What you could not forget when you face with a patient with phacomatoses.

Poster No.: C-2154
Congress: ECR 2014
Type: Educational Exhibit
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Keywords: Pathology, Diagnostic procedure, Ultrasound, MR, CT, Thorax, Neuroradiology brain, Abdomen
DOI: 10.1594/ecr2014/C-2154

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Learning objectives

The objective of this educational exhibit is to show the main radiological features of the phakomatosis. As highly variable and age dependant, imaging techniques have an important role in the diagnosis and follow-up of these patients.
Background

The phakomatosis include a group of diseases related with a genetic defect in a tumor suppression gene.

They characteristically affect the neuroectodermic tissue, but is not rare that other organs are involved. The clinical picture varies depending on the diseases but has common factors like skin lesions, fibrous tumors, malformations of the nervous system and tumors.

This group includes neurofibromatosis type 1, neurofibromatosis type 2, tuberous sclerosis, von Hippel-Lindau syndrome and Sturge-Weber syndrome.
Findings and procedure details

TUBEROUS SCLEROSIS

Tuberous sclerosis (TS) is a multisystem, autosomal dominant neurocutaneous syndrome affecting children and adults and characterized by the presence of benign congenital tumors in multiple organs. It results from mutations in one of two genes, TSC1 (encoding hamartin) or TSC2 (encoding tuberin). (1,2). Approximately one in 8,000 adults and one in 6,000 newborns are affected by TS (3) and about two thirds are sporadic (4). The clinical course and the prognosis depend on the organs or systems affected. The prognosis is still quite poor and nearly 40% of patients die by the age of 35 years. (1). Classical triad of epilepsy, mental retardation, and adenoma sebaceum is rarely seen at clinical examination, so radiologic findings play an important role in the diagnosis and treatment.

Cardiac rhabdomyoma, renal angiomyolipoma, and neurologic involvement (including cortical or subependymal tubers and white matter abnormalities) are the most common radiologic findings. (1).

Four common central nervous system (CNS) abnormalities are:

- 1. **Cortical-subcortical tubers**: are developmental abnormalities of the cerebral cortex, present in over 80% of patients that present as areas of gyral thickening that resemble potatoes ("tubers") (1,2,5). They are typical findings in infancy, persist throughout life but do not become malignant tumors. Neurologic manifestations intimately related to the cerebral cortical tubers include epilepsy (which occurs in more than 70-80% of patients), cognitive disability, and neurobehavioral abnormalities such as autism (2). On CT are iso-hypodense and may calcify (5). MRI is better than CT in the detection of tubers (6). In neonates and infants, before myelination, they can be better seen on T1-WI as areas of hyperintensity. In older children and adults, the peripheral component is frequently isointense in all sequences while the inner part is iso-hypointense to white matter on T1-WI and markedly hyperintense on T2-WI and FLAIR (1) Fig. 1 on page 17 . Only 10% show enhancement (7). Tubers can calcify Fig. 2 on page 34 or undergo cystic degeneration (2) Fig. 3 on page 35 .

- 2. **Subependymal nodules**: are asymptomatic small nodular hamartomas that protrude from the walls of the lateral and third ventricles (2), are usually multiple and tend to calcify with age (1). Unenhanced CT shows multiple small nodular foci along the walls of the ventricles bilaterally, usually with dense calcification. On MR, before myelination they are hyperintense on T1-WI and iso to hyperintense on T2. With myelination they tend to become isointense unless calcified. Once calcified they are better seen on T2*/SWI...
- **3. White matter abnormalities**: are better identified on MRI

- **Superficial white matter abnormalities**, seen as high-intensity areas on T2-WI and decreased-intensity areas on T1-WI, associated with cortical tubers.
- **Radial white matter bands**, seen as curvilinear bands of hyperintensity on T2-WI and iso- to hypointensity to normal white matter on T1-WI that run from ventricular or juxtaventricular white matter toward the cortex Fig. 7 on page 39.
- **Cyst-like white matter lesions**: seen as small well-demarcated lesions of similar intensity to cerebrospinal fluid, located in deep white matter and typically near the lateral ventricles (1) Fig. 8 on page 40.

- **4. Subependymal giant cell astrocytomas**: are derived from subependymal nodules almost always at the foramen of Monro (1,2), and tend to become larger tumors (>1 cm) with more enhancement. (1). These lesions are composed of proliferative astrocytes and giant cells but do not become malignant glial tumors (8). Yet they may cause obstructive hydrocephalus and require surgery. At MR they are observed as well-demarcated lesions hyperintense in T2-WI and usually enhance (1,5) (Fig. 10 on page 42, Fig. 11 on page 43, Fig. 12 on page 44, Fig. 13 on page 45, Fig. 14 on page 46 and Fig. 15 on page 47).

