugural Video Olympics at the 2008 MDS International congress, the yearly event now known as the MDS Video Challenge continues to be the one of most popular and educational sessions at the International Congress. The event centers on the presentation of complex and challenging cases from around the world and most often the educational impact centers on the phenomenology or other clinical aspect of the history or examination and the way in which the selected experts navigate the case. Occasionally, however, these cases center on an unusual

or important imaging finding which serves not to distract from the phenomenology and other clinical findings, but instead augments them, creating a rich layered picture which can be gradually revealed to the attendant audience and movement disorders experts at this highlight of the International Congress. We have therefore compiled selected “imaging pearls” from prior Video Challenge events into two anthologies. The first anthology discussed imaging pearls in which the patient had an underlying genetic condition. This second anthology will focus on unusual

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or important imaging findings in those Video Challenges cases where the underlying condition was acquired.

We present here six cases of acquired movement disorders presented at previous Video Olympics/Video Challenge events. Rather than focus on the clinical history and examination findings, the descriptions below will predominantly focus on the relevance of the neuroimaging findings to these conditions. The cases include autoimmune disorders (case 1 and 2), disorders of hemodynamics or CSF dynamics (cases 3 and 4), movement disorders secondary to neoplasia (case 5), a toxic exposure (case 6) and an infection (case 7). Each case is presented in the same format: brief details of the clinical case are presented first along with neuroimaging findings; the characteristic imaging findings of that disorder are then outlined; and finally the differential diagnosis for the imaging findings seen is discussed.

Case 1: Marked Progressive Cerebellar Atrophy in anti-GAD Antibody-Associated Neurological Disorder

Summary of Case

A 54 year-old woman with a history of sickle cell anemia and hyperthyroidism status post radioactive iodine treatment presented with progressive dystonia and ataxia. Initial presentation was at 47 years old with sudden onset of left sided weakness, dysarthria, dysphagia and diplopia presumably from a right capsular stroke (although imaging did not show a convincing causative lesion). Months later, she developed episodic dystonic facial and right limb contractions triggered by physical activity and anxiety. On examination, she had a left hypertropia and bilateral exotropia, gaze evoked nystagmus, cerebellar dysarthria, limb dysmetria, and postural instability. Initially she was able to tandem walk with minimal assistance. Over the next few years, dystonia progressed with predominant findings of contractions of her face, jaw, hands and feet resulting in profound slowness of movement. At last follow-up, she was wheelchair bound due to profound generalized cerebellar ataxia, dystonia and spasticity.

Multiple investigations failed to provide a diagnosis until anti-GAD65 antibodies were found to be strongly positive in the serum (>1:4800) and CSF (high positive). After this result became available further questioning revealed that she had experienced episodic trunk stiffness and discomfort that had interfered with her ability to sit in her wheelchair. Examination at that time confirmed persistent excessive activity in her paraspinal and abdominal muscles.

Imaging

Fluid-attenuated inversion recovery (FLAIR) images from MRI of the brain performed from 2007 to 2013 demonstrated progressive atrophy of the cerebellar hemispheres, with progressively increasing size of the cerebellar sulci and the fourth ventricle

(Fig. 1). There was also progressive volume loss of the middle cerebellar peduncles and the pons.

Characteristic Imaging Findings of anti-GAD65-Associated Disorders

Reported imaging findings in anti-GAD65-associated disorders have been wide-ranging. These include classical T2-weighted hyperintensities in the mesial temporal lobes in the setting of autoimmune encephalitis¹ and more rarely T2-weighted hyperintensities in extralimbic areas (including thalamus, brainstem, striatum and middle cerebellar peduncle).^{1,2} Generalized atrophy, cortical/subcortical T2-weighted hyperintensity and hippocampal atrophy/hyperintensity are the most common findings in anti-GAD65-associated autoimmune epilepsy.³ Brain MRI is, however, frequently normal⁴ even in the setting of cerebellar ataxia with high anti-GAD65 titres.⁵ Cerebellar atrophy may, however, be present in up to 60% of patients with anti-GAD65-associated cerebellar ataxia,⁶ but this tends to be mild to moderate in severity.⁷ The degree of atrophy which evolved over time in this patient is unusual for an immune-mediated cerebellar disorder. Whether this degree of cerebellar atrophy contributed to this patient's progressive dystonia, a feature infrequently seen in this disorder,^{8–10} is unclear.

Differential Diagnosis of Imaging Findings

The differential diagnosis of preferential cerebellar atrophy includes neurodegenerative processes including hereditary ataxias and multiple system atrophy; toxic causes including exposure to alcohol, lithium, or phenytoin; post-radiation injury; chronic vertebrobasilar insufficiency; other antibody-mediated encephalopathies, which may be paraneoplastic or non-paraneoplastic; and JC virus granule cell neuronopathy.^{11,12}

Case 2: Tonic Spasms Secondary to Longitudinally Extensive Transverse Myelitis in Primary Sjogren Syndrome

Summary of Case

A 23 year-old woman presented with a one-month history of intermittent, involuntary, painful flexion of both wrists and metacarpophalangeal joints. This tonically flexed hand position, giving the appearance of clenched fists, would be maintained for 1–2 min and would recur 2–3 times/hour. The spasms predominantly occurred spontaneously but could also be triggered by sudden movements. Consciousness was preserved during the episodes. Two months prior to symptom onset, she presented with holocranial headaches, hiccups, and intractable vomiting. Examination revealed normal fundi, left hemi-sensory loss, bilateral brisk deep tendon reflexes, and upgoing plantars. Neuroimaging findings are discussed below. CSF aquaporin-4 antibodies were negative. Peripheral blood film demonstrated microcytic,

