with noncontrast imaging sequences generally sufficient for screening for SEGA, we recommend avoiding contrast agents until there is a growing lesion or clinical suspicion of SEGA. In the latter circumstances, gadolinium can better define the lesion size, characteristics, and margins and nearby anatomical structures, which may be important for decision-making and for planning and monitoring treatment response.

Focal seizures and epileptic spasms occur in most (63% to 78%) infants with TSC, and caregivers should be educated to recognize these even if none are reported at the time of diagnosis.[10] A helpful resource is the Infantile Spasms Action Network (https://infantilespasms.org/what-can-is-look-like/). Also, at the time of diagnosis, children with TSC should undergo routine baseline electroencephalography (EEG), prolonged if necessary to include both awake and sleep stages, even if patient has never reported clinical seizures or epileptic spasms previously. If epileptic spasms or focal seizures are suspected but cannot be confirmed clinically or the baseline EEG reveals abnormalities that are nonspecific, the patient should have an eight- to 24-hour video-EEG that includes sleep, which may detect electrographic seizures or interictal epileptiform discharges that have been shown to be strongly predictive of impending epilepsy.[29,30] Early recognition and control of seizures is highly correlated with improved developmental and neurological outcomes,[31-33] and pre-emptive treatment with vigabatrin before the onset of clinical seizures may provide additional benefit of preventing or delaying seizure onset in at-risk infants diagnosed with TSC and epileptiform activity on EEG.[34] However, pre-emptive treatment with vigabatrin may not be able to improve developmental and neurological outcomes over that achieved by early recognition and control of clinical seizures alone[34,35] (Category 2A).

Children with TSC should be referred initially to a pediatric neurologist with expertise in epilepsy associated with TSC. Likewise, adults with TSC should be evaluated by an adult neurologist with expertise in epilepsy associated with TSC. Ongoing management may then be coordinated with a general pediatrician or general neurologist if preferred or necessary (e.g., in regions or countries with limited availability or access to epilepsy or TSC specialists).

TSC-associated neuropsychiatric disorders (TAND)

The term, "TAND," and related terminology was introduced in 2013[8] and readily accepted as an umbrella term encompassing interrelated neuropsychiatric manifestations common in TSC, including behavioral, psychiatric, intellectual, academic, neuropsychological, and psychosocial difficulties and disorders (Fig). TAND issues are common and are often the most impactful aspect of TSC, yet they are least likely to be addressed and controlled by existing treatments.[36] The TAND Checklist (lifetime version, TAND-L) was developed in 2015[37,38] as a screening tool to identify neuropsychiatric concerns in a person of any age by encouraging and guiding conversations between individuals or caregivers and a health care provider. The TAND Checklist is freely available and can be downloaded in 19 languages (https://tandconsortium.org/checklists/).

At diagnosis, all patients should receive comprehensive assessment for TAND manifestations to identify areas needing immediate or early intervention[37] (Category 1). Patients should be referred as appropriate to suitable professionals to initiate evidence-based interventions for any difficulties or disorders identified (Category 1), and parents or caregivers of children and dependent adults should be educated about TAND to ensure that families know what to look for as potential emerging TAND manifestations[37,39] (Category 2A). Family members may also need psychological and social support while coming to terms with the diagnosis of TSC and TAND, so strategies should be in place to support caregiver well-being[40,41] (Category 2B).

Kidney

At the time of diagnosis, abdominal imaging should be obtained regardless of age. MRI is the preferred modality for the evaluation of angiomyolipoma because 25% to 30% can be fat poor[42] and may be missed when abdominal ultrasonography is performed.[43] In the event MRI is not possible an abdominal CT would be the next preferred modality. Intravenous contrast can help with identification of renal cysts and lipid-poor angiomyolipoma on abdominal CT and is likely less harmful than previously feared,[44]especially in patients with normal renal function (glomerular filtration rate [GFR] >60 mL/min/1.73 m^2).[45,46]

MRI of the brain and abdomen can be coordinated, thereby limiting the need for multiple sessions of anesthesia if needed for successful MRI. MRI of the abdomen may also reveal aortic aneurysms or extrarenal hamartomas of the liver and neuroendocrine tumors in the pancreas and other abdominal organs that also can occur in individuals with TSC.[47] In addition to imaging, accurate blood pressure assessment is important because of the increased risk of secondary hypertension.[48,49] To assess kidney function at time of diagnosis, blood tests should be obtained to determine GFR using creatinine or cystatin C equations for adults[50,51] or children.[52,53] Patients with reduced muscle mass for any reason, including significant developmental delays, can have artifactually increased estimated GFR if a creatinine equation is used. In such situations, measurement of serum cystatin C concentration can be used to more accurately evaluate GFR[52,54] (Category 1).

Lung

Clinical assessment for LAM and chest CT should be performed in all females, and symptomatic males, 18 years or older. Ultra-low-dose CT acquisition protocols are recommended when possible to limit radiation exposure.[55] High-resolution CT (HRCT) is not needed to diagnose cysts that are characteristic of LAM but can be useful for the differentiation of dependent abnormalities such as pleural/chylous effusions or dependent atelectasis.[56] Minimum intensity projection-reformatted images[57] also can be used to better identify extremely small cysts.

Key elements of history include information about family history of lung diseases, occupational and environmental exposures, tobacco use, features of connective tissue diseases, dyspnea on exertion, cough, hemoptysis, chest pain, and history of pneumothorax. Baseline pulmonary function tests (PFTs) including prebronchodilator spirometry and postbronchodilator spirometry, lung volumes, and diffusion capacity of the lung for carbon monoxide, and six-minute walk test should be performed in individuals with lung cysts consistent with LAM on the screening CT. Although in cross-sectional studies serum vascular endothelial growth factor-D (VEGF-D) has excellent positive and moderate negative predictive value for the presence of LAM in women with TSC,[58-60] it has not been tested prospectively as a screening tool to signal the need for a CT and cannot yet be routinely recommended for that purpose (Category 2A).

Multifocal micronodular pneumocyte hyperplasia (MMPH) refers to benign, nodular proliferation of type II pneumocytes that occurs in both men and women with TSC.[61] Radiologically, MMPH appears as multiple, often diffusely distributed, discrete solid and ground glass nodules, typically ranging between 2 and 14 mm in diameter, with no consistent central/peripheral or apical/basilar distribution.[62] Given that MMPH has rarely been reported in