Imaging of Drug-Related Vasculopathy

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KEYWORDS

• CNS • Vasculitis • Vasculopathy • Drug-related • Cocaine-induced • Levamisole • RCVS • PRES

KEY POINTS

- Cocaine-induced CNS vasculitis is produced by additives/contaminants added to cocaine, mainly levamisole.
- Cocaine-induced midline destructive lesion should be considered in any structural lesion of the sinonasal complex in the context of a positive toxicologic screening or confirmed cocaine-snorting habit.
- Marijuana is the most prevalent triggering factor in reversible vasoconstriction syndrome secondary to substance abuse.
- The risk of CNS vasculopathy associated with sympathomimetic or immunosuppressant drug therapy increases in patients with impaired renal and hepatic function.

INTRODUCTION

Illicit drugs and medications represent an important etiologic factor in patients with vasculopathy. This type of vascular injury has been recognized as a separate entity under the 2012 revised Chapel Hill Consensus Conference Nomenclature of Vasculitides.[1] Drug-associated antineutrophil cytoplasmic antibodies (ANCA) vasculitis has been described with cocaine, antithyroid drugs, and hydralazine. Other drugs may have direct toxicity on the vascular endothelium (immunosuppressants and oncologic medications) or affect the integrity of the vessels through their sympathomimetic mechanism (marijuana, amphetamines, sympathomimetic drugs). This article reviews the pathomechanism, clinical presentation, and imaging findings of vasculopathy related to recreational drug abuse and prescribed medications.

IMAGING TECHNIQUE AND PROTOCOL

Magnetic resonance (MR) imaging is the modality of choice for the evaluation of patients with suspected central nervous system (CNS) vasculopathy. Recommended sequences include diffusion-weighted imaging (DWI), susceptibility-weighted imaging (SWI), T2-weighted images (WI), fluid-attenuated inversion recovery (FLAIR), and T1WI-post intravenous contrast administration. MR time of flight (TOF) or MR angiography (MRA) is recommended to visualize the vessels' lumen to detect stenosis, occlusion, or aneurysms. CT, combined with CT-angiography (CTA), is an alternative to MR imaging when this is contraindicated or unavailable.

Vascular lumen imaging has been the cornerstone in evaluating intracranial and extracranial vascular diseases. Imaging modalities such as

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CTA, digital subtraction angiography (DSA), and MRA rely on the opacification of the vascular lumen following intra-arterial (DSA) or intravenous (CTA, MRA) contrast administration. Alternatively, the development and dissemination of MR pulse sequences with high spatial resolution, multiplanar 2D or 3D acquisition, multiple tissue weightings, and suppression of signal in luminal blood and CSF have allowed the use of specific MR sequences to evaluate the vascular wall of the circle of Willis and second-third order intracranial arterial vessels.[2] As a result, the direct visualization of the vessel wall on vessel wall MR imaging (VW-MR) is a valuable adjunct to conventional imaging to differentiate among causes of intracranial arterial narrowing such as atherosclerosis, vasculitis, reversible cerebral vasoconstriction syndrome (RCVS), and arterial dissection.

ILLICIT DRUG-ASSOCIATED VASCULOPATHY

Central Nervous System Complications Associated with Cocaine Abuse

Cocaine is the most common illegal stimulant drug worldwide. It is highly addictive and has a high lipid solubility, which accounts for its rapid diffusion across cell membranes. This substance blocks catecholamine absorption, resulting in the vasoconstriction of blood vessels, elevation of blood pressure, tachycardia, and increased cardiac output.[3,4] Most commonly, cocaine is sniffed as cocaine hydrochloride, although it can also be smoked (the alkaloidal form known as crack) or injected.[4,5] Drug effects include a brief but intense euphoria, enhanced energy, and alertness.

Cocaine abuse has been associated with various neurologic complications, mainly ischemic and hemorrhagic strokes, induced directly or indirectly by additive substances in contaminated samples. For unknown reasons, the drug's hydrochloride form is linked to significantly greater rates of hemorrhagic strokes than its alkaloidal form, which causes an equal frequency of ischemic and hemorrhagic events.[6]

Around 40% to 50% of patients with hemorrhagic strokes (intraparenchymal and subarachnoid) have concurrent pathology, such as cerebral arteriovenous malformations or aneurysms (**Fig. 1**), which rupture as a result of cocaine's sympathetic effects.[4,7,8] In cases where it is impossible to document concomitant vascular pathology, intraparenchymal bleeding is most commonly located in the basal ganglia and thalami.[9]

The causes of ischemic stroke are diverse and include drug-induced thrombosis caused by increased platelet aggregation, vasospasm, cardioembolism, accelerated atherosclerosis, and cerebral vasculitis.[5,10,11] Brain infarcts are primarily located in the subcortical white matter (watershed infarctions), in the middle cerebral artery territory (see **Fig. 1**), and in the mesencephalon. The latter is more frequently involved when cocaine is combined with amphetamines.[9]

Cocaine-induced CNS vasculitis, which seems to be produced by additives/contaminants added to cocaine, mainly levamisole, is usually associated with intranasal drug administration.[12] In addition to brain infarcts found in cross-sectional imaging studies, focal constrictions of the main arteries might be identified in angiographic studies. In contrast, VW-MR imaging identifies concentric enhancement of the vessel wall, a feature that distinguishes this condition from isolated drug-induced vasospasm.[9]

Rarely, cocaine produces a toxic encephalopathy from direct effects after intravenous or nasal administration. Brain MR imaging shows diffuse high-signal intensity lesions on T2-WI involving the subcortical and deep white matter, the corpus callosum, and the deep gray matter (pallidum) associated with diffusion restriction (**Fig. 2**).[13] Cocaine-induced blood pressure imbalance can even cause reversible cerebral vasoconstriction syndrome (RCVS) and posterior reversible encephalopathy syndrome (PRES) (**Fig. 3**).[8,14] Finally, transitory spinal cord ischemia or infarction has been described in cocaine users, and it should be considered in the differential diagnosis of acute nontraumatic myelopathy.[15]

Levamisole-induced Multifocal Inflammatory Leukoencephalopathy

Levamisole is an anthelmintic agent with significant immunomodulatory properties, commonly used as an additive to cocaine[16] as it enhances and extends its stimulating effects. Chronic exposure to levamisole may cause serious side effects, including skin necrosis, agranulocytosis, cutaneous and CNS vasculitis, and a potentially lethal MIL.

The physiopathology of levamisole-induced MIL likely depends to a large extent on an immunologic mechanism, given that biopsy specimens show lymphocytic infiltrates, the condition responds to immunosuppressive therapy, and it typically has a latent period of at least 2 weeks after cocaine use.[17]

Imaging findings in MIL include multiple inflammatory-demyelinating-like lesions, predominantly involving the frontal and parietal subcortical and periventricular white matter (**Fig. 4**), the basal ganglia, and the brainstem.[18] The lesions show