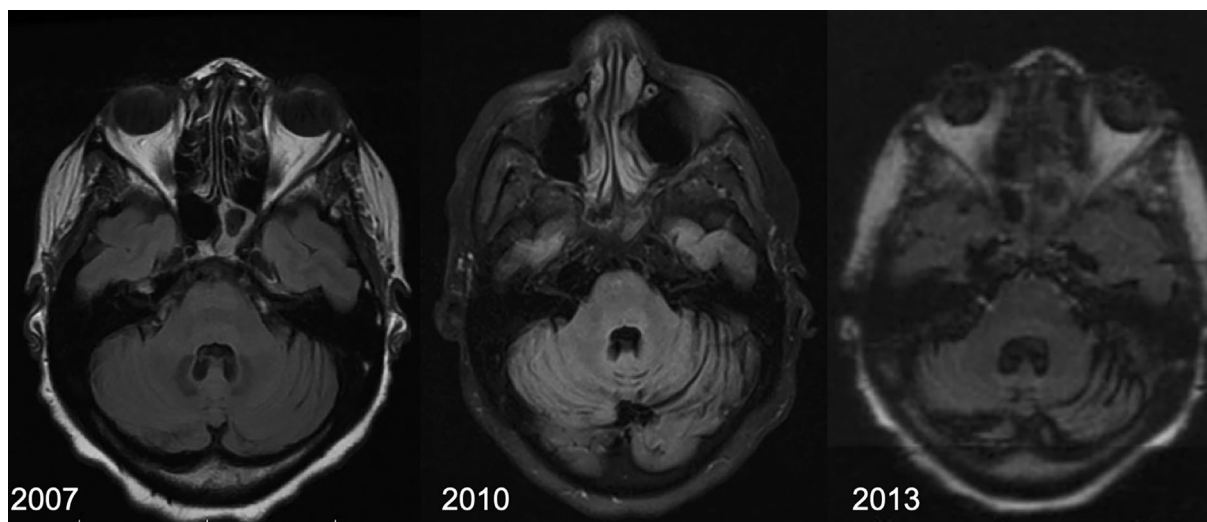


FIG. 1. Case 1: Sequential axial FLAIR images demonstrating progressive atrophy of cerebellar hemispheres, prominence of cerebellar sulci and fourth ventricle and volume loss in middle cerebellar peduncle and pons.

hypochromic anemia. Further testing for inflammatory causes revealed a strongly positive anti-Ro52 antibody and a diagnosis of Sjogren syndrome was made.

Imaging

MRI brain was unremarkable but MRI of the cervical spine revealed confluent T2 hyperintensity from C2 to C4/C5 without expansion of the cord (Fig. 2).

Characteristic Imaging Findings in Primary Sjogren Syndrome

Involvement of the nervous system in the primary Sjogren syndrome is rare, and predominantly affects the peripheral nervous system (5%–15%). Involvement of the central nervous system occurs in fewer than 5% of cases.¹³ Hyperintense signal changes in the deep, periventricular, and subcortical white matter (which may follow a perivascular distribution) on T2-weighted and

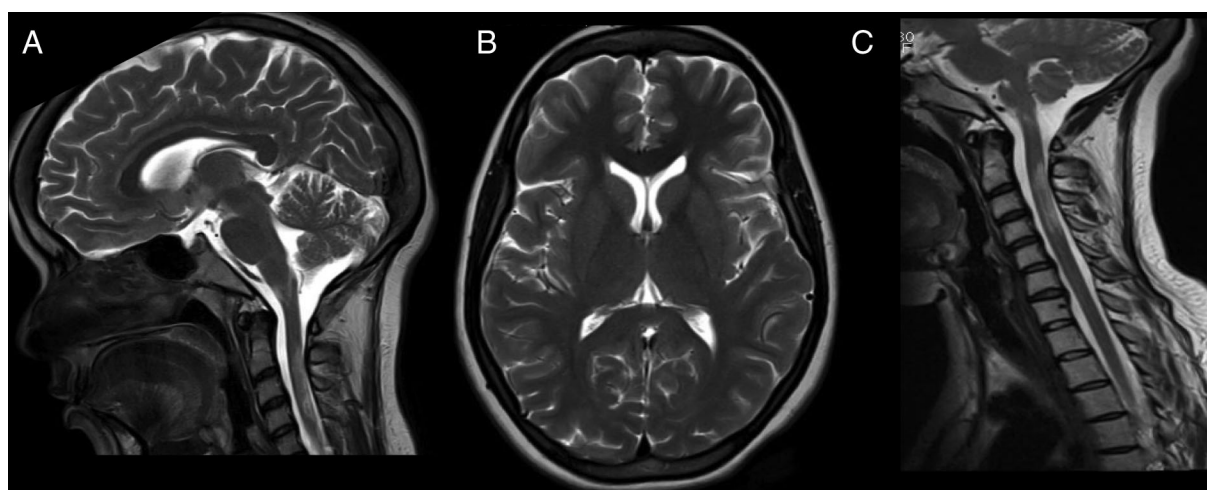


FIG. 2. Case 2: Axial and sagittal T2 imaging of the brain demonstrates normal appearance of the gray and white matter. In particular, the corpus callosum is unremarkable. Sagittal T2 imaging of the cervical spine demonstrates hypersignal within the cord, extending from the mid-C2 level to the C4-5 level (>2 vertebral bodies in length). There is no significant cord expansion.

FLAIR sequences are the most frequent MRI brain abnormalities seen in Sjogren syndrome.^{14–16} Punctate contrast-enhancing foci may be present in the pons, mesencephalon, middle cerebellar peduncles, and cerebellum.¹⁷ Hyperintense, non-enhancing, bilateral basal ganglia, thalamic, and brainstem lesions have also been reported.^{18,19}

Other MRI brain findings described include cranial nerve involvement (e.g. optic nerve T1-weighted hyperintensity with the enhancement of the optic chiasm), bilateral temporal lobar and hippocampal T2/FLAIR hyperintensities seen in the setting of limbic encephalitis, tumefactive lesions, and marked cerebellar atrophy.^{14,15,18–24} Central pontine myelinolysis, hemorrhage, lacunar infarcts, and leptomeningeal enhancement, have also been reported in some case series.^{14,15,18–24}

In Sjogren-related myelopathy, spinal cord involvement typically appears as longitudinally extensive T2 hyperintensities in the posterior columns without T1 gadolinium enhancement (although enhancement has also been described).^{16,22} Extensive lesions involving the entire spinal cord have also been rarely reported.²⁵ Sjogren's syndrome is therefore important to keep in mind in the differential of longitudinally extensive transverse myelitis (LETM).

Differential Diagnosis of Imaging Findings

The main imaging differential diagnosis for Sjogren syndrome is multiple sclerosis. The lesions in Sjogren syndrome are usually smaller than those in MS (although tumefactive lesions have been reported), they may affect cranial nerves, and generally do not involve the corpus callosum.²⁶ Larger, confluent lesions in Sjogren syndrome have to be distinguished from entities such as progressive multifocal leukoencephalopathy, acute disseminated encephalomyelitis (ADEM), lymphoma, metastases, abscesses, cysts and glioma.²⁶ The presence of a tumefactive lesion or multiple hyperintensities may make one consider adrenoleukodystrophy in the differential. Multiple hyperintensities in the posterior fossa, particularly when contrast-enhancing, may be concerning for vasculitis, e.g. Behçet's disease.^{14,20} Tuberculosis and brain metastases are important differential diagnoses for other contrast-enhancing posterior fossa lesions.¹⁴