The first three abnormalities can be seen in almost all patients. The main differential diagnosis is Taylor-type cortical dysplasia (type IIb) that can be indistinguishable from tubers.

**Cardiac** rhabdomyomas are intracavitary or intramural benign striated muscle tumor characterized by the presence of "spider cells", which can be single or multiple and the most common location is on the ventricular septum. (1, 2, 9). They are observed in nearly 50-70% of infants with TS and they typically appear during the first year of life. Spontaneous regression or disappearance of the tumor is described in up to 70% of children at the age of 4 years (9).

Rhabdomyomas may be detected on fetal ultrasonography and are the most common cardiac tumor diagnosed in utero (2). Echocardiography is noninvasive and can be useful in its detection and follow-up, however MRI can provide additional information regarding tumor extension, size or in the assessment of cardiac function (1).

TS can also affect lungs, kidneys, bones, liver, and the alimentary gastrointestinal tract.

**Pulmonary** involvement includes:
- **Lymphangioleiomyomatosis (LAM)**. It affects women almost exclusively. The diagnosis is usually made during early adulthood. Its more common clinical manifestations are dyspnea or pneumothorax. Clinical course is slow and progressive, ultimately leading to respiratory failure (1,2).

CT features are a diffuse interstitial proliferation and round, thin-walled cysts of variable size and contour with a symmetric and uniform distribution in the pulmonary parenchyma. Reticular opacities can be seen, reflecting interstitial edema secondary to obstruction of the lymphatic vessels. (1,10). Thin-section CT may demonstrate characteristic features and can avoid a lung biopsy Fig. 16 on page 48.

- **Multifocal micronodular pneumocyte hyperplasia (MMPH)**: is another pulmonary manifestation. It is not frequent and at thin-section CT it is seen as multiple tiny nodules (1-8 mm in diameter) with a diffuse and a random distribution (11) Fig. 18 on page 50.

Patients with TS can also develop a number of **renal** lesions being the most common angiomyolipomas and cysts (12).

- **Renal angiomyolipomas (AML)**. Appear in 55-75% of patients. They are a benign tumors. They usually manifest at a younger age and usually are multiple, larger, and bilateral (1,2). It has been described that they grow in adults and may cause renal architecture distortion, which compromises function. Renal failure is the leading cause of death in adults with TS (12). The most alarming complication is hemorrhage, especially in those that measure more than 3 cm in diameter. It is due to the rupture of an abnormal vessel (frequently associated with aneurysms). Typical CT findings are noncalcified cortical tumors containing fat with a CT value of less than -20 HU Fig. 19 on page 51 and Fig. 20 on page 52. However, intratumoral fat cannot be detected in approximately 4.5% of AML. Sometimes it is difficult to differentiate them from renal cell carcinomas on CT scans so in these cases MRI is recommended Fig. 21 on page 53. (1,2,13).

- **Renal cysts** are also a common CT finding Fig. 17 on page 49. Bilateral and multiple renal cysts in younger patients also raise suspicion of TS (1) Fig. 22 on page 54. They usually are asymptomatic and are associated to hypertension and renal failure (2).

- The overall incidence of **renal carcinoma** in TS is similar to that in the general population. However in patients with TS it is diagnosed at a younger age (2).

A careful **skin** examination of patients at risk for TS must be performed because a variety of skin lesions can be detected in more than 90% of patients. Skin lesions include large hypomelanotic macules, confetti-like lesions, facial angiofibromas, shagreen patches, forehead #brous plaques, and ungual or periungual fibromas. Oral manifestations may be also detected like teeth enamel pitting or gingival fibromas. (1, 15).

**Hepatobiliary and gastrointestinal** area are also involved. Some of the abnormalities reported include:
- The gastrointestinal alimentary tract typically presents multiple polyps at any point (78%). Early malignant changes in these polyps have been described (14).
- Hepatobiliary system anomalies include hepatomegaly, liver angiomyolipomas Fig. 23 on page 55, lipomas, hamartomas Fig. 24 on page 56, and fibromas.
- In the pancreas angiomyolipomas Fig. 25 on page 57, hypoplasia, islet-cell tumors, hamartomas have been described, and mucoviscidosis also.

**Bone** manifestations of TS include cyst-like lesions, hyperostosis of the inner table of the calvaria, osteoblastic changes, periosteal new bone formation, and scoliosis. These lesions can appear anywhere but the most common are in the calvaria, short tubular bones of the hand or foot, spine, and pelvis. On skeletal radiographs and CT images, cortical or medullary cyst-like radiolucent areas or sclerotic deposits are found focally or diffusely (1) Fig. 26 on page 58.