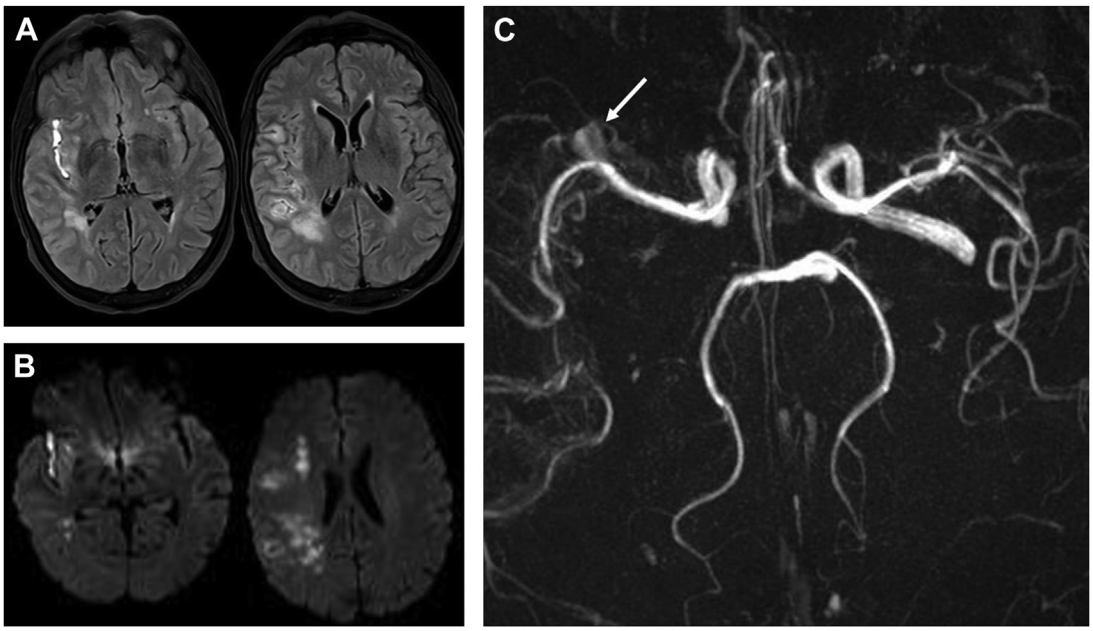

Fig. 1. Acute infarctions associated with subarachnoid hemorrhage in a patient with a history of cocaine abuse. Axial FLAIR (*A*) and diffusion-weighted (*B*) images show acute infarcts in the right MCA territory and subarachnoid hemorrhage within the right Sylvian fissure. MRA shows a small saccular aneurysm at the right MCA bifurcation (*arrow* in C).

variable degrees of surrounding vasogenic edema and peripheral restricted diffusion, with mild or no mass effect. Ring enhancement can be detected in up to one-third of cases.[18] Single or multifocal tumefactive and Balo-like demyelinating lesions, with the typical concentric rings on T2-WI, associated with peripheral diffusion restriction and contrast enhancement, are unusual findings (**Fig. 5**).[19,20]

The diagnosis of levamisole-induced MIL based on MRI findings is complex, and it should always be considered in the context of the patient's clinical setting (chronic cocaine use) or following positive results of toxicologic screening tests. Differential diagnosis includes inflammatory-demyelinating disorders such as multiple sclerosis (MS) or acute disseminated encephalomyelitis (ADEM). Patients with levamisole-induced MIL are commonly treated with steroids and have a good clinical outcome.[20]

Cocaine-induced Midline Destructive Lesions

The recurrent vasoconstrictive effect in the nasal mucosa induced by chronic intranasal cocaine use has the potential to produce the so-called CIMDL. This repetitive vasoconstriction causes progressive damage leading to ischemia and subsequent necrosis of the mucosa lining and underlying structures.[21,22] Additional pathomechanisms include chemical irritation, mechanical trauma from high-velocity inhalation, the toxic effect of adulterants mixed with cocaine (amphetamines or caffeine), secondary bacterial infection, antineutrophil cytoplasmic antibodies formation, immunosuppression, and osteoblast inhibition.[22–24]

Patients with CIDML present self-limiting epistaxis, rhinorrhea, and scabs, sometimes associated with olfactory dysfunction (hyposmia or anosmia), likely induced by direct damage to the neuroepithelium by cocaine or its adulterants or by the potential obstruction of the olfactory cleft by inflammation and mucosal edema.[25,26]

The typical features of CIDML are usually detected on CT. Common imaging findings include the opacification of the paranasal sinuses and mucoperiosteal thickening of the nasal cavity and paranasal cavities. Progressive involvement of the sinonasal region with eventual erosion and destruction of the mucosa and bony structures is typical. The starting point of CIDML seems to be the nasal septum, which may spread across the inferior third of the sinonasal complex, including the nasal floor and the inferolateral nasal wall (inferior turbinate and maxilla) (**Fig. 6**). From this point, the disease may extend superiorly toward the middle third of the sinonasal complex (middle

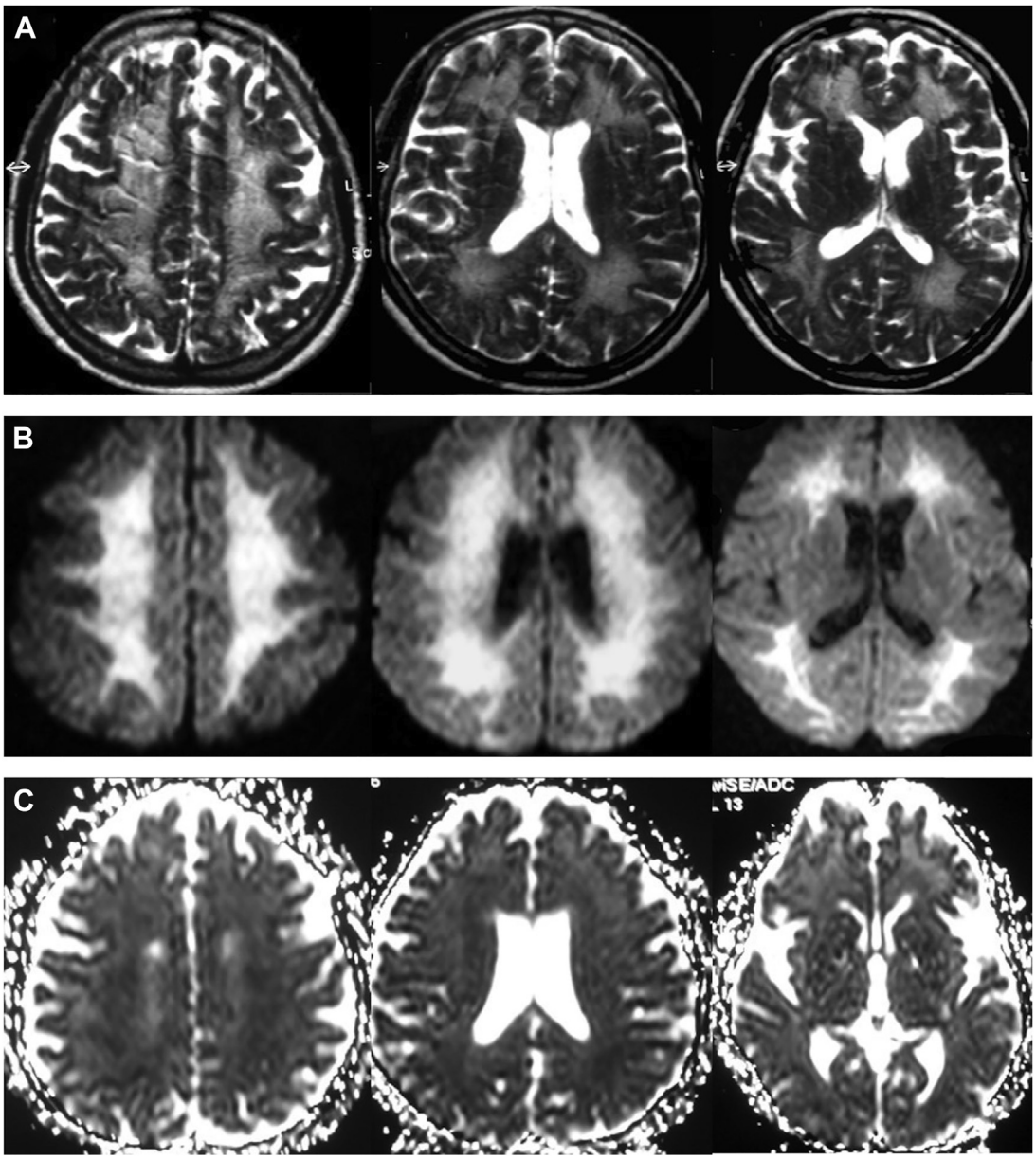

Fig. 2. Cocaine-induced encephalopathy. MR imaging shows diffuse symmetric and confluent T2WI hyperintense lesions (*A*) involving the subcortical and deep white matter of both hemispheres, associated with high signal intensity on diffusion-weighted images (*B*) and mild low signal on the ADC maps (*C*), indicating partial restricted diffusion.