LETM involving multiple spinal segments in Sjogren syndrome may mimic neuromyelitis optica spectrum disorder (NMOSD). Aquaporin-4 antibodies are frequently positive in Sjogren syndrome and these two conditions can co-exist.^{14,26} LETM may also be seen in other autoimmune inflammatory disorders (MS, ADEM or anti-MOG encephalomyelitis), systemic inflammatory disorders (Behçet's disease, systemic lupus erythematosus, antiphospholipid syndrome and sarcoidosis), infectious/parainfectious disorders (including coronavirus disease 19, tuberculosis, treponema pallidum, varicella-zoster, cytomegalovirus, Epstein Barr virus, HIV, HTLV-1, Lyme disease, schistosomiasis), neoplastic/paraneoplastic syndromes (B-cell lymphoma, astrocytoma, ependymoma), vascular diseases (spinal cord infarction, dural arteriovenous fistula), traumatic spinal cord injury, post-radiotherapy or in nutritional deficiencies (B12, copper deficiencies).^{27–30}

Case 3: Dementia and Parkinsonism Secondary to Intracranial Dural Arteriovenous Fistula

Summary of Case

A 64 year-old man with a 10-year history of left-sided tinnitus (noticed after minor trauma) presented with a six-month history of a progressive cognitive decline and personality change. He became apathetic, irritable, and dismissive. Three months later he became increasingly slow, unsteady, and had problems with dexterity. He was previously independent but now needed help with dressing. Family history was not contributory. Examination revealed a right-sided Horner's syndrome, scleral injection and parkinsonism. Masked facies, poverty of speech, utilization behavior, and bilateral bradykinesia (right>left) were present. His Luria test was impaired, he had a stooped posture, reduced arm swing, and postural instability.

Imaging

MRI brain showed nonspecific FLAIR hyperintensities within the white matter of the bilateral cerebral hemispheres (Fig. 3). Axial T1-weighted imaging post-gadolinium showed prominent enhancing vessels along the tentorium and within the temporo-occipital lobes bilaterally suggestive of a pseudophlebitic pattern in keeping with venous congestion. Axial T2-weighted imaging post-contrast showed corresponding prominent flow voids in keeping with venous congestion. Four vessel digital subtraction angiography showed extensive left sigmoid and transverse sinus dural AVF (dAVF), supplied by branches of vertebral arteries, ECA, tentorial branches of ICA (not shown). Embolization and ligation of the intracranial dAVF resulted in a complete resolution of symptoms.

Characteristic Imaging Findings of Intracranial Dural Arteriovenous Fistulae

Clinical symptoms of dAVF vary depending on the site of the fistula and the involved vessels. Dementia and parkinsonism occur relatively rarely (3%–12% of cases).³¹ Most cases are due to a high-grade dAVF located in the superior sagittal, transverse or sigmoid sinuses or rarely the straight sinus.^{32–36} The connection with the superior sagittal sinus may result in ischemia localized to the frontal and temporal lobes and basal ganglia.^{33,37}

The most common MRI brain imaging features suggestive of dAVF are diffuse T2-weighted/FLAIR hyperintensities and tortuous flow voids of venous channels.³¹ While FLAIR hyperintensities are most commonly found in the white matter, they may also occur in the basal ganglia (in isolation or in combination). The hyperintensities may also be minimal or absent.^{36,38} A combination of parkinsonism and T1-weighted hyperintensities (likely related to venous congestion) in the basal ganglia is also suggestive of dAVF.³⁹ The signal abnormalities may fluctuate

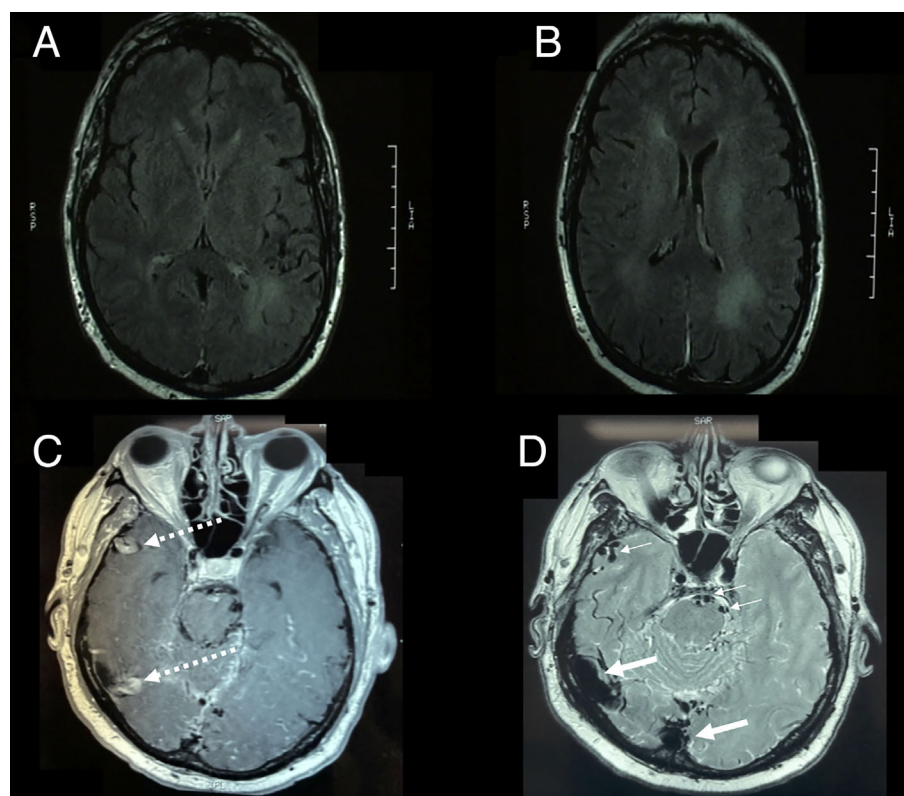


FIG. 3. Case 3: Axial FLAIR MRI brain at the level of the basal ganglia (A), the corona radiata (B); gadolinium-enhanced T1-weighted imaging showing enhancement of engorged vessels (dashed arrows) (C); axial T2-weighted imaging with gadolinium showing small flow voids anterior to the brainstem and in the right temporal lobe from engorged vessels (small arrows), and large flow void from dilatation of the torcula, right transverse and sigmoid sinuses (large arrows) (D).

and importantly reverse with endovascular treatment.³⁹ Additional findings may include engorged veins, venous infarction, intracranial hemorrhage, dilated leptomeningeal or medullary vessels or vascular enhancement.⁴⁰ Dilatation of the ventricular system was described in a single case associated with dementia.⁴¹