**NEUROFIBROMATOSIS TYPE 1 (NF1)**

Neurofibromatosis type 1 (NF1), also known as von Recklinghausen disease or peripheral neurofibromatosis, is the most common of the phakomatoses. This disorder is relatively common and affects one in 3000 person approximately and has the same prevalence in both sexes (16). NF1 is an inherited autosomal dominant disorder but 50% of patients have no positive family history and the disease appears as a spontaneous mutation (17).

In NF1 the skin, the nervous system, the bones, the endocrine glands and other organs can be affected by benign or malignant neoplasm as a result of abnormal tumor suppression. The NF1 gene, a tumor suppressor gene located on chromosome 17q11.2, encodes neurofibromin, a negative regulator of the Rasoncogene, the inactivation of which leads to cell proliferation and tumor development (18).

NF1 has a variety of systemic manifestations due to the ubiquity of the peripheral nerves. Therefore, this neurocutaneous syndrome can simulate several diseases that we should keep in mind when the diagnosis is performed (19).

The diagnostic criteria of NF1 were defined by the National Institute of Health Consensus Development Conference on Neurofibromatosis (20).

**Radiologic features in The Central Nervous System**
A variety of findings in the CNS are noted in patients with NF1, both tumoral and non-tumoral. Brain tumors are the second most common tumor that occurs in individuals with NF1, following peripheral nervous system neurofibromas. Most of the brain tumors are low-grade astrocytomas, typically optic pathway pilocytic astrocytoma. Non-tumoral alterations include dysplastic white matter lesions, bone dysplasias, meningocele, dural ectasia, aqueductal stenosis and vascular malformations. CNS pathology is a significant cause of morbidity in patients with this disorder (21).

**Optic nerve gliomas** are typically noted and most of them correspond to pilocytic astrocytoma. Optic pathway gliomas may be suspected because of ailing vision or an abnormal eye exam and they are detected by MRI. At MR they appear like tortuous enlargement of the optic nerve isointense at T1 and usually hyperintense at T2-WI. The enhancement after administration of gadolinium contrast is heterogeneous. Fat saturated T1-weighted sequences after contrast administration is most sensitive in their detection. They frequently involve the posterior visual pathways, spreading to the optic tracts, geniculated bodies and optic radiations. **Fig. 27 on page 17**. (22) Contrast administration is necessary in MR studies to maximize tumor detection and characterization and in the follow-up of these patients (23).

In patients with NF1 areas of hyperintensity are on T2-WI have been also described in white matter, also called unknown bright objects. (24). They are isointense in T1-WI and predominantly located in the basal ganglia, the brainstem and cerebellum. They typically don’t cause mass effect and doesn’t enhance after contrast administration. They correspond histopathologically to myelin vacuolization. These lesions are very suggestive of NF1 and will be useful as an additional criteria for its diagnosis **Fig. 28 on page 18** (25). Although usually small they may be hard to differentiate from diffuse infiltrating astrocytomas. They usually enlarge during childhood and disappear later in life, being uncommon in adults.

**Radiologic features in Thorax**

The manifestations of NF1 in the thorax may involve the ribs, the chest wall, the lungs or the mediastinum.

The **subcutaneous neurofibromas** are a common finding in NF1. They appear as soft nodules with low attenuation in the chest wall and are, they are often numerous. **Fig. 29 on page 19**. Subcutaneous neurofibromas can mimic metastatic soft tissues implants from primary tumor like melanoma or breast cancer or also be similar to sebaceous cysts (26).

The **plexiform neurofibromas** are smooth elliptic benign tumors in the paravertebral, axilar or intercostals regions **Fig. 30 on page 20** and **Fig. 31 on page 21**. The differential diagnosis includes extensive adenopathy of lymphoma, tuberculosis, sarcoidosis or metastatic cancer. In MRI neurofibromas show a low to intermediate
At T1-WI they show high signal intensity that corresponds to areas of mixoid tissue. The sarcomatous degeneration of the neurofibromas is rare and is estimated to occur in 5-15% of patients with NF1 (27).

The **meningoceles** are also frequent in NF1. They appear due to the different pressure between thorax and the subarachnoid space. They appear as well circumscribed paravertebral masses.

The most common **skeletal manifestations** of NF1 in the thorax involve the thoracic spine and the ribs. The characteristic abnormalities include well-margined erosion due to plexiform neurofibromas. Typically the spinal deformities include scoliosis. The **cervical and dorsal spine** is frequently involved and it usually appears along childhood and can increase along the years. *Fig. 32 on page 22* Enlargement of one or more neural foramen can also appear (28).

**Radiologic features in Abdomen**

Gastrointestinal involvement in NF1 is reported to occur in 10-25% of patients. A variety of organs may be affected including the development of with a diverse group of neoplasm. This is why a complete abdominopelvic scanning CT with intravenous and oral contrast should be performed in NF1 patients because they frequently present have additional asymptomatic neoplasm (29).