turbinate and ethmoid) (**Fig. 7**). Finally, there could be the involvement of the neurocranium (anterior skull base, lamina papyracea, and orbit).[27,28]

CIMDL should be considered, according to Seyer and colleagues[21] when two of the following three findings are present: nasal septal perforation, palatal perforation, or lateral nasal wall destruction. An alternative and more simplistic diagnostic criteria of CIMDL include demonstrating any structural lesion of the sinonasal complex in the context of a positive toxicologic screening or confirmed cocaine-snorting habit.[29] A classification based on this distribution pattern has also been proposed (**Table 1**) (**Fig. 8**).[28]

Differential considerations of midline destructive lesions include granulomatosis with polyangiitis (GPA), Churg-Strauss Syndrome (CSS), T-cell lymphoma, and trauma. Although a positive antineutrophil cytoplasmic antibodies (ANCA) test would support the diagnosis of GPA, positive ANCA

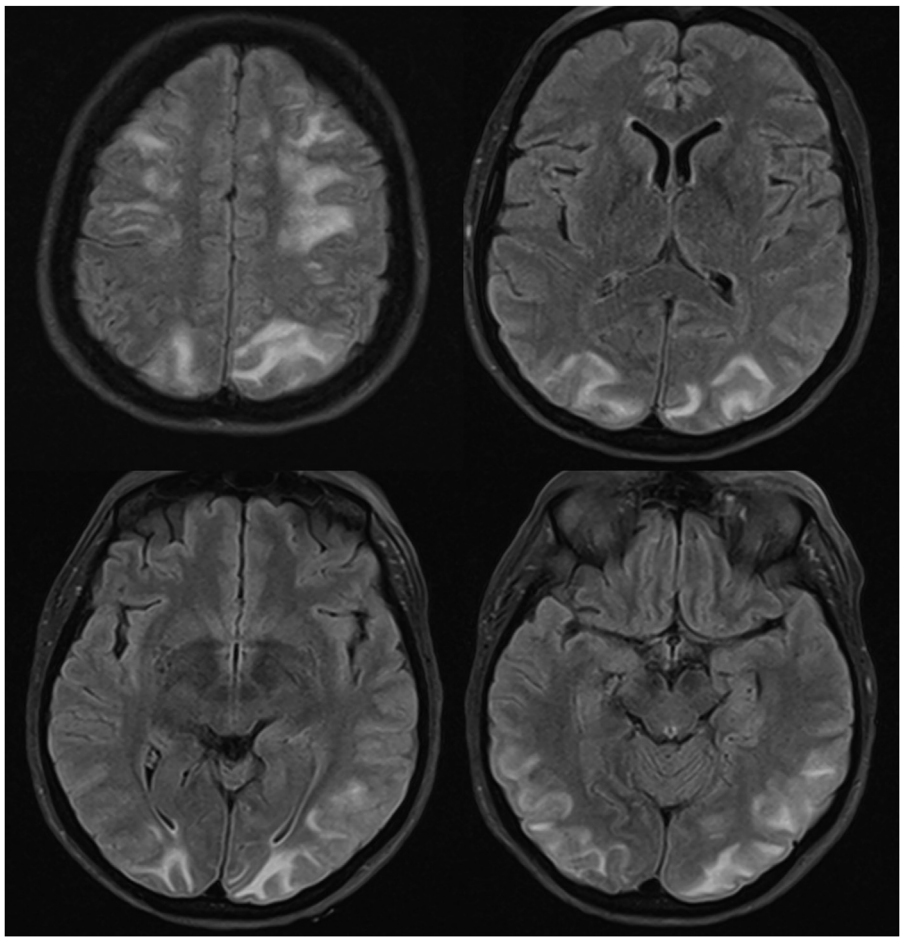

Fig. 3. PRES in a middle-aged cocaine abuser female. Axial FLAIR images show bilateral asymmetric subcortical white matter signal abnormality consistent with vasogenic edema in the parieto-occipital regions and frontal lobes.

test results have also been found in an unexpectedly large proportion of patients with CIMDL,[27,30] which makes the discrimination between the 2 challenging in the absence of documented cocaine addiction. Ultimately, the absence of systemic manifestations and the lack of response to treatment for GPA will lead to the confirmation of CIMDL in a cocaine user. On imaging, early destruction of the nasal septum, nasal floor, and inferolateral nasal wall supports CIMDL, given that these structures are more likely preserved in other diseases, such as GPA.[29] Given patients' noncompliant lifestyle, CIDML management is complex. Regular debridement of necrotic tissues and crusts and local and systemic antibiotic medication are all part of the conservative treatment. Surgical reconstruction of bone and cartilaginous lesions and correction of mucosal and cutaneous defects can be performed in complex cases.[31] However, surgical treatment should be withheld until there is evidence of lesion stability for at least 12 months, along with the confirmation of cocaine abuse discontinuation.

Marijuana-related Reversible Cerebral Vasoconstriction Syndrome

RCVS often affects young adults. Patients present with severe thunderclap headaches, which may or may not be associated with neurologic deficits. Intracranial arterial segmental vasoconstriction may result in multifocal luminal narrowing with a beading appearance on imaging studies (**Fig. 9**). These findings are expected to resolve within 12 weeks from onset.[32] While most patients follow a benign course, some may experience permanent neurologic deficits or death from intracranial hemorrhage or ischemic stroke.[33]