Diffusion-weighted imaging (DWI) can demonstrate increased, but not restricted diffusion (secondary to venous congestion) and susceptibility-weighted imaging (SWI) can show marked dilatation and hyperintensity within the sinus/vein suggestive of arterialized flow. Time-of-flight magnetic resonance angiography may show hypertrophied feeding arteries adjacent to the fistula.^{32,36,42}

The gold standard tool for diagnosis and endovascular treatment planning remains digital subtraction angiography (DSA).³² Distinctive features may include the dAVF location at the transverse-sigmoid sinus, reflux into the straight sinus, leading to congestion of the basal ganglia and parkinsonism as in the current case.³²

Differential Diagnosis of Imaging Findings

Collateral venous drainage mimicking dAVF is also an imaging feature of both acute and chronic dural thrombosis

(when the proximal segment recanalizes, while the distal outflow remains obstructed in chronic dural thrombosis).⁴³ Other differential imaging diagnoses include cerebral arteriovenous malformations (especially pial AVM/fistula), cavernous malformations, highly vascular tumors, jugular bulb pseudo-lesions, and, in cases of a dAVF adjacent to the brainstem, an infiltrating glioma.^{43,44} Finally, the confluent white matter lesions may also mimic acute leukoencephalopathy.⁴⁵

Case 4: Hemichorea Secondary to Intracranial Hypotension

Summary of Case

A 35 year-old man presented with a 4-month history of decreased left-hand dexterity, specifically for holding objects and performing fine motor tasks. The symptoms progressed, with involuntary movements of the left hand emerging. He developed near-constant “fidgetiness,” and these involuntary movements resulted in balance problems and falls. His past medical history included depression, ADHD and asthma. There was no history

of trauma. He did not take any medications, and his family history was non-contributory.

Examination revealed a vertical supranuclear gaze palsy, absent vertical OKN, left hemichorea, brisk deep tendon reflexes with crossed adductor reflexes, non-sustained bilateral ankle clonus, and an upgoing left plantar (downgoing on the right). Coordination was impaired with tasks involving the left upper extremity, with hemichorea interfering with most movements of the left side.

Imaging

Contrast-enhanced MRI of the brain showed inferior displacement of the brainstem, the splenium of the corpus callosum and cerebellar tonsils with associated venous distension (Fig. 4). MRI of the spine showed an epidural fluid collection suggestive of a CSF leak in the thoracic region (Fig. 4). Treatment with a single blood patch provided partial improvements in both balance and involuntary movement.

Characteristic Imaging Findings in Intracranial Hypotension Due to Spinal CSF Leak

The neuroimaging hallmark of intracranial hypotension is supra- and infratentorial pachymeningeal contrast enhancement which is found in 83% of cases.^{46,47} The enhancement is typically linear, non-nodular and becomes less prevalent over time.^{46–48} Spinal CSF loss leads to so-called “brain sagging” resulting from inferior displacement of the optic chiasm, cerebral aqueduct, cerebellar tonsils, and brainstem (pontomesencephalic angle $<50^\circ$, interpeduncular angle $<40.5^\circ$) which can be seen in 61% of cases.⁴⁸ This can result in development of subdural hematomas or hygromas or a pressure effect on the basal ganglia and their connections and hence movement disorders (including chorea which has been reported in three individuals to date).^{48–53}

Other features of intracranial hypotension include decreased ventricular size, effacement of the perichiasmatic/prepontine cisterns, and subarachnoid spaces.^{49,54,55} Compensatory venous

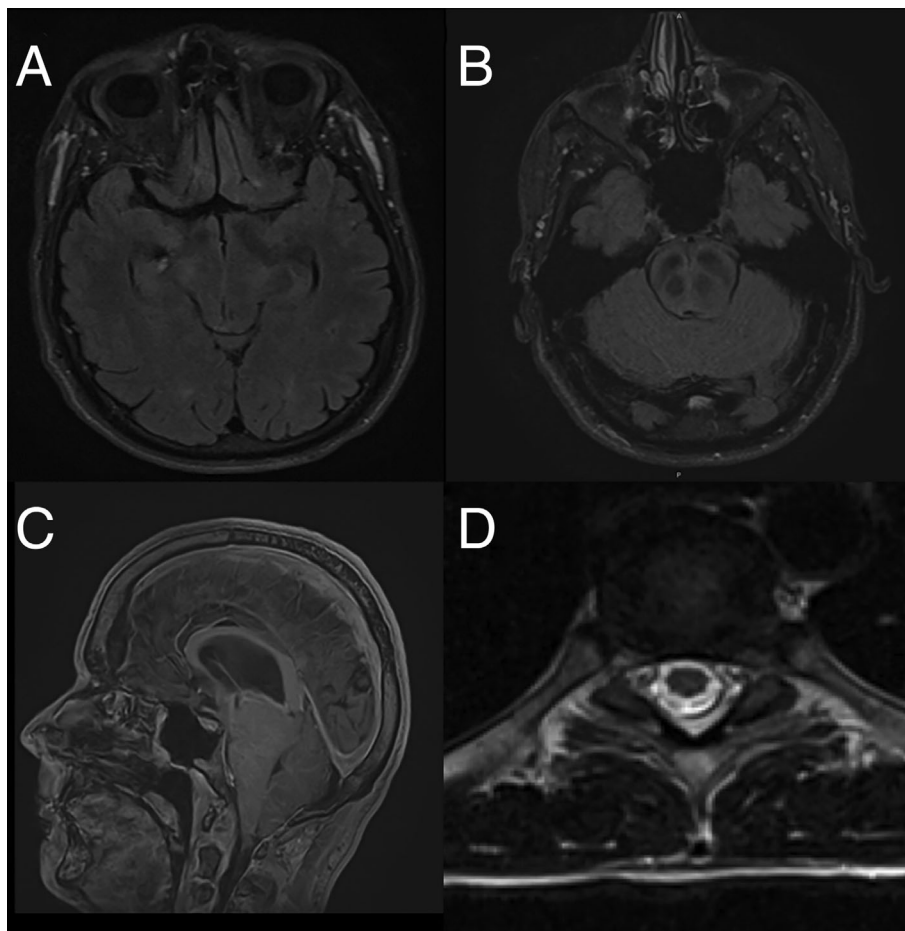


FIG. 4. Case 4: Axial T2 FLAIR MRI brain (A, B) and contrast-enhanced sagittal T1 (C) showing inferior displacement of the brainstem, splenium of the corpus callosum and cerebellar tonsils with associated venous distension. Axial T2 post-contrast MRI spine at the T6 level (D) demonstrating an epidural fluid collection suggestive of CSF leak.