**Neurofibromas** are the most common neoplasm of the gastrointestinal tract in patients with NF1. The clinical manifestations may vary depending on the location and the extension of the neurofibromas. The most common location is paraespal and presacral regions but may occur in the retroperitoneum or visceral organs. On CT they appear as hypoattenuating masses adjacent to the psoas muscles *Fig. 33 on page 23*. In MRI they show characteristically low intensity on T1-WI and heterogeneous signal intensity on T2-WI. Sometimes they are so so extensive that can not be differentiated from adenopathies of lymphoma or soft tissues sarcomas. *Fig. 34 on page 24* (30).

In patients with NF1 a malignant peripheral nerve sheath tumor can be originated from a neurofibroma. The tumor appears in the second decade and has a poor prognosis.

Ganglioneuromas, neuroendocrine tumors and gastrointestinal stromal tumors has also been recognized in the literature in NF1.

**NEUROFIBROMATOSIS TYPE 2 (NF2)**

Neurofibromatosis type 2 (NF2) is an autosomal dominant neurogenetic disease that predisposes to multiple central and peripheral nervous tumors (mainly schwannomas,
malignant meningiomas and ependymomas) and to ocular abnormalities (cataract) (32,33). The prevalence is around 1 in 60,000 (34). It is caused by mutations in the NF2 tumor suppressor gene located on chromosome 22q12 encoding a protein called schwannomin or merlin (33,35). About 50% of patients represent new germ line mutations, although about 20% represent somatic mosaicism (35).

The most common clinical onset is hearing loss due to vestibule-cochlear schwannomas, which is usually unilateral at onset and may be accompanied by tinnitus. In other cases, dizziness, imbalance, reduced visual acuity or cataract may be the first clinical symptom (34).

The prognosis is adversely affected by early age at onset, a higher number of meningiomas and when a truncating mutation is present.

Surgical removal of symptomatic cranial and spinal tumors is the main stay of management. However, it is important to balance the use of microsurgery and/or radiation treatment particularly in aggressive tumors, those with high surgical risks, or in patients who refuse surgery. (36).

MRI is considered the best imaging modality for detecting vestibular schwannomas so it should be used in patients with NF-2 (35). Screening for vestibular schwannomas should begin in adolescence (39).

The criteria of diagnosis of NF 2 is one of the following:

- Bilateral eighth cranial nerve (CN8) masses seen with appropriate imaging techniques (CT or MRI).

- NF-2 in a first-degree relative and either a unilateral CN8 mass or two of the following: neurofibroma, meningioma, glioma, schwannoma, or juvenile posterior subcapsular lenticular opacity (32).

The most common abnormalities related with NF2 are:

**Intracranial tumors:**

- **Vestibular schwannomas:** occur in about 95% of adult patients. Initial symptoms include tinnitus, hearing loss, and balance dysfunction. They originate inside the internal auditory canal but later extend medially into the cerebello-pontine angle (ice-cream cone appearance). Without treatment they may cause compression of the brain stem and
hydrocephalus. The great majority of patients develop bilateral vestibular schwannomas by the age of 30 years (34,37,38).

On CT these lesions are hypodense to isodense and may calcify. On MRI these tumors are iso-hypointense on T1-WI and hyperintense on T2-WI. Homogeneous enhancement is present after contrast administration Fig. 35 on page 59, Fig. 36 on page 60, Fig. 37 on page 61, Fig. 38 on page 62 and Fig. 39 on page 63. When the tumors are large, the signal characteristics may be more heterogeneous with cystic degeneration Fig. 40 on page 64, necrosis or hemorrhage. (41).

The main differential diagnosis of bilateral enhancing lesions in internal auditory canals is leptomeningeal metastases (carcinomatosis) (5).

- **Non-vestibular schwannomas**: Schwannomas may also develop on other cranial and peripheral nerves, with sensory nerves more frequently affected than motor nerves. They rarely, if ever, undergo malignant transformation to neurofibrosarcoma. (34,37,38). Intracranial non-vestibular schwannomas are usually located in trigeminal or oculo-motor nerves. Multiple tiny schwannomas of cauda equina roots is also frequent (5).

- **Meningiomas**: Lifetime risk may approach 80%. Most are intracranial, however, spinal meningiomas occur (40). They can be multiple, range in size and tend to occur at a younger age. These lesions are hyperdense on CT and avidly enhance after contrast. On MRI they are usually isointense with gray matter on both T1- and T2-weighted images but may cause displacement of the brain and associated hyperostosis or erosion of the skull Fig. 38 on page 62. After gadolinium administration, they enhance homogeneously (41) Fig. 39 on page 63, Fig. 41 on page 65, Fig. 42 on page 66 and Fig. 43 on page 67.