While RCVS occurs spontaneously in about 40% of cases, 60% of RCVS cases may be

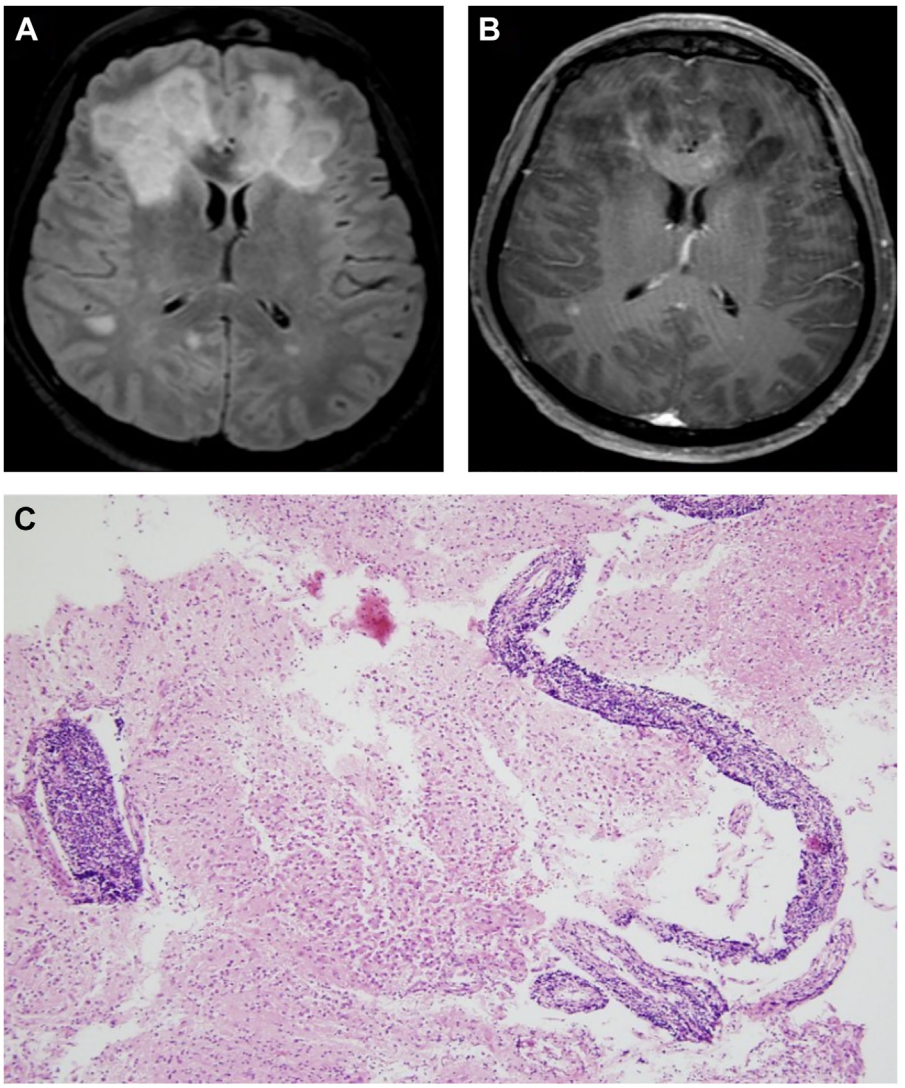

Fig. 4. Levamisole-induced MIL. Young male with a history of daily cocaine abuse who presented with progressive confusion, behavioral change, and visual hallucinations. Axial FLAIR (*A*) and contrast-enhanced T1-weighted (*B*) images show confluent white matter lesions mainly affecting the frontal lobes, with minimal mass effect and mild contrast enhancement. Brain biopsy shows perivascular lymphocytic infiltration (CD3+ and CD4+) (hematoxylin-eosin, original magnification X10) (*C*). (*From* Pessini LM, Kremer S, Auger C, et al. Tumefactive inflammatory leukoencephalopathy in cocaine users: Report of three cases. Mult Scler Relat Disord. 2020;38:101496.)

associated with vasoactive substances, pregnancy, uncontrolled hypertension, head trauma, and neurosurgical procedures.[34] Use of vasoactive substances, including marijuana, selective serotonin reuptake inhibitors, exercise stimulants, energy drinks, alcohol, triptans, methamphetamines, or sympathomimetic drugs, is the most frequently documented cause of RCVS. Among these substances, marijuana is the most prevalent triggering factor, reported in up to 30% of secondary RCVS cases.[35]

Intracranial VW-MR imaging is a valuable adjunct to conventional imaging to distinguish between RCVS and its relevant differential diagnosis of vasculitis. On MR imaging, these two entities may show multiple, likely bilateral, parenchymal infarctions of different ages and in different vascular territories (**Fig. 10**). CTA, MRA, or DSA demonstrate focal or multifocal segmental narrowing of small and medium size arterial vessels (**Fig. 11**). Differentiation between RCVS and vasculitis has clinical relevance; RCVS is treated with observation or

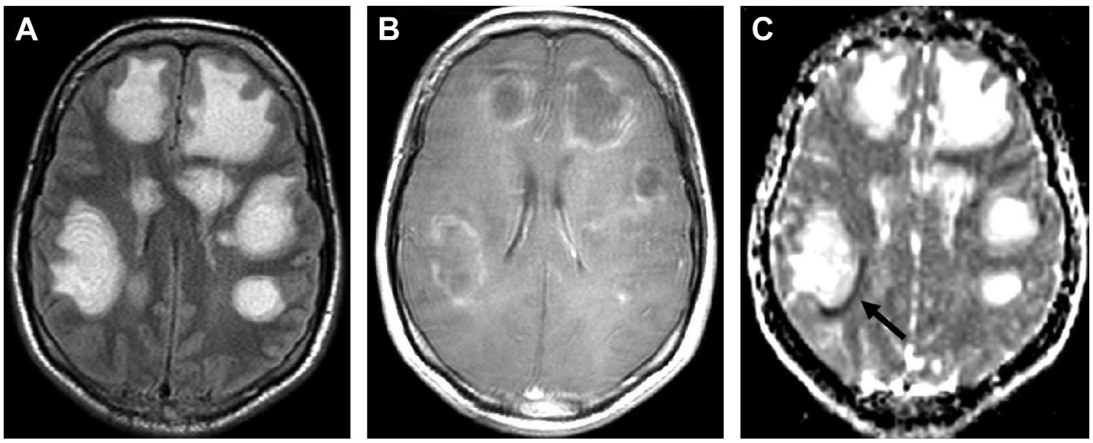

Fig. 5. Levamisole-induced MIL with Baló-like lesions. A middle-aged male with a history of chronic cocaine abuse presented with confusion, disorientation, speech, and behavioral impairment. Axial FLAIR (*A*) and contrast-enhanced T1-weighted (*B*) images show several pseudo tumoral lesions affecting the subcortical frontoparietal white matter of both cerebral hemispheres, with incomplete ring-enhancement and peripheral diffusion restriction on the ADC map (*arrow* in C). A concentric ring pattern (onion bulb appearance) is noted on the FLAIR image (*A*). Postmortem hair samples showed significant concentrations of cocaine and levamisole. (*From* Pessini LM, Kremer S, Auger C, et al. Tumefactive inflammatory leukoencephalopathy in cocaine users: Report of three cases. Mult Scler Relat Disord. 2020;38:101496.)

calcium channel blockers, whereas vasculitis is treated with steroids and immunosuppressive drugs. VW-MR imaging may help differentiate these entities; while both disorders may result in arterial wall thickening, the vessel wall in RCVS typically does not enhance, in contrast to the characteristic intense concentric vessel wall enhancement in vasculitis.[36] The relative paucity of arterial wall enhancement is concordant with limited histopathologic data in RCVS, which has shown a lack of arterial wall inflammation.

Heroin Toxicity

Heroin is a semi-synthetic opioid made from chemically processed morphine. It can be sniffed, inhaled, or injected. Heroin may cause acute or chronic effects on the brain, including neurovascular disorders, leukoencephalopathy, and atrophy.[37] Ischemia is the most commonly encountered acute neurovascular complication, typically seen following intravenous injection. Proposed pathomechanisms include vasospasm as a direct effect of heroin in vascular smooth muscle receptors, vasculitis from immune-mediated responses, or embolic events from impure additives.[9]

Symmetric spongiform degeneration occurs in the setting of heroin-induced leukoencephalopathy affecting the cerebral and cerebellar white matter and the corticospinal and solitary tracts.[38] This is exclusively seen after drug inhalation ("chasing the dragon"), and the clinical manifestations

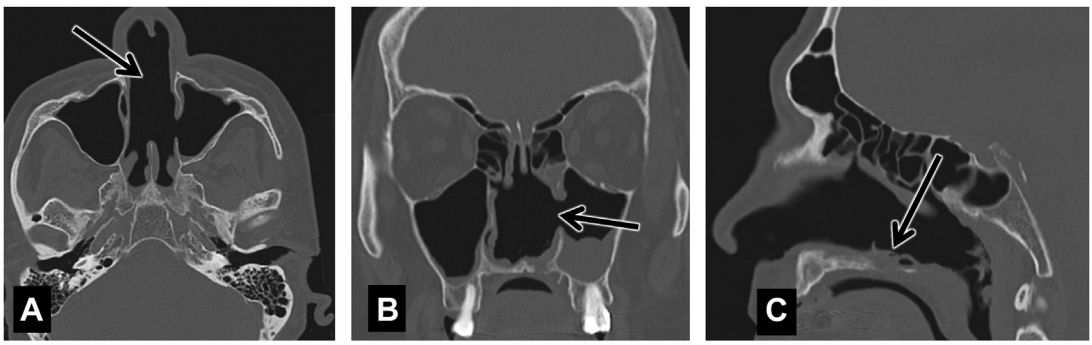

Fig. 6. 59-year-old man with a significant history of cocaine abuse *and cocaine-induced midline destructive lesions (CIMDL)*. Noncontrast bone algorithm CT images through the nasal vault demonstrate a widely perforated nasal septum (*arrow*, *A*). Coronal image shows the absence of middle and inferior turbinates (*arrow*, *B*). Sagittal reconstruction to the left of midline shows the osseous destruction of the posterior hard palate (*arrow*, *C*), which is also seen on the coronal B image.