dilatation (a convex distention of the inferior portion of the midpoint of the dominant transverse sinus) is found in 75%, and results in the enlarged dural venous sinuses, cranial nerves, and pituitary gland (which may enhance on post-contrast MRI and may demonstrate hemorrhage within).^{50,56} While MRI brain is a sensitive method of detecting intracranial hypotension (sensitivity 83%), it does not provide information on the CSF leak location and needs to be complemented by spinal MRI (94% sensitivity) and/or CT myelography.^{48,49,57} The most common location of the CSF leak is the thoracic spine (41%), followed by the cervicothoracic junction (25%), cervical spine (14%), and lumbar spine (12%) (leaks may be multiple).^{48,58} A CSF leak may go undetected in up to 50%.⁵⁹

Differential Diagnosis of Imaging Findings

The inferior displacement of the cerebellar tonsils is a common finding in intracranial hypotension and may be mistaken for a Chiari I malformation.⁶⁰ It is important to look for other features of intracranial hypotension, in order to avoid unnecessary surgery. The engorgement of the pituitary gland may be associated with hormonal changes and may be mistaken for a pituitary adenoma (similarly risking unnecessary resection).⁵² Dilatation of the inferior intercavernous sinus (suggesting a possible focal pituitary lesion), found in up to 50% of intracranial hypotension, may be seen in healthy individuals.⁶¹ In contrast to the smooth and diffuse dural enhancement seen in intracranial hypotension, the enhancement found in metastatic/granulomatous disease or prior subdural hematoma is either nodular or irregular, or limited to one region.⁶² It should be differentiated from post-lumbar puncture enhancement (seen in 5% of patients), and from infectious/carcinomatous meningitis which typically involves the leptomeninges (or neurosarcooidosis where leptomeninges are involved in up to 40%).^{62,63} Collagen disorders, infections (fungal, tuberculosis, syphilis, Lyme disease), intrathecal infusions, idiopathic hypertrophic pachymeningitis, hemodialysis, ventricular shunting and leukemia/lymphoma can all also cause diffuse pachymeningeal enhancement (albeit more irregular, nodular, and thin).^{49,63}

Case 5: Primary Central Nervous System Lymphoma Presenting As Rapidly Progressive Steele-Richardson-Olszewski Syndrome

Summary of Case

A 70-year-old man had shown abnormal behavior, bradyphrenia and a loss of verbal fluency beginning one month before presentation. On admission, there was a vertical supranuclear gaze palsy with impairment of convergence, marked facial hypomimia, hypophonia, neck and truncal rigidity and generalized bradykinesia. He had a wide-based gait with start hesitation, but he had no ataxia or tremors. Several days after admission, his level of consciousness declined. Following MRI (discussed

below) a transventricular endoscopic biopsy was performed. Histological examination revealed the characteristic findings of diffuse large B-cell lymphoma (DLBL). Treatment with a course of high-dose systemic methotrexate led to improvement in the imaging abnormalities as well as his clinical symptoms.⁶⁴

Imaging

Figure 5A,B,C: Sagittal T1 post-contrast image through the midline of the brain demonstrates two avidly enhancing mass lesions, one located at the pineal gland region with involvement of the tectum, and one located within the third ventricle with involvement of the midbrain tegmentum. The third ventricular lesion is also seen on axial T2 image where it demonstrates low signal. There is extensive bilateral and symmetric edema within the globus pallidus, internal capsules, thalami, hypothalami, cerebral peduncles and midbrain on axial T2 images. There is obstructive hydrocephalus at the level of the third ventricle with enlargement of the lateral ventricles.

Figure 5D,E,F: Following chemotherapy there is a marked improvement in the pre-treatment abnormalities.

Characteristic Imaging Findings of Progressive Supranuclear Palsy (PSP)

The hallmark imaging feature of PSP (particularly the Richardson syndrome variant (i.e. PSP-RS)) is preferential atrophy of the midbrain tegmentum.⁶⁵ The resulting morphology of the tegmentum on mid-sagittal MR imaging—flattening or concave contours at the rostral and caudal aspects with elongation of the interpeduncular fossa and preservation of pontine volume—has been termed the “hummingbird” or “penguin silhouette” sign.^{66,67} On axial imaging, atrophy with resulting concavity of the lateral margins of the midbrain tegmentum, with preservation of the cerebral peduncles and tectum, is referred to as the “morning glory flower sign” or “Mickey mouse” sign.^{65,68} In addition to midbrain atrophy, preferential atrophy of the superior cerebellar peduncles has been documented in PSP and is thought to correlate with disease duration.⁶⁹ Large scale studies aimed at evaluating the sensitivity and specificity of these imaging features for diagnosis of PSP are challenging to perform given the need for neuropathological comparison as the gold standard for diagnosis. While the identification of typical imaging features increases diagnostic confidence for PSP, imaging remains a supportive feature rather than a major component of the diagnostic criteria.⁷⁰

Differential Diagnosis of Imaging Findings

Neoplastic or inflammatory disorders that may cause a PSP-like syndrome include processes that result in compression or infiltration of the brainstem, particularly those localized in the pineal region. The main differential for the imaging findings seen here is germinoma which typically involves both the pineal gland and the floor of the third ventricle. Germinomas are, however,

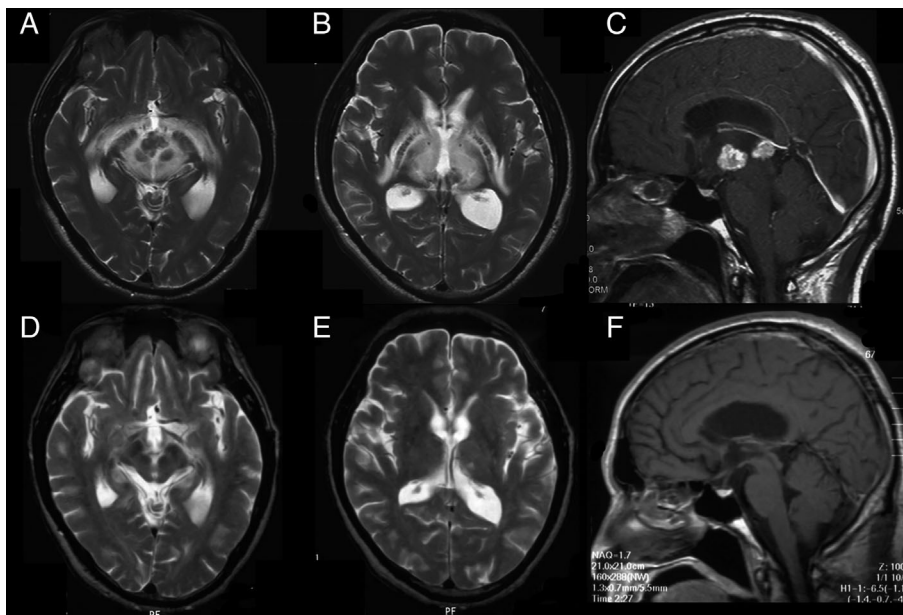


FIG. 5. Case 5: (A, B, C): Pretreatment axial T2 and sagittal T1 post-contrast images demonstrating two avidly enhancing mass lesions and extensive bilateral and symmetric edema within the globus pallidus, internal capsules, thalami, hypothalamus, midbrain and cerebral peduncles with obstructive hydrocephalus (see text for details) (D, E, F): Post-chemotherapy axial T2 and sagittal T1 post-contrast images demonstrating marked improvement in the pre-treatment abnormalities.

