Köhlmeier–Degos disease or Degos disease or malignant atrophic papulosis is a rare chronic obliterator vasculopathy of uncertain etiology. It affects skin and other organs such as the gastrointestinal tract and the central nervous system, in addition to the heart, lungs, kidneys, and eyes. It can be classified as (i) malignant Degos disease with systemic manifestations which is further subclassified as (a) autoimmune: when there are associated clinical and/or laboratory features of either connective tissue disease or vasculitis, (b) coagulopathy-associated, and (c) virally induced, and (ii) benign cutaneous type which lacks systemic manifestations even after years of onset. The disease usually manifests in adults, has male preponderance, and has been more commonly reported from the Caucasian population.

We describe the clinical course in a patient with Degos disease having neurological involvement and highlight the imaging and histological findings.

A 44-year-old gentleman developed one episode of focal-to-bilateral tonic-clonic seizure. Examination four hours after the seizure was normal. He had diffuse skin lesions for about 2 years. He did not have preexisting scarring acne on the face. Brain MRI showed enhancing multifocal T2/FLAIR hyperintense lesions. Stereotactic biopsy of the right temporal lesion showed areas of coagulative necrosis/infarct which was indicative of vasculopathy/vasculitic process. Brain MRI after 2 months showed an increase in the size of the lesions. The histopathological findings of skin biopsy are depicted in Figure 3. He was treated empirically with intravenous methyl prednisolone (1 g/day for 5 days). One month later, he developed sudden onset, non-progressive, impaired vision in the right eye. Examination revealed bilateral optic disc edema, soft retinal exudates, and right inferior temporal quadrantanopia. Brain MRI done 4 days after the onset of new deficits showed no new lesions. There was evidence of “blooming” in susceptibility-weighted images within these lesions. Hematological and biochemical investigations were significant for an elevated erythrocyte sedimentation rate (52 mm/first hour). Work up for immune-mediated and granulomatous disorders and serological testing for human immunodeficiency virus, hepatitis B, and hepatitis C viruses were negative. Cerebrospinal fluid analysis showed normal opening pressure and slightly elevated protein (50.9 mg/dL, ref.: 15–45 mg/dL). CT scan of chest and abdomen was normal. Based on the clinical and histological findings of the characteristic skin lesions, the patient was diagnosed to have Degos disease. He was treated with monthly pulsed intravenous methylprednisolone along with levetiracetam, clopidogrel, and cilostazole. His visual deficits remained status quo. There was no recurrence of seizures. Skin lesions increased in number. He developed gastrointestinal symptoms in the form of vomiting and diarrhea alternating with constipation and he succumbed to his illness around one year after onset of neurological symptoms.

Neurological involvement is reported in 20–60% of patients with Degos disease. In a case series from the Mayo Clinic, 10 out of 15 patients had neurological manifestations, including fatal hemorrhagic or ischemic strokes, polyradiculoneuropathy, and nonspecific symptoms. More than half the patients had only cutaneous manifestations. As noted in our patient, the skin lesions antedate neurological manifestations by weeks to years. Uncommonly, neurological features can precede or occur simultaneously with skin lesions. Any part of the neuraxis can be affected and the clinical manifestations correspond to the site of involvement. Our patient manifested with neurological and ophthalmological features in the form...
of seizures, quadrantanopia, and multifocal brain lesions, which were secondary to vasculopathy of the leptomeningeal and cortical vessels. He also developed optic disc edema in the absence of raised intracranial pressure raising the possibility of optic nerve head ischemia secondary to retinal artery involvement. Table 1 summarizes the neurologic manifestations reported in literature.\[^2-9\]

The clinical course is progressive, sometimes fulminant, with the appearance of new neurological deficits as was noted in our patient. Fatal outcome has been reported in majority of the patients.\[^5,7\] Death occurs from bowel perforation, large cerebral infarcts, or massive cerebral hemorrhage. Rarely patients have mild or transient deficits.\[^6,10\] The key determinant of mortality is the degree of vascular involvement and ischemic complications. The factors that determine whether the disorder remains benign and confined to the skin or becomes malignant with other organ system involvement are not known.