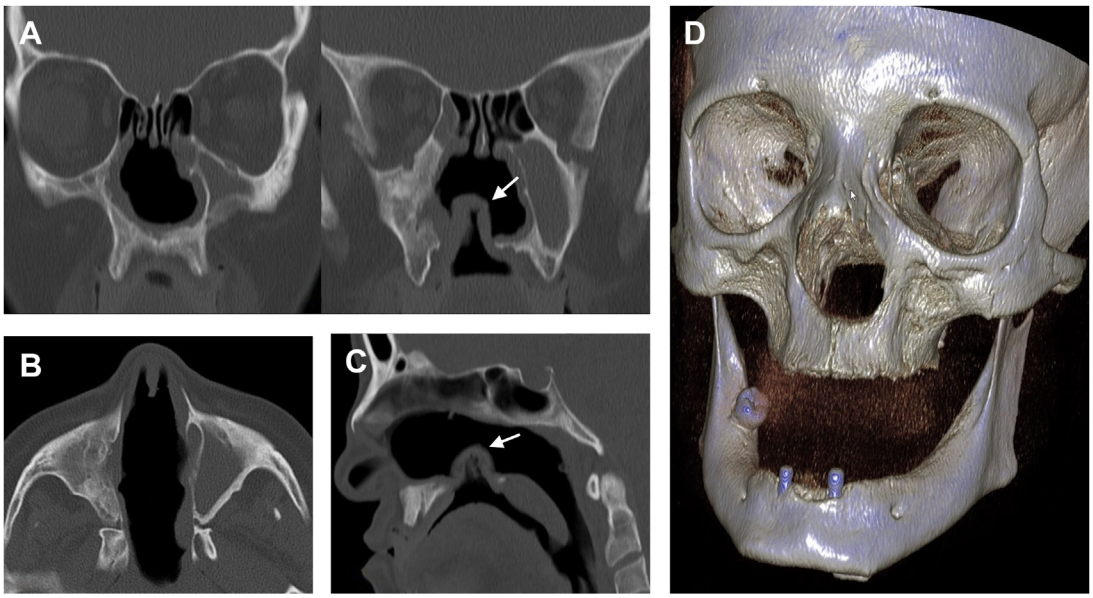

Fig. 7. CIMDL in a patient with a history of chronic intranasal cocaine abuse. Coronal (*A*), axial (*B*), and sagittal (*C*) bone window views of a CT scan of the facial bones show absence of the nasal septum, of the bilateral inferior, middle, and superior turbinates, of the medial walls of the maxillary sinuses, as well as palatal perforation with herniation of oral cavity mucosa into the nasal cavity (*arrows* in *A* and *C*). Volume-rendered 3D image (*D*) was acquired to help plan the surgical repair of the sinonasal cavity.

develop days to months after consumption.[37] On MR imaging, this is seen as symmetric T2WI and FLAIR hyperintensity in the cerebellum and posterior limbs of the internal capsules, sparing the anterior limbs (Fig. 12). Sparing of the subcortical white matter is typical.[39] These findings are presumed to reflect mitochondrial toxicity as MR spectroscopy typically shows reduced N-acetyl aspartate and increased lactate in the affected areas.[40]

Table 1
Classification Proposal for lesion location and grading of cocaine-induced midline destructive lesions

Localization	Grade	Frequency
Nasal septum	1	99%
Grade 1 + inferolateral region (inferior turbinate and medial wall of maxillary sinus)	2a	59%
Grade 1 + palate	2b	30%
Grade 2 + ethmoid bone, middle turbinate, and superior turbinate	3	23%
Grade 3 + neurocranium (lamina papyracea, orbit or anterior skull base)	4	8%

Modified from Nitro L, Pipolo C, Fadda GL, et al. Distribution of cocaine-induced midline destructive lesions: systematic review and classification. Eur Arch Otorhinolaryngol. 2022;279(7):3257-3267.

MEDICATION-ASSOCIATED CENTRAL NERVOUS SYSTEM VASCULOPATHY

Sympathomimetic Drugs

Sympathomimetic agents are used to augment the endogenous catecholamines of the sympathetic CNS for therapeutic purposes. Sympathomimetic drugs, such as pseudoephedrine, can cause intracranial vasculopathy. Pseudoephedrine relieves cold, flu, sinusitis, asthma, and bronchitis symptoms. Cerebral angiography studies in patients with stroke, associated with over-the-counter sympathomimetic medications, have shown "vasculitis-like" abnormalities, including widespread segmental narrowing and beading, usually in both the carotid and vertebrobasilar territories.[41] Sympathomimetic drug use has been identified as a risk factor for intracranial hemorrhage[42,43] and occasionally for ischemic stroke (Fig. 13).[44] The risk of complication increases in patients with impaired renal and hepatic function. Proposed mechanisms by which these drugs cause cerebrovascular complications include the development of hypertensive crisis[45] due to direct vasoconstrictive action and the result of angiitis.[46,47]

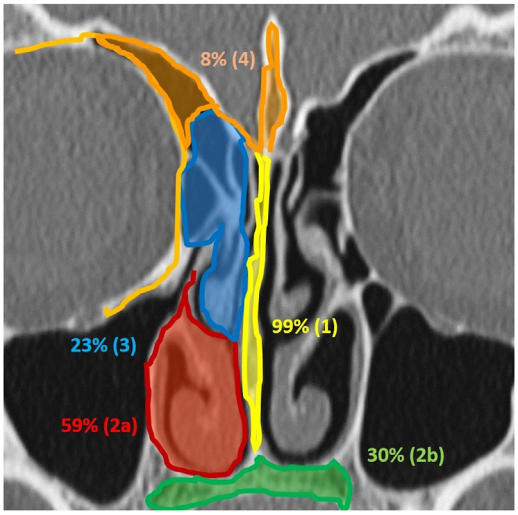

Fig. 8. Prevalence of CIMDL according to location. Coronal CT scan from a healthy subject is used as an anatomic reference. Yellow: grade 1 (nasal septum); red: grade 2a (inferior turbinate and medial wall of maxillary sinus); green: grade 2b (palate); blue: grade 3 (ethmoid bone, middle turbinate, and superior turbinate); orange, grade 4 (lamina papyracea, orbit or skull base). (*Modified from* Nitro L, Pipolo C, Fadda GL, et al. Distribution of cocaine-induced midline destructive lesions: systematic review and classification. Eur Arch Oto-Rhino-Laryngology. 2022;279(7):3257-3267.)

Antithyroid Drugs

Methimazole (MMI) and propylthiouracil (PTU) have long been used to treat hyperthyroidism secondary to Grave's disease (GD). ANCA-associated vasculitis is a rare and potentially life-threatening complication associated with these drugs. The median time between drug initiation and disease onset is 42 months, with PTU reported to have a higher incidence of vasculitis than MMI.[48] The pathogenesis is not well understood. Still, it has been postulated that MMI and PTU influence the production of myeloperoxidase (MPO)-ANCA, leading to vascular injury.[48] MPO-ANCA-associated vasculitis affects a single organ in 44% of patients, two organs in 34%, and more than two in 22%. In approximately 2% of cases, CNS vasculitis can occur, and it is seen in patients with more than two-organ involvement.[48] Typical manifestations include multiple lower cranial nerve deficits, cerebral hemorrhage, or hypertrophic pachymeningitis.