typical of younger patients with 90% of the cases presenting before the age of 20.⁷¹ Other differential diagnoses include high grade glioma, rosette-forming glioneuronal tumor, chordoid glioma of the third ventricle, pineal tumors with CSF dissemination and other, rarer tumors. As shown in the current case, CNS lymphoma may rarely present as a pineal region mass with low signal on T2 weighted imaging, avid enhancement, and mass effect with edema of the midbrain, thalami and basal ganglia. Differential diagnostic considerations include pineal-based tumors (pineocytoma, pineoblastoma), other extra-axial tumors that have a predilection for the pineal region (germ cell tumors, meningioma), or intra-axial tumors affecting the midbrain (glioma, metastases).⁷² Inflammatory or infectious disorders such as Whipple's disease, sarcoidosis, anti-IgLON5-associated disease or neurocysticercosis may also manifest with a PSP-like presentation.^{73–76}

Acknowledgement: this patient has been reported previously in a book chapter.⁶⁴

Case 6: T2-Weighted Thalamic Hypointensity in the Setting of Toluene Abuse

Summary of Case

A 16 year-old boy presented with an 8-month history of progressive difficulty walking and imbalance with frequent falls. He

was dysarthric with mild cognitive difficulty and outbursts of anger. He had normal birth and development and no prior medical history. No family members were affected.

Examination revealed interrupted pursuit with gaze-evoked horizontal nystagmus. He had a postural tremor of his right more than left upper limb in the wing beating position and an intention tremor with dysmetria, more prominent on the left than right. In addition, bilateral upper and lower limbs were spastic with upgoing plantars. His gait was ataxic.

Routine blood tests and copper studies were normal. Multiple bottles of eraser fluid (which contain toluene) were discovered in the patient's bedroom and it transpired that the duration of abuse was approximately 2 years prior to presentation.

Imaging

MRI brain demonstrated relative hypointensity of the thalami on FLAIR and T2-weighted imaging, with a similar appearance in the dentate nuclei, as well as hyperintensity of the white matter on FLAIR/T2 imaging best seen within the posterior limbs of the internal capsules bilaterally (Fig. 6). There was marked generalized atrophy of the brain parenchyma.

Characteristic Imaging Findings of Chronic Toluene Abuse

Chronic toluene abuse leads to progressive neurologic symptoms including cognitive impairment, cerebellar dysfunction,

extrapyramidal features and optic neuropathy.⁷⁷ The most common imaging finding is of periventricular white matter hyperintensities of variable extent which occur in 46% of chronic abusers.⁷⁸ These may be symmetric or asymmetric and potentially reversible on discontinuation of toluene.^{79,80} Corticospinal tract involvement and most notably Internal capsule hyperintensity (particularly of the posterior limb) appears to be a common finding, most likely as a result of demyelination and axonal degeneration.^{81–87} Cerebral infarction and perfusion abnormalities have also been reported.^{88,89} Less commonly, the cortical and deep gray matter may be involved.^{90,91} Generalized cerebral atrophy, thinning of the corpus callosum and cerebellar atrophy are common.⁷⁷ Thalamic T2 hypointensity is seen in approximately 20% of patients.⁷⁸ The combination of thalamic T2 hypointensity and adjacent internal capsule hyperintensity may represent an important diagnostic clue to the abuse of this substance.^{82,84,87,92,93} The “face of the giant panda sign,” a characteristic finding in Wilson’s disease has also been demonstrated in the setting of toluene abuse.⁸² Enquiry regarding epistaxis, facial rash, behavioral changes and observing for blisters around the nose and mouth,

unusual fetor, and conjunctival injection may increase diagnostic suspicion.

Differential Diagnosis of Imaging Findings

Bilateral symmetric T2 hypointensity of the thalami is an uncommon finding that has been reported in metabolic processes such as lysosomal storage disorders⁹⁴ (specifically GM1 and GM2 gangliosidosis, Krabbe’s disease, aspartylglucosaminuria, mannosidosis, fucosidosis, mucopolipidosis IV, and subtypes of neuronal ceroid lipofuscinosis), aceruloplasminemia, and metachromatic leukodystrophy.⁹⁵ Acquired processes including neoplasia (e.g. lymphoma) or hemorrhage (e.g. secondary to arterial or venous infarction, or hypertension) affecting bilateral thalami may also demonstrate low T2 signal, however these processes would typically be associated with mass effect, edema or enhancement, and are less likely to be bilaterally symmetric. T2 hypointensity of gray matter is not a common finding but has been previously described.⁹¹ T2 hypointensity in the basal ganglia most often occurs in the setting of iron deposition, and can be seen in normal aging,⁹⁶ Parkinson’s disease and Huntington’s