Establishing an early and accurate diagnosis is important to ensure close follow-up for extracutaneous organ involvement. Diagnosis rests on identifying the characteristic skin lesions as noted in our patient, which is further supported by histological studies. Other neurological disorders where cutaneous lesions aid in the etiological diagnosis are listed in Table 2. Treatment of Degos disease includes immunosuppressive agents, antiplatelets, anticoagulants, rheological agents, and prostaglandins like treprostinil.\[^1\] There is no effective treatment for Degos disease since the understanding of the underlying pathophysiology is incomplete. Increased platelet aggregation and fibrinolytic dysfunction have been noted.\[^1,11\] Familial occurrence with autosomal dominant inheritance has been reported. Autoimmunity appears to play a major role as evidenced by presence of autoantibodies like antiphospholipid antibodies. Besides, as noted in our patient, histopathological findings of the skin and brain suggest vasculopathy. Other studies including autopsy-based studies provide evidence for

| Site               | Presentation                                                                                                                                 |
|--------------------|----------------------------------------------------------------------------------------------------------------------------------------------|
| Brain              | Venous thrombosis, hemorrhage, infarct involving supra- or infratentorial regions leading to headache, seizures, cognitive decline, dysarthria, aphasia, hemiparesis, amaurosis fugax, brainstem dysfunction |
|                    | Tear drop calcifications in cerebral parenchyma                                                                                                                                                 |
|                    | Progressive unilateral occlusion of cerebral vessels leading to hemispheric atrophy and thinning of overlying calvarium                                                                       |
| Spinal cord        | Myelopathy with patchy peripheral lesions (“saw-tooth” or “moth-eaten” appearance) and thinning of cord                                                                                         |
| Peripheral nervous system | Optic neuropathy, Radiculopathy, Sensori-motor polyneuropathy, Myopathy                                                                     |
| Extra-axial        | Enhancing leptomeningeal nodules, Diffuse meningeal enhancement, Ependymal enhancement, Subdural effusion (due to blockage of CSF flow) can mimic battered baby syndrome in infants |
| Disease/Syndrome       | Neurological features                                                                 | Cutaneous features                                                                 | Histological findings                                                                 |
|------------------------|----------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| **Inflammatory disorders** |                                                                                        |                                                                                      |                                                                                        |
| APLA                   | Ischemic strokes, Sneddon’s syndrome, transverse myelitis, chorea                      | Livedo reticularis, acrocyanosis, Degos-like lesions, erythematous macules, purpura, ecchymoses, and subungual splinter hemorrhages | Oclusive vascular changes, thrombotic microangiopathy, arterial intimal fibrous hyperplasia |
| SLE                    | Encephalopathy, chorea, strokes, psychosis, optic neuropathy, peripheral neuropathy, myopathy, myasthenia gravis | Photosensitivity, malar rash, discoid lupus, alopecia, mucosal ulcers, Raynaud phenomenon, angioneurotic edema, palpable purpura, subcutaneous nodules, gangrene, erythema multiforme | Vasculopathy, micro-/macroinfarction, focal/diffuse vasculopathy                        |
| Sarcoïd                | Cranial neuropathies, chronic meningitis, peripheral neuropathy, myopathy, hypothalamic involvement | Dry skin, hypodidrosis, cicatricial alopecia, erythema nodosum, vesicles, maculopapular rash, lupus pernio, plaques, keloids | Noncaseating granuloma                                                                  |
| Behcet’s disease        | Aseptic meningitis, encephalitis, myelitis, CVT, isolated trigeminal neuralgia          | Erythema nodosum, genital ulcers, oral aphthous ulcers, dermatographia, vesicles, pustules, folliculitis, pyoderm, acneiform eruptions, and necrotising vasculitis |                                                                                       |
| Sjögren’s syndrome      | Aseptic meningitis, CVT, peripheral neuropathy, dorsal ganglionopathy                  | Raynaud’s phenomenon, purpura, xerostomia                                           | Necrotic lesions, perivascular cuffing                                                  |
| Rheumatoid arthritis    | Pachymeningitis, leptomeningitis, CNS vasculitis, myelopathy, mononeuritis multiplex    | Subcutaneous nodules, liver palms, vivid washable yellow discoloration                 | Rheumatoid nodules, pachymeningitis, leptomeningitis, vasculitis                        |
| **Genetic disorders**   |                                                                                        |                                                                                      |                                                                                        |
| Tuberous sclerosis      | Subependymal giant-cell astrocytomas, behavioral problems, autism, West syndrome       | Ash leaf spots, confetti-like hypopigmented patches, café-au-lait spots, shagreen patches, periungual fibromas, facial angiofibromas | Cortical tubers, neuroglial hamartomas                                                  |
| Neurofibromatosis 1 and 2 | Optic nerve gliomas, radiculopathy, acoustic neuromas, schwannoma                | Café-au-lait spots, fibromatous dermal tumors, and Lisch nodules, axillary or inguinal region freckling, neurofibromas, violaceous papillary skin neurofibromas | Micronodular capillary and arteriolar proliferations. Gial proliferations are hamartomatous in nature |
| Hereditary hemorrhagic telangiectasia (HHT)/Osler–Weber–Rendu syndrome | Ischemic strokes, subarachnoid hemorrhages                                       | Mucocutaneous telangiectasias                                                        | Vascular dysplasia                                                                      |
| Homocystinuria          | Ischemic strokes, mental retardation, seizures, personality disorders, depression     | Cutaneous hypopigmentation, malar flush, and livedo reticularis                      |                                                                                        |
| Porphyrias              | Encephalopathy, psychosis, neuropathic abdominal pain, peripheral neuropathy          | Blisters, postinflammatory hyperpigmentation                                         |                                                                                        |
| Sturge–Weber            | Leptomeningeval venous malformation, epilepsy, developmental delay                  | Congenital port wine stain over the face                                            |                                                                                        |
| Ataxia Telangiectasia/Louis-Bar syndrome | Ataxia, choreoathetosis, seizures, oculomotor abnormalities | Cutaneous telangiectasia, café-au-lait spots, progeric and sclerodermatous changes    |                                                                                        |