Prognosis is, however, favorable if the condition is detected early, if antithyroid drugs are discontinued, and if patients are treated with corticosteroids or immunosuppressants.[48,49]

Oncologic Drugs

Methotrexate (MTX) is an anti-metabolite agent that inhibits the enzyme dihydrofolate reductase (DHFR), which catalyzes the conversion of dihydrofolate into tetrahydrofolate, the active form of folic acid. Tetrahydrofolate is necessary for the synthesis of nucleotides of both DNA and RNA.[50] The incidence of MTX neurotoxicity ranges from 3% to 8%.[51,52] Acute MTX neurotoxicity, most often seen 10 to 11 days after intrathecal MTX administration,[51,52] usually results in stroke-like symptoms, such as aphasia, weakness, sensory deficits, ataxia, and seizures. Symptoms typically resolve within 24 to 36 hours. The inhibition of tetrahydrofolate by MTX also appears to affect the synthesis of macromolecules, such as myelin. Therefore, the presence of MTX-induced leukoencephalopathy is considered to be secondary to the impairment of myelin turnover. DHFR inhibition also leads to increased levels of homocysteine, which is toxic to vascular endothelium and may cause direct vascular damage. This is the proposed mechanism behind mineralizing angiopathy (**Fig. 14**) and vascular occlusion.[53]

On MR imaging, acute MTX-related leukoencephalopathy often demonstrates restricted diffusion in the deep periventricular white matter without corresponding FLAIR signal abnormality. Interestingly, in the subacute stage, high T2WI/FLAIR signal abnormality appears in a delayed fashion in the same regions of DWI signal change, a finding that is seen in 15% to 75% of patients (**Fig. 15**). These imaging findings, however, do not consistently correlate with neurologic deficits.[51] DWI abnormalities in acute MTX neurotoxicity indicate cerebral dysfunction but not necessarily overt structural injury to the cerebrum.[54] Most patients have a benign course with no long-term sequelae and can usually resume MTX therapy.[52]

Immunosuppressive Drugs

Immunosuppressive drugs (eg, cyclosporine, tacrolimus) are common precipitants of PRES. Although the pathophysiology remains unclear, these drugs are believed to have a direct toxic effect on vascular endothelial cells with secondary damage to the blood-brain barrier.[55] Hypertension and renal failure are risk factors for developing neurologic symptoms in patients treated with immunosuppressants.[55] Patients present with headache, mental confusion, vomiting, visual disturbances, or seizures. On imaging, subcortical vasogenic edema is typically seen in the parieto-occipital regions on CT or MR imaging, often with the additional involvement of the posterior

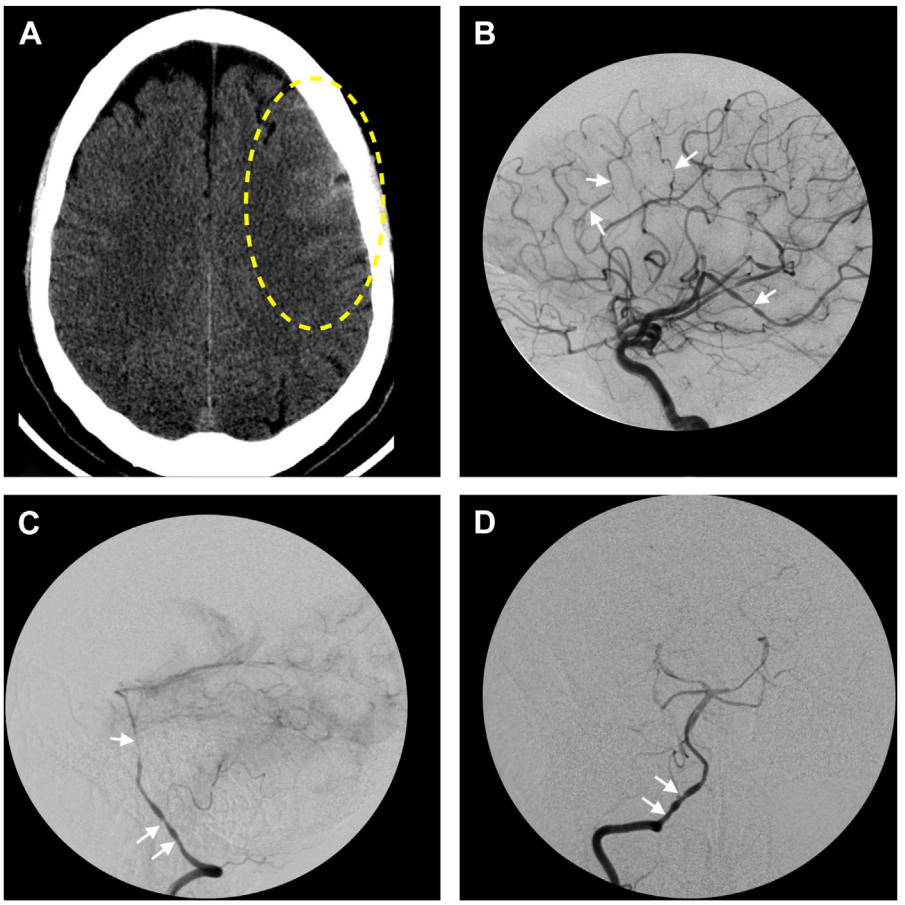

Fig. 9. Marijuana-induced RCVS. 27-year-old male patient with post-coital headache and marijuana consumption. Non-contrast CT head shows acute subarachnoid hemorrhage in the left frontal region (*dashed circle* in *A*). DSA shows multifocal narrowing of ipsilateral distal ACA and MCA branches (*arrows* in *B*). There is also multifocal narrowing of the basilar artery (*arrows* in *C and D*) and both proximal posterior cerebral arteries, giving a "beaded appearance" of the vessels.

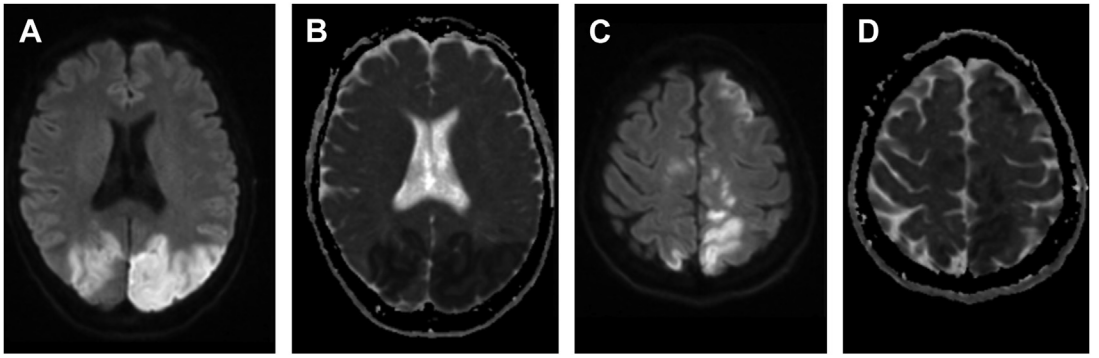

Fig. 10. A 38-year-old patient presented to the emergency department with severe thunderclap headache, vision loss, and mental status changes. The patient disclosed daily exposure to smoked marijuana and caffeinated energy drinks. DWI MR imaging (*A-D*) at admission demonstrates multifocal acute and subacute infarcts involving the bilateral occipital and parietal lobes, as well as the frontal lobes, the latter left more than right.

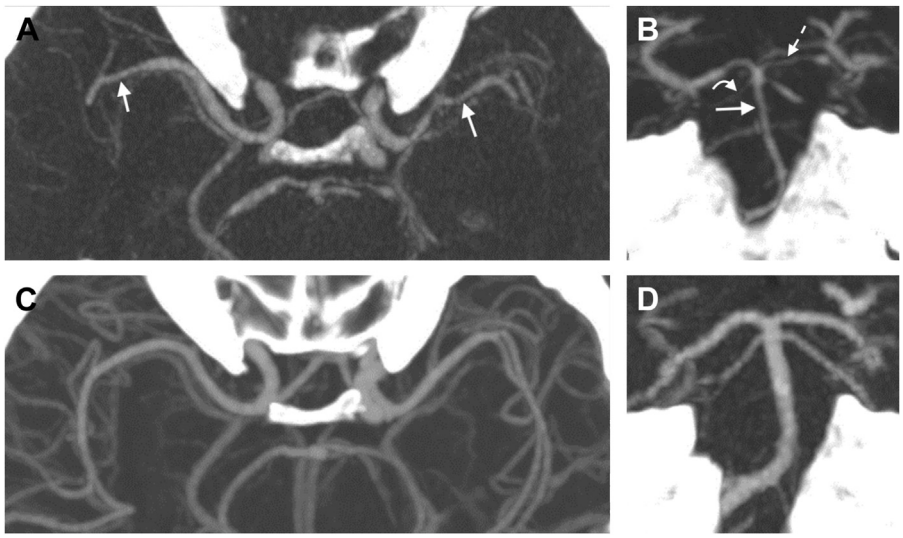

Fig. 11. Same patient from **Fig. 10**. Thick 10 mm axial (*A*) and coronal (*B*) MIP reconstructions of CTA COW at admission demonstrate moderate to severe multifocal short and long segment luminal narrowing, representing vasospasm, involving the left supraclinoid ICA, the bilateral MCAs, left worse than right (*arrows* in *A*), the basilar artery (*arrow* in *B*), the right superior cerebellar artery (*curved arrow* in *B*) and left PCA (*dashed arrow* in *B*). 12 weeks follow up CTA (*C* and *D*) demonstrate complete resolution of vasospasm.