**Spinal tumors**: at least two thirds of individuals develop them. They are often multiple and of various histologic types, including ependymomas, schwannomas and meningiomas.

- **Intramedullary tumors** are usually low-grade ependymomas and occur in 5% to 33% of individuals. These tumors can be located at any level of the spinal cord (39,41) and are usually isointense with respect to normal cord parenchyma on nonenhanced T1-WI and hyperintense in T2-WI. They are centrally located within the cord, demonstrate intense enhancement, and can be multiple Fig. 44 on page 68 and Fig. 45 on page 69.

- **Peripheral schwannomas** arise from the dorsal nerve roots. On MRI, schwannomas are isointense to skeletal muscle on T1-WI, hyperintense on T2-WI, and enhance significantly Fig. 46 on page 70, Fig. 47 on page 71.
- **Meningiomas** demonstrate signal intensity similar to the normal spinal cord on T1- and T2-WI and enhance intensely after gadolinium injection (5,41).

Ocular involvement and mononeuropathy are also related with NF2. Posterior subcapsular lens opacity is the most common ocular finding. Retinal hamartoma and epiretinal membrane are also observed.

About 70% have skin tumors, but only 10% have more than ten. The tumors appear to be as three different types, the most frequent is a plaque-like lesion, which is a intracutaneous lesion, but we can also observe subcutaneous nodular tumors or intracutaneous tumors similar to those in NF1. Most of these tumors are schwannomas, but occasional definite neurofibromas do occur (34). In contrast to neurofibromatosis type 1 (NF1) neurofibromas and astrocytomas are relatively infrequent.

**VON HIPPEL-LINDAU**

Von Hippel- Lindau disease (VHL) is a rare autosomal dominant disease associated with an inactivation of a tumor suppression gene, predisposing to the development of several tumors. The estimated prevalence is one in 31,000 (42). Only 20% are non-familial "de novo" mutations.

The diagnostic criteria for VHL disease include:
- More than one hemangioblastoma in the CNS.
- One hemangioblastoma of CNS and visceral manifestations of the disease.
- Manifestations and family history of VHL disease (43).

The mortality of patients with VHL disease has been reduced in the last 20 years but the median life expectancy is still 49 year (44).

**Radiologic features in The Central Nervous System**

The **retinal hemangioblastoma** is the most frequent tumor detected in VHL patients. The prevalence in patients with VHL disease is 45-59% approximately. In MR at T1-WI they appear as high signal intensity lesions compared with the normal vitreous intensity. Enhancement after contrast administration can be seen in severe lesions (45).

The **CNS hemangioblastoma** is one of the most typical manifestations of VHL disease. They usually appear in the cerebellum and the spinal cord. Only 10% are supratentorial. When they are correlated with VHL disease they occur in younger patients and the prognosis is worse. They are highly vascular lesions that present readily enhancement.
after contrast administration and may associate dilated draining veins. Two-thirds of them show an associated non-neoplastic cystic component with the typical appearance of cyst with a solid mural nodule abutting the leptomeninges. At MR the solid portion demonstrates low signal intensity on T1-WI and high signal intensity on T2-WI and after contrast administration. Fig. 48 on page 25 and Fig. 49 on page 73. Treatment of CNS hemangioblastomas is "en bloc" surgical resection, usually limited to symptomatic lesions as in patients with VHL disease the surgical management is more difficult (46).

Endolymphatic sac tumors (ESC) appear in 10-15% of patients with VHL. ESC are slow-growing benign tumors of the endolymphatic sac, located in the posterior surface of the petrous temporal bone and locally invasive. The typical clinical presentation is a unilateral hearing loss and vestibular dysfunction. In CT a retrolabyrinthine mass with bone erosion is typical. In MRI it shows heterogeneous signal and enhancement and may associate asymmetrical signal intensity between membranous labyrinths Fig. 50 on page 72 and Fig. 51 on page 26. The early diagnosis is important because an early surgical intervention can prevent more hearing loss (45).

Radiologic features in Abdomen

Renal lesions:

Renal cysts are frequent in patients with VHL and occur in 60% approximately. In a big number of patients they can be bilateral(47). But solid tumors and renal cell carcinoma (RCC) have also been described in younger patients with VHL, this is why a screening is important. Different imaging techniques might help us to differentiate between cystic and solid lesion. US is useful to distinguish them but CT might help us in the detection of small lesions or when the kidney has been distorted by multiple renal cysts (47). Cysts demonstrate little or no wall enhancement and solid components enhance after contrast material administration(48).