Contd...
obstructive vasculopathy of small and medium-sized vessels, with variable degree of inflammation, sparing the tunica media. Histological changes in the skin evolve in early, fully developed, and late lesions. Based on the available evidence, various mechanisms have been proposed to explain the clinical manifestations of this disease including vasculitis, coagulopathy, and endothelial dysfunction triggered by viral or bacterial infections. How the interplay of genetics, autoimmunity and coagulopathy drives the disease process and contributes to the obstructive vasculopathy of Degos disease still remains to be understood.

We highlight the clinical, radiological, and histological findings in a patient with systemic Degos disease and stress on meticulous skin examination as a crucial step in the diagnostic algorithm. It is important to establish an accurate diagnosis for counseling the patient regarding the prognosis. Knowledge gaps in the disease pathophysiology need to be filled so as to develop effective targeted therapies.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and anonymity cannot be guaranteed.

| Disease/Syndrome        | Neurological features                                                                 | Cutaneous features                                    | Histological findings                                                                 |
|-------------------------|----------------------------------------------------------------------------------------|--------------------------------------------------------|---------------------------------------------------------------------------------------|
| Fabry disease           | Painful small fiber neuropathy with autonomic involvement, seizures                    | Purpuric, skin rash, angiokeratoma diffusum            | Hydric deep white matter, neuronal ballooning due to glycolipid storage                |
|                         |                                                                                        |                                                        | Angiopathy of subarachnoid arteries due to medial thickening from glycolipid deposition |
|                         |                                                                                        |                                                        | Adventitial fibrosis with lymphocytic infiltration                                     |
| Pseudoxanthoma elasticum| Stroke, retinopathy                                                                    | Pseudoxanthoma, multiple papules, peau d’orange, angioid streaks, subcutaneous calcification usually in blood vessels | Skin shows calcium deposits and swollen, fragmented elastic fibers                      |
| Infections              |                                                                                        |                                                        |                                                                                        |
| Syphilis                | Aseptic meningitis, late meningovascular syphilis, tabes dorsalis                      | Primary: Chancre. Secondary: maculopapular nonpruritic scaling rash, patchy alopecia, condyloma lata, mucous patches, erythema multiforme, split papules | Extensive leukocyte infiltration into the meninges, with perivascular leukocyte infiltration. Fischer’s plaques |
| Tuberculosis            | Chronic meningitis, vasculitic infarcts, Pott spine, CNS tumefactomatous                | Primary tuberculous chancre, verrucosa cutis, lupus vulgaris, scrofuloderma, erythema nodosum, erythema multiforme | Lymphohistiocytic meningitis with or without caseous necrosis. Tubercular granuloma with multinucleate giant cells |
| Varicella zoster        | Meningitis with cerebellar ataxia                                                      | Vesicles with oral lesions                             | Multifocal vasculopathy, lymphocytes, and macrophages infiltrating the arterial media  |
| Cryptococcosis          | Chronic meningitis                                                                      | Macules and nodules (in 10-15% of cases)               | Meninges diffusely infiltrated with numerous cryptococci and mononuclear cells, occasional granulomatous reaction, and necrosis |
| Lymes disease           | Aseptic meningitis, polyneuropathy, delayed demyelinating disease                     | Target lesion                                           | Visible ep shreddal granulation, irregular nodular protrusions of subependymal glia. Leptomeninges show mild fibrosis and chronic infiltrate of lymphocytes |
| HIV                     | HIV-1-associated neurocognitive disorder (HAND), peripheral neuropathy, progressive multifocal encephalopathy, tuberculosis, toxoplasmosis, and infection with cytomegalovirus | Molluscum contagiosum, seborheic dermatitis, verruca vulgaris, Kaposi sarcoma, herpes zoster | Multinucleated giant cells, microglial nodules/myelin loss                            |
| Neoplastic              |                                                                                        |                                                        |                                                                                        |
| Leukemia                | Meningeal leukemia is common form of relapse, seen in ALL                              | Erythema nodosum, Sweet syndrome                       |                                                                                        |
| Lymphoma, cutaneous (T cell) | Subacute meningitis, vertebral metastases                                              | Scler erythematosus patches, leonine facies, poikiloderma, hypopigmented and hyperpigmented patches with atrophy and telangiectasia |                                                                                        |
Letters to the Editor