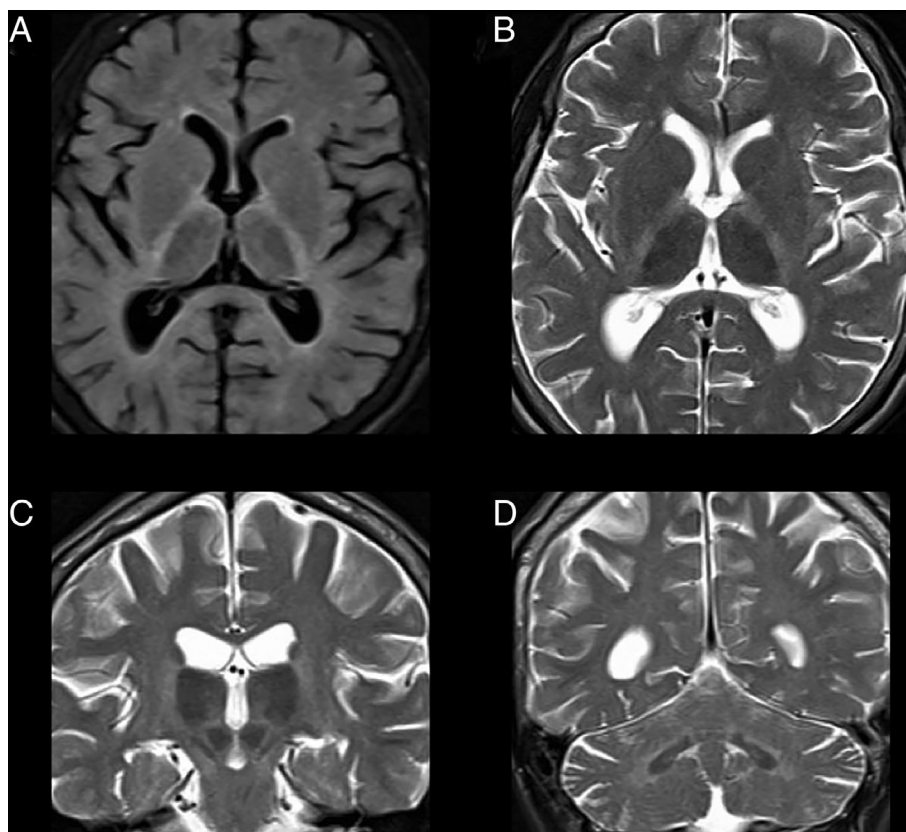


FIG. 6. Case 6: Axial FLAIR (A), axial T2-weighted imaging (B) and coronal T2-weighted imaging (C) demonstrating hypointensity of thalami bilaterally and hyperintensity of the white matter (most notably of the posterior limbs of the internal capsules) and marked generalized atrophy. Coronal T2-weighted imaging through the dentate nuclei (D) shows similar hypointensities in the dentate nuclei.

disease,^{97,98} multiple sclerosis,⁹⁹ Pantothenate kinase-associated neurodegeneration.¹⁰⁰ None of these conditions, however, with the possible exception of multiple sclerosis, typically result in concurrent T2 hypointensity within the thalamus.⁹¹

Confluent white matter hyperintensity involving the internal capsule can be seen most commonly in the setting of hypoglycemia^{101,102} but also in amyotrophic lateral sclerosis and Krabbe disease (both of which can affect the corticospinal tracts diffusely)^{103,104} and neuronal ceroid lipofuscinoses.¹⁰⁵ Symmetrical white matter hyperintensities involving the posterior limbs of the internal capsule and lateral brainstem are also seen in heroin vapor inhalation (“chasing the dragon”).¹⁰⁶ Hyperintensity of the posterior limb of the internal capsule is commonly seen in amyotrophic lateral sclerosis¹⁰⁷ but none of the above disorders (apart from Krabbe disease) demonstrate concomitant thalamic T2 hypointensity.

Case 7: Holmes’ Tremor Due to Hemorrhagic Pontine Gnathostomiasis Causing Hypertrophic Olivary Degeneration

Summary of Case

A 46 year-old Thai woman developed a sudden onset of right-sided weakness and numbness with diplopia and intermittent throbbing headache 8 months previously. As the symptoms were

not severe at the beginning, she did not seek any medical attention. While weakness gradually improved, she noticed abnormal movements of her right hand developing 2 months after the initial onset. No prior medical history was available. On examination, a low-frequency right-sided tremor was most noticeable in her right hand, present both at rest and with action. There was also abnormal posturing of her right fingers in association with a flexion-extension tremor of the fingers. With posture and action, tremor amplitude became more pronounced with associated overflow and right finger-to-nose ataxia. Low-frequency palatal tremor was also evident on examination. Eye movement examination demonstrated vertical pendular nystagmus. Laboratory investigations revealed elevated WBC of 10,200 with 15% of eosinophils. CSF showed no pleocytosis with normal protein and sugar. Given the imaging findings below and eosinophilia, CSF gnathostomiasis IgG Ab was tested and was positive.

Imaging

Selected images from axial T2-weighted sequence at the level of the midbrain/pons demonstrates heterogeneous, predominantly low T2 signal abnormality with a linear morphology in the dorsal pons, preferentially localized to the left of midline (Fig. 7). On coronal gradient echo sequence, there is associated blooming artifact suggestive of hemorrhage (or mineralization). There is an adjacent T2 hyperintense focus at the right pontomesencephalic junction that may represent an associated cyst or edema. Axial T2 weighted image at the level of the medulla demonstrates hypersignal and enlargement of the left inferior olivary nucleus.

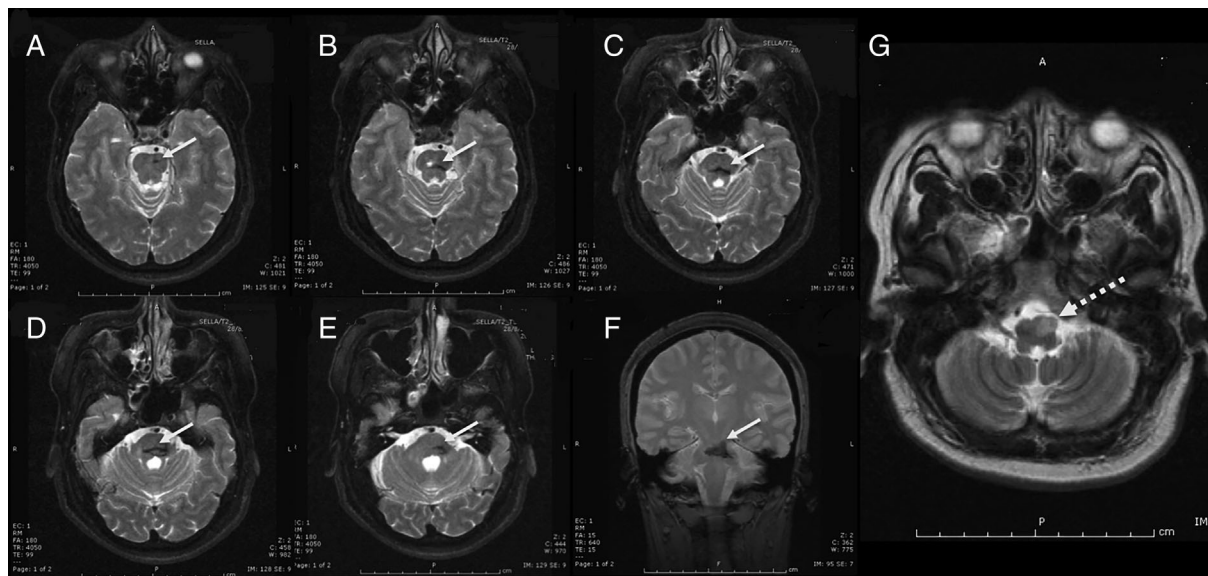


FIG. 7. Case 7: Axial T2-weighted images demonstrating focal area of predominantly T2 hypointensity in the left midbrain and pons (see text for details) (A–E); coronal gradient echo sequence demonstrating associated blooming artifact (F); (G): Axial T2-weighted image at the level of the inferior olive showing olivary hypertrophy and hyperintensity (hatched arrow).