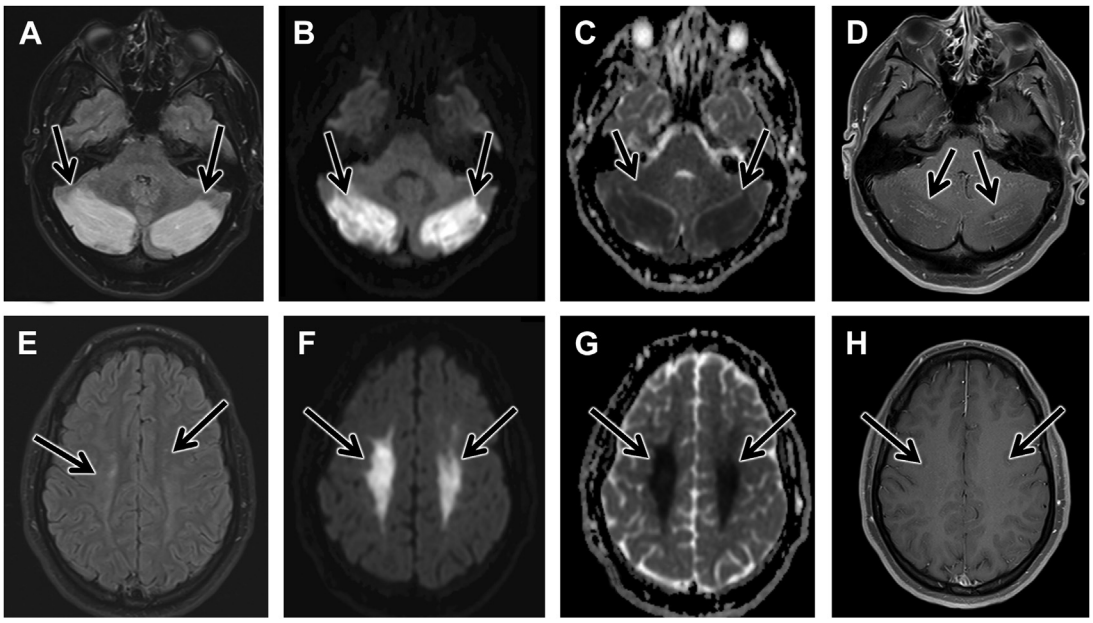

Fig. 12. Heroin-induced leukoencephalopathy in a 23-year-old woman with a history of heroin abuse, Adderall overdose, and hypnotic toxidrome. Top row (*A-D*): the posterior fossa demonstrates abnormally increased FLAIR signal intensity bilaterally within the cerebellar hemispheres (*arrows*, *A*), with bright diffusion signal intensity (*arrows*, *B*) and low signal intensity on ADC (*arrows*, *C*). There is linear enhancement of small folia on axial T1-post contrast fat-saturated image (*arrows*, *D*). Lower row (*E-H*) demonstrates subtle increased FLAIR signal within the bilateral centrum semiovale (*arrows*, *E*) but significant restricted diffusion (*arrows* in *F* and *G*). There are small foci of enhancement on postcontrast T1WI (*arrows* in *H*).

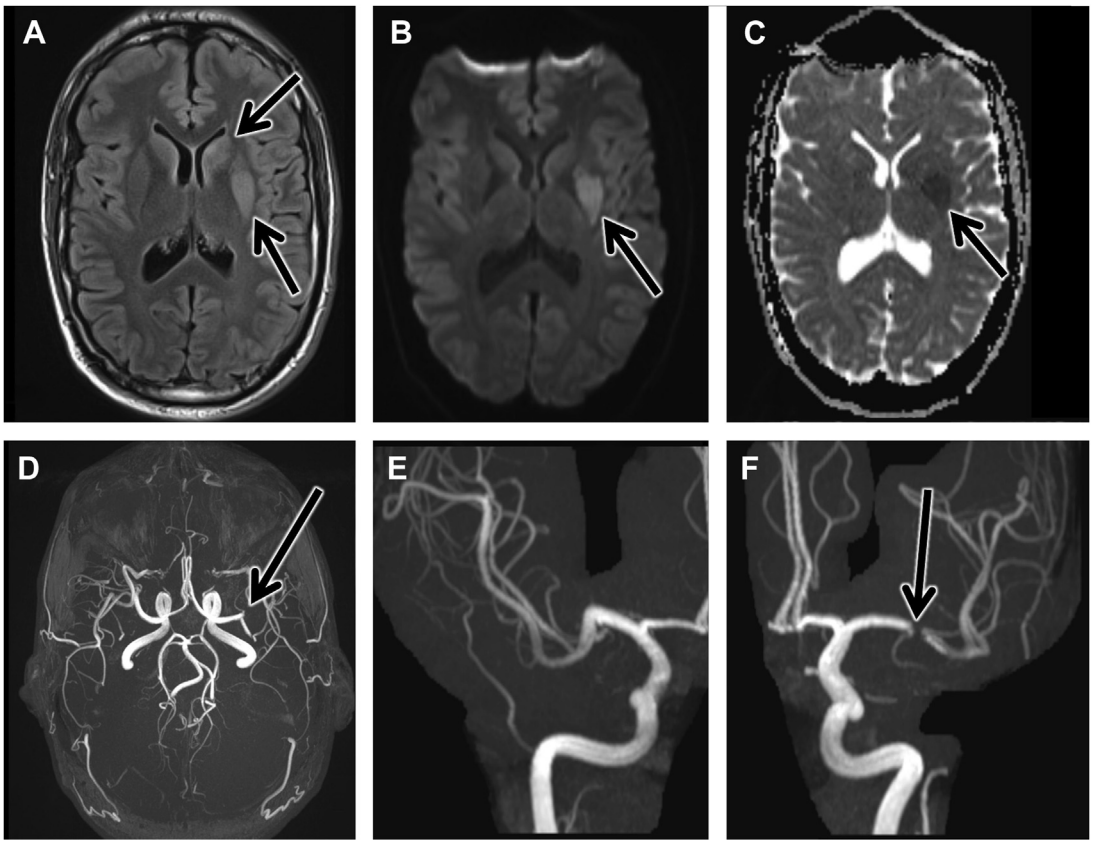

Fig. 13. Acute infarct in a 27-year-old woman with a history of methamphetamine abuse presenting with severe dysarthria and right-sided weakness. Axial FLAIR image demonstrates bright signal intensity within the left caudate head and putamen (*arrows* in *A*). DWI shows corresponding restricted diffusion (*arrows* in *B* and *C*) consistent with an acute infarct. MRA shows focal occlusion of the distal left M1 segment (*arrows* in *D* and *F*). Contralateral normal M1 segment for comparison (*E*).