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

Doddallur Mallikarjuna Sundhur*, Sumanth Shivaram*, Shilpa Rao†, Madhu Nagappa, Doniparthi V. Seshagiri, Vani Santosh1, Madhukara J*, Shreedhara AS1, Maya D. Bhat4, Rose D. Bharath*, Sanjib Sinha

Department of Neurology, National Institute of Mental Health and Neurosciences (NIMHANS), 1Department of Neuropathology, National Institute of Mental Health and Neurosciences (NIMHANS), 2Department of Dermatology, St John’s Medical College Hospital, 3Department of Neurology, Columbia Asia Hospital, 4Department of Neuroimaging and Interventional Radiology (NIIR), National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, Karnataka, India

*Both authors have contributed equally.

Address for correspondence: Dr. Sanjib Sinha, Department of Neurology, National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, Karnataka, India. E-mail: sanjib_sinha2004@yahoo.co.in

References
1. Theodoridis A, Makrantonaki E, Zouboulis CC. Malignant atrophic papulosis (Köhler-Degos disease)-A review. Orphanet J Rare Dis 2013;8:10.
2. Annato C, Ferri R, Elia M, Cosentino F, Schepis C, Siragusa M, et al. Nervous system involvement in Degos disease. AJNR Am J Neuroradiol 2005;26:646-9.
3. Subbiah P, Wijdicks E, Muenter M, Carter J, Connolly S. Skin lesion with a fatal neurologic outcome (Degos’ disease). Neurology 1996;46:636-40.
4. Ye L, Lekgabe E, Tsui A, Gaillard F. The evolution of cerebrovascular changes in Köhlermeier-Degos disease: An 11-year follow-up case report. J Clin Neurosci 2018;48:114-7.
5. Dastur DK, Singhal BS, Shroff HJ. CNS involvement in malignant atrophic papulosis (Kohlemeyer-Degos disease): Vasculopathy and coagulopathy. J Neurol Neurosurg Psychiatry 1981;44:156-60.
6. Caviness Jr VS, Sagar P, Israel EJ, Mackool BT, Grabowski EF, Frosch MP. Case 38-2006: A 5-year-old boy with headache and abdominal pain. N Engl J Med 2006;355:2575-84.
7. Moss C, Wassmer E, Debbel G, Hackert S, Goodyear H, Malcomson R, et al. Degos disease: A new simulator of non-accidental injury. Dev Med Child Neurol 2009;51:647-50.
8. Yeo TH, Vassallo G, Judge M, Laycock N, Kelsey A, Crow YJ. Infantile neurological Degos disease. Eur J Paediatr Neurol 2011;15:167-70.
9. Matsuura F, Makino K, Fukushima T, Matsubara N, Shibuya M, Higuchi T, et al. Optic nerve and spinal cord manifestations of malignant atrophic papulosis (Degos disease). J Neurol Neurosurg Psychiatry 2006;77:260-2.
10. Sharma S, Brennan B, Naden R, Whelan P. A case of Degos disease in pregnancy. Obstet Med 2016;9:167-8.