Characteristic Imaging Findings of Gnathostomiasis and Hypertrophic Olivary Degeneration

Gnathostomiasis is a parasitic infection caused by *Gnathostoma spinigerum*, which is endemic to Southeast Asia, Central and South America, and is predominantly acquired by consumption of raw freshwater fish or shellfish.¹⁰⁸ Several case reports and case series have described imaging findings of neurologic gnathostomiasis.^{109,110} Brain imaging in affected patients has revealed several typical features, including: linear signal abnormality suggesting spread along a white-matter tract, with associated hemorrhage; multifocal hemorrhage; prominent Virchow-Robin spaces; periventricular T2 hyperintensities; brainstem involvement; and multifocal nodular enhancement in affected areas. Imaging abnormalities of the spinal cord have also been reported, specifically long-segment T2 hyperintense signal change with cord expansion consistent with myelitis. Involvement of the cauda equina has also been reported with hemorrhage, enhancement, and nerve root clumping (arachnoiditis).¹¹¹

Hypertrophic olivary degeneration (HOD) is a unique form of neuronal degeneration most commonly resulting from a lesion along the dento-rubro-olivary pathway, also referred to as the Guillain-Mollaret triangle.¹¹² Cerebellar or brainstem destructive lesions, typically involving the outflow from the dentate nucleus, decussating in the midbrain around the red nucleus to the contralateral central tegmental tract result in denervation of the inferior olivary nucleus. The most common clinical manifestation is symptomatic palatal tremor; oculopalatal tremor (palatal tremor with pendular nystagmus) may also be present.¹¹³ The characteristic MRI findings of HOD follow three phases: (1) high T2 signal within the ION without hypertrophy, generally within the first 6 months post-ictus; (2) high T2 signal and hypertrophy of the ION, lasting from 6 months to 3–4 yr post-ictus; and (3) high T2 signal with resolution of hypertrophy, which can persist indefinitely.¹¹⁴ This is accompanied by a brainstem or cerebellar lesion that is most commonly vascular in origin, usually hemorrhagic rather than ischemic, with a wide variety of other potential pathologies including traumatic, neoplastic, surgical, inflammatory or demyelinating.¹¹³ Histologic studies have demonstrated macroscopic hypertrophy of the inferior olivary nuclei with corresponding neuronal swelling and vacuolization, gliosis and demyelination, ultimately leading to atrophy.^{113,114} While HOD is most commonly unilateral, it may be bilateral. Bilateral HOD is also a characteristic feature of sporadic progressive ataxia and palatal tremor (sporadic PAPT), in the absence of a structural cerebellar or brainstem lesion.¹¹⁵

Differential Diagnosis of Imaging Findings

As suggested above, the dorsal pontine linear signal abnormality and associated hemorrhage is consistent with gnathostomiasis. The presence of an associated pontomesencephalic cyst in addition to the elevated white cell count and eosinophilia forces other infective causes to be considered in this case. Eosinophilic meningoenzephalitis may also be caused by parasitic infection

with *Angiostrongylus cantonensis*, *Baylisascaris procyonis*, other helminthic parasitic infections including toxocariasis, trichinosis, cysticercosis, schistosomiasis, fascioliasis, and paragonimiasis, or fungal infection with coccidioidomycosis.¹¹⁶ While neuroimaging findings of angiostrongyliasis and gnathostomiasis may overlap, reports suggest gnathostomiasis more commonly manifests with intracerebral hemorrhage and myelitis patterns (without clinical evidence of meningitis, as in our case), whereas angiostrongyliasis may show normal neuroimaging or abnormalities limited to the meninges.^{110,117} Infection with *Baylisascaris procyonis* is less common, with several case reports describing a predilection for the periventricular white matter with FLAIR/T2 signal abnormality and enhancement evolving to chronic atrophy.¹¹⁸ Imaging manifestations in neurotoxocariasis are highly variable, ranging from isolated myelitis, to multiple ring-enhancing lesions, to leptomeningeal enhancement with hydrocephalus, to vasculitis with multifocal ischemia.¹¹⁹ Given the wide range of imaging manifestations of causative organisms and the possibility of significant overlap in imaging appearance, the diagnosis is generally made on the basis of clinical features, detailed exposure history, CSF and serologic testing, and potentially even tissue biopsy.

Differential diagnosis of a focal T2 hyperintense lesion with hypertrophy of the inferior olivary nucleus could include subacute vertebrobasilar perforator infarct, focal neoplasm (astrocytoma, metastasis or lymphoma), or an infectious or inflammatory process (multiple sclerosis, rhombencephalitis, sarcoidosis, etc.). However, other entities may show restricted diffusion (infarct, infection) or enhancement (subacute infarct, neoplasm, active inflammation or infection), which would not be expected in HOD, and also would not follow the typical temporal progression of imaging findings expected in HOD. Additionally, the presence of an associated brainstem lesion and the typical clinical features of oculopalatal tremor would help confirm the diagnosis of HOD.

Discussion

Neuroimaging continues to be an essential paraclinical aid in the diagnosis of many movement disorders. As next generation sequencing continues to become more widely available, diagnoses in movement disorders are increasingly being made via genetic panels or whole exome sequencing approaches, often bypassing the need to exclude alternative diagnoses through an exhaustive work-up. Acquired movement disorders lack this luxury and neuroimaging remains an essential part of the diagnostic work-up for these conditions. The cases presented here along with those presented in our accompanying anthology (“Neuroimaging Pearls from the MDS Congress Video Challenge I: Genetic Disorders”) are an attempt to capture and document some of the key imaging pearls that have been presented at the MDS Video Challenge but which could easily be forgotten given the emphasis on the videotape documentation of critical phenomenology in this session.

Author Roles

(1) Research project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript: A. Writing of the first draft, B. Review and Critique.

C.F.: 1A, 1B, 1C, 3A

S.R.: 1A, 1B, 1C, 3B

D.A.O.: 1A, 1B, 1C, 3A

P.A.L.: 3B

D.S.K.: 3B

S.S.: 3B

S.K.J.: 3B

J.M.K.M.: 3B

A.D.H.: 3B

R.S.S.: 3B

V.S.C.F.: 3B

C.S.: 3B

L.A.: 3B

T.H.: 3B

Y.O.: 3B

N.H.: 3B

S.S.: 3B

H.K.: 3B

R.B.: 3B

C.L.: 3B

A.E.L.: 1A, 1B, 1C, 3B

Disclosures

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