RCC associated with VHL disease are multicentric and bilateral solid hypervascular masses or complex cystic masses with mural nodules and thick septa. MR is also useful especially in patients with renal failure (48)Fig. 52 on page 27. Simple Cysts are hypointense in T1-weigthed images and hyperintense in T2-weighed images with no enhancement after administration of gadolinium contrast material. Complex or solid lesions demonstrate enhancement after contrast T1-weighed images (48). The treatment of choice in VHL patients with renal cell carcinoma is surgery (partial nephrectomy or enucleation or nephrectomy) and the follow-up is necessary (49).

Pancreatic lesions:
The prevalence of pancreatic involvement in VHL disease varies from 0% to 77%. The pancreatic cysts are frequent in VHL patients. They are typically asymptomatic and they are detected during screening examination. They usually don’t show significant progression and conservative management is recommended (50). Cystic lesions are commonly detected with CT or US. The walls of simple cysts enhance poorly or not at all. **Fig. 53 on page 28** Microcystic adenomas are usually well circumscribed, with numerous small cysts normally < 2 cm. Enhancement occurs at the periphery of these microcysts (51).

**Adenocarcinomas** and pancreatic neuroendocrine tumors have also been described. Pancreatic adenocarcinomas have a poor prognosis and only 10%-15% are potentially resectable. Lesions are typically detected with US and CT. **Fig. 54 on page 29 and Fig. 55 on page 30**. Neuroendocrine pancreatic tumors, or islet cell tumors, occur in 5-17% of VHL patients. When associated with VHL disease, neuroendocrine pancreatic tumors have low rates of malignancy and metastasis (<10%), so an expectant therapeutic can be adopted. When these lesions are functional, they can secrete insulin, glucagon, gastrin and somatostatin, causing symptoms and thus allowing early diagnosis (52). Neuroendocrine pancreatic tumors have well defined margins, round morphology and frequently are hypoechoic relative to pancreatic parenchyma. In US these tumors are homogeneous and hypo or isodense compared to normal pancreatic parenchyma. Typically, there is intense contrast enhancement in the arterial phase. In MRI these lesions are hypointense on T1-weighted MR images and hyperintense on T2-weighted images (53).

**Pheochromocytomas** have a prevalence that can vary from 0% to 60%. Pheochromocytomas associated to VHL disease appear at a younger age, are usually multiple, ectopic (15%-18%) and can be bilateral (50%-80%) (54). They arise from the neural crest and may produce elevated levels of catecholamines in the serum and urine. Nevertheless, many lesions are asymptomatic and results of biochemical tests are normal. The symptoms/signs are headaches, palpitations, episodic sweating, pallor, nausea and intermittent or sustained hypertension. The typical appearance at CT is a solid or complex cystic mass that may have areas of necrosis, haemorrhage, and calcifications. Marked enhancement is also typically seen, although small areas of the tumor may remain with low attenuation. At MR imaging, 95%-100% of lesions have low or intermediate signal intensity on T1-weighted images and high signal intensity on T2-weighted images and show marked gadolinium enhancement (55).

**Papillary Cyst-adenomas** of the epididymis are common in men with VHL disease (found in 10%-60%). If there are bilateral cyst-adenomas of the epididymis, it is pathognomonic of VHL disease(14). Usually no treatment is required because they don’t have malignant potential. In US they are mixed echotexture, with both solid and cystic components. Calcifications and ductal ectasia within the rete testis may be present(55).
Sturge Weber syndrome is a vascular neurocutaneous syndrome also known as encephalotrigeminal angiomatosis. It differs from the other phakomatoses previously described here, as it correspond to a congenital but not inherited disease and it is not associated with the development of tumors.

The pathogenesis is believed to be a vascular steal secondary to a cortical angiomatous malformation. (56)

It is clinically characterized by facial nevus and neurologic features. Facial nevus usually is present at birth and gradually darkens to a port-wine nevus, often in the distribution of a trigeminal nerve division. (56). Only 5% of patients do not present facial nevus.

The most common neurological symptoms are focal seizures. Hemianopsia is also common because of the involvement of the leptomeninges overlying the occipital lobe. Poor intellectual function and progressive mental retardation may also be present. Eye abnormalities, such as glaucoma, choroidal hemangioma, and tortuosity of episcleral, iris and retinal vessels may be present. (57)

Neuroradiologic findings are related to the pial angioma and used to confirm the diagnosis, to evaluate the extension of the cortical angiomatous malformation and to evaluate associated abnormalities. (57)

Typical findings include characteristic progressive cerebral atrophy and calcification in the area of the pial angioma, usually located in the parieto-occipital region.