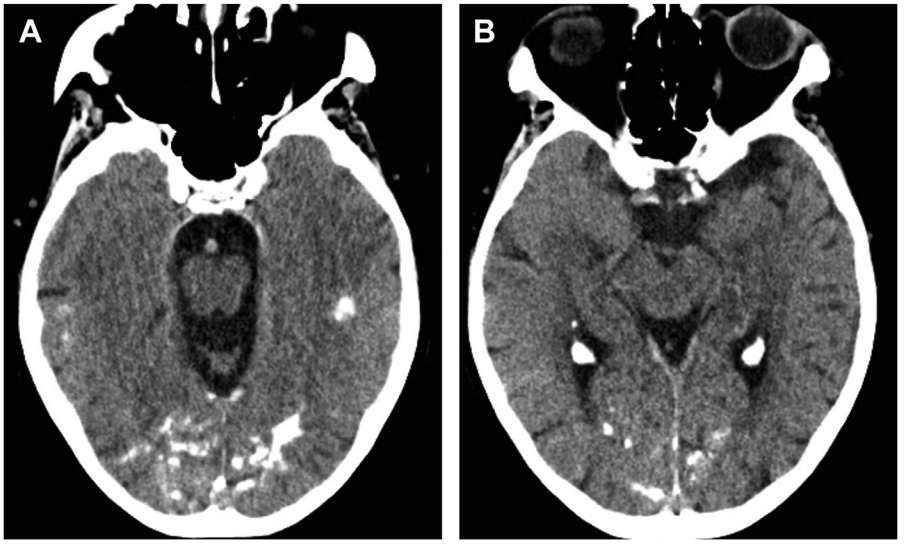

Fig. 14. Mineralizing microangiopathy. CT brain images (*A* and *B*) show multiple parenchymal calcifications in both occipital and temporal lobes in a patient with remote history of MTX treatment.

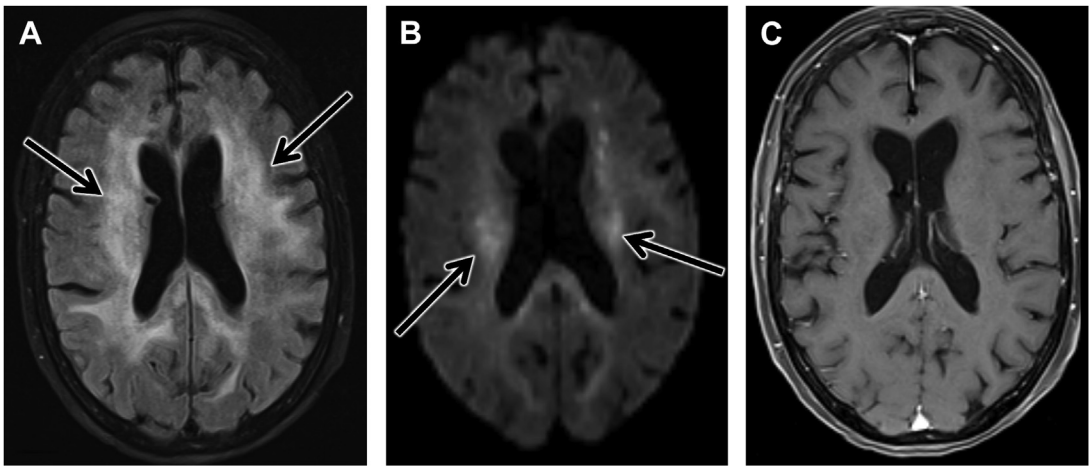

Fig. 15. MTX-related leukoencephalopathy. 69-year-old woman with a history of chronic lymphocytic leukemia recently started on methotrexate therapy who presented with falls, confusion, and weakness. Axial FLAIR image shows diffuse high signal intensity of the deep white matter (*arrows* in *A*), associated with patchy restricted diffusion (*arrows* in *B*). There is no enhancement on axial T1 post-contrast fat-saturated image (*C*).

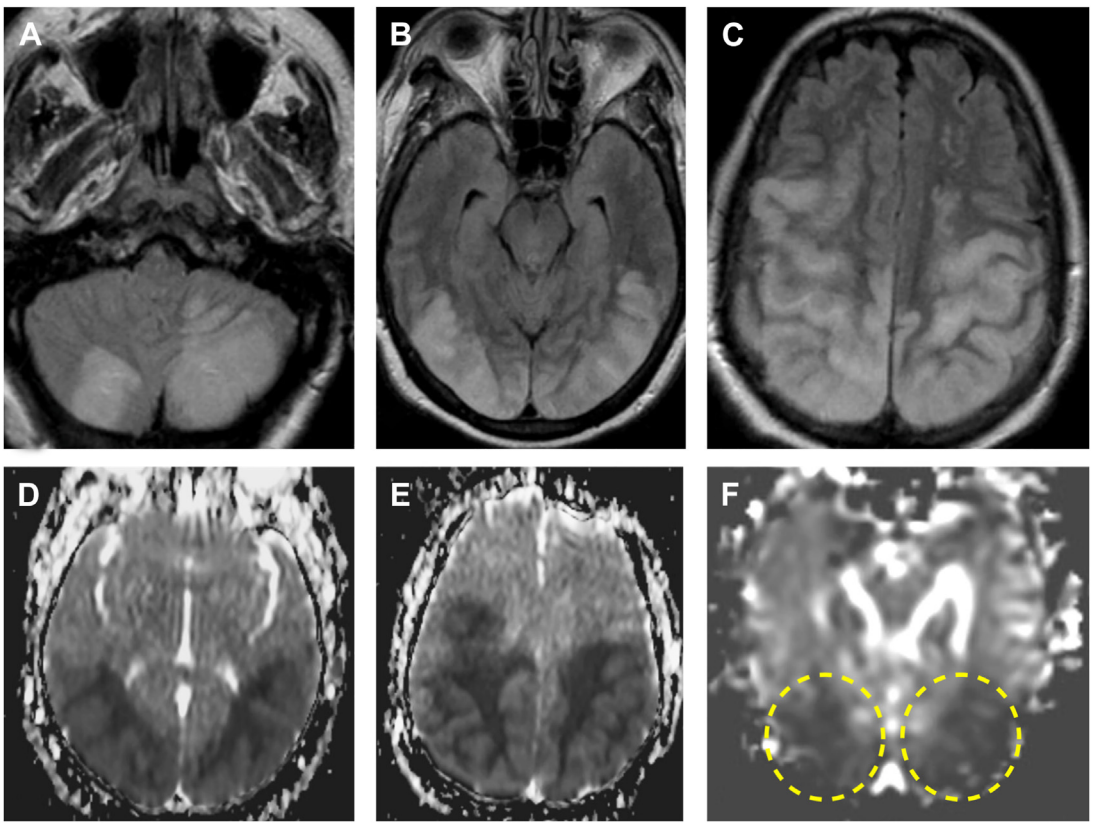

Fig. 16. Cyclosporine-induced PRES. Axial FLAIR (*A–C*) images demonstrate diffuse bilateral slightly asymmetric subcortical edema in the cerebellum, occipitotemporal and frontoparietal regions associated with restricted diffusion on ADC map (*D–E*) and low perfusion on dynamic susceptibility contrast perfusion (*dashed circles* in *F*).

temporal, parietal, or frontal lobes (**Fig. 16**).[56] Additional structures such as the brainstem, cerebellum, and basal ganglia can also be affected.[56] Most patients usually have a full gradual resolution of symptoms after drug withdrawal, and imaging abnormalities resolve within 2 weeks.

SUMMARY

Vasculopathy secondary to the use of recreational drugs or certain medications can lead to significant complications in the central nervous system (CNS) and sinonasal cavity, including intracranial hemorrhage and stroke. MR imaging, VW-MR, and CT/CTA are valuable tools for the evaluation of patients with suspected drug-induced vasculitis or vasculopathy. The management of drug-associated vasculopathy relies on drug withdrawal and supportive therapy to avoid secondary toxic effects. Most patients have a benign course with no long-term sequelae.

CLINICS CARE POINTS

- Approximately half of patients with hemorrhagic strokes due to cocaine abuse have a concomitant pathology such as cerebral vascular malformations or aneurysms.
- The pattern of involvement of the sinonasal complex helps differentiate CIMDL from its primary differential diagnosis, GPA.
- Over-the-counter sympathomimetics medications to relieve cold, flu, or asthma symptoms have been identified as a risk factor for CNS vasculopathy, intracranial hemorrhage, or ischemic strokes, especially in patients with impaired renal and hepatic function.

DISCLOSURE

The authors have nothing to disclose.

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