CT is the most useful imaging technique to evaluate calcifications in the Sturge Weber Syndrome. These calcifications have a common pattern: dense, gyriform and subjacent to the abnormal meninges. Other CT features include: diffuse high attenuation of the superficial and deep white matter, presumably due to microcalcifications; gyriform enhancement after the administration of iodinated contrast material (reflecting pial angiomatosis) and brain atrophy as a consequence of vascular steal phenomena of the pial angioma. (58)

Nevertheless MRI is considered to be the standard imaging of reference in the Sturge Weber Syndrome. A very characteristic sign is the leptomeningeal enhancement in contrast-enhanced T1-WI, which assesses the extent of the pial disease Fig. 57 on page 31 and Fig. 58 on page 32. T2* and SWI sequences are useful in the detection of calcifications. Cavernous angioma and other venous abnormalities may also be identified. Gadolinium enhanced MRI is also useful to demonstrate choroid plexus enlargement, a confirmatory finding in the Sturge Weber Syndrome. T2-WI is used to detect related gliosis and cerebral atrophy in chronic isquemia. (58)

The treatment of Sturge Weber syndrome is directed to adequate pharmacologic control to the seizures. Surgery may be needed for medical refractory seizure activities. It can
range from cortical excision to hemispherectomy, depending on the extent of vascular malformation. (58)
Fig. 1: Cortical tubers spread in both hemispheres and seen as hyperintense cortical areas on T2-WI and hypointense to white matter on T1-WI. After gadolinium contrast they do not show any enhancement.

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Fig. 27: Optic nerve glioma in patient with NF-1. a) Axial T2 FLAIR image shows an hyperintense well defined expansive mass that involves the right optic nerve. b) Axial T1-WI MR image after administration of gadolinium. The lesion shows enhancement, suggestive of glioma.

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**Fig. 28:** Unknow bright objects in patient with NF-1. Axial T2 FLAIR images show small areas of increased signal in the basal ganglia, thalami, cerebelum and pons.

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**Fig. 29:** Subcutaneous neurofibromas in a patient with Neurofibromatosis type 1. Axial CT scan demonstrates small subcutaneous neurofibromas in the anterior chest wall.

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**Fig. 30:** Axial CT scan obtained in a patient with neurofibromatosis type 1 demonstrates an intercostal neurofibroma and little small subcutaneous neurofibromas.

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**Fig. 31:** Neurofibromas: Coronal T1-WI MR images after contrast administration shows a paravertebral soft tissue mass.

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Fig. 32: Axial CT scan demonstrates bilateral neurofibromas within the psoas muscles.
Fig. 33: Coronal and axial CT scan demonstrates an extensive and diffuse retroperitoneal mass composed by multiple plexiform neurofibromas encompassing all the retroperitoneal vessels in a patient with severe scoliosis and neurofibromatosis type 1.

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**Fig. 34:** Coronal and axial T2-weighted MR scan demonstrates multiple nodular lesions following the neural path nerves of both lower limbs consistent with neurofibromas.

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**Fig. 48:** Axial T2-FLAIR MR images and axial T1-WI MR images after contrast administration shows an hemangioblastoma in the right cerebellum in a patient with Von hippel lindau disease.

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Fig. 51: Axial T2-WI MR images shows an asymmetry in the signal intensity of the membranous labyrinth on the left side. The patient was diagnosed with low-grade adenocarcinoma of endolymphatic sac and surgery was performed.

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**Fig. 52:** 10a. 10b. Axial contrast-enhanced CT scans show a solid enhance lesion in the left kidney in the venous phase consistent with a renal cell carcinoma.

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**Fig. 53:** Axial contrast-enhanced CT scans show multiple pancreatic cysts that appears as high signal intensity lesions on axial T2-WI TRUF1 images in a patient with Von Hippel Lindau disease.

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**Fig. 54:** US show a solid nodule in the pancreas in a patient with Von Hippel Lindau disease

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**Fig. 55:** Axial CT scan demonstrates a big multinodular mass in the pancreas hipodense after contrast administration in a patient with Von Hippel Lindau disease. A biopsy was performed and a pancreatic cistoadenoma was diagnosed.

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**Fig. 57:** Axial and sagital CT images shows dense and gyriform calcifications in the right temporo-occipital lobes in a patient with Sturge-Weber syndrome.

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**Fig. 58:** Axial SWI sequences MR shows hipointensity due to calcifications in the right temporo-occipital lobes in a patient with Sturge-Weber syndrome.

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**Fig. 56:** Axial T2 weighted, axial T2 FLAIR and sagittal T1 weighted MRI images in a patient with choroidal angioma and Sturge-Weber syndrome.

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Fig. 2: Cortical tubers in the left cerebellar lobe seen hyperintense on T2-WI with hyposignal in SWI indicating calcification.

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Fig. 3: Multiple cortical-subcortical tubers with a diffuse distribution in both hemispheres are identified as hypointense lesions on T1-WI and hyperintense on FLAIR. We can observe cystic degeneration in some of these lesions localized at the level of the occipital lobes.

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**Fig. 4:** Small bilateral subependymal nodules at the atrium ventricular level.

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**Fig. 5:** Subependymal nodules in the walls of the lateral ventricular systems without any pathological enhancement after paramagnetic contrast.

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Fig. 6: Subependymal nodules observed as isointense on FLAIR image and seen as multiple subependymal nodules in the lateral ventricular systems regarding calcified nodules on SWI. We can also objetify abnormalities of the white matter in the posterior areas of the occipital horns of the lateral ventricles and less marked in the anterior region on the frontal horns.

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**Fig. 7:** Radial white matter bands seen as curvilinear bands of hyperintensity on T2-FLAIR and iso- to hypointensity to normal white matter on T1-WI that run from juxtaventricular white matter toward the cortex.

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**Fig. 8:** Cystic white matter lesion near the lateral ventricles seen as hypointense lesions on T1-WI and hyperintense on T2-WI.
Fig. 9: Subependimal nodules and astrocytoma in a patient with ET.

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Fig. 10: Subependymal giant cell astrocytoma at the left foramen of Monro observed as hyperintense lesion in T2-WI.

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**Fig. 11:** The same lesion with high enhancement after contrast administration.

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**Fig. 12:** On CT we can observe multiple bilateral and small nodular foci along the walls of the ventricles which are typical of ET and a hypodense lesion at the left ventricle suggestive of subependymal giant cell astrocytoma. At MRI it is seen hyperintense in T2-WI.

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**Fig. 13:** We can observe that the lesion enhances after contrast administration.

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Fig. 14: Hyperechoic and homogeneous lesion of 15 mm, located in the front side of left ventricular system, suggestive of subependymal astrocytoma. At MRI it is seen as hypointense on T1-WI.

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**Fig. 15**: MRI shows the same lesion located on the left ventricular astrocytoma left system, adjacent of the foramen of Monro seems to have increased in size (maximum diameter 15 mm), with enhancement after contrast administration and with incipient left lateral ventricle dilation.

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Fig. 16: High resolution chest TC showing the pulmonary parenchyma that is almost entirely replaced by multiple thin-walled cyst images of different size.

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Fig. 17: In the same patient, abdomen CT demonstrates practical replacement of both kidneys' parenchymal and hepatic cysts, in relation with hepatorenal polycyst disease. The presence of hepatorenal polycystic disease associated with cystic lung lesions is described in association with tuberous sclerosis.

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**Fig. 18:** High resolution chest TC demonstrates multiple small ground glass pulmonary nodules with bilateral distribution that given the underlying disease of the patient are suggestive of multifocal micronodular pneumocyte hyperplasia.

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Fig. 19: Coronal and axial CT images demonstrate multiple bilateral angiomyolipomas with characteristic fatty components (attenuation values -56 UH and -43 UH).

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Fig. 20: Renal angiomyolipomas.

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**Fig. 21:** Axial T1-WI, STIR and VIBE MR images demonstrate some hyperintense well defined nodules in both kidneys in T1-WI, that loss of signal in STIR sequence and without enhancement after gadolinium administration (VIBE sequence). They are suggestive of angiomyolipomas.

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Fig. 22: Ultrasounography demonstrates bilateral renal cysts in a one year old child.

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**Fig. 23:** Axial CT scan demonstrate a hepatic angiomyolipoma with characteristic fatty components.

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**Fig. 24:** Coronal CT scan demonstrates multiple small nodular hepatic lesions, some of them calcified (hamartomas likely) and other predominantly fatty (lipomas).

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Fig. 25: Axial and coronal CT scan demonstrate pancreatic angiomyolipomas with characteristic fatty components.

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Fig. 26: Sagital and axial CT scans demonstrates sclerotic deposits.
**Fig. 35:** Axial MRI show bilateral vestibular schwannomas seen as two masses inside the internal auditory canals. On the right side it extends medially into the cerebello-pontine angle (ice-cream cone appearance). Homogeneous enhancement is seen after contrast administration.

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Fig. 36: Coronal MPR curve where bilateral vestibular schwannomas can be objetified.

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Fig. 37: Bilateral vestibular schwannomas seen as two hyperintense tumors inside the internal auditory canals on T2-FLAIR sequence.

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**Fig. 38:** Bilateral vestibular schwannomas seen as iso-hyperintense tumor on T2-WI. On the right posterior lobe of the cerebellum a meningioma is observed as a heterogeneous mass on T2-WI.

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**Fig. 39:** Bilateral vestibular schwannomas seen as iso-hyperintense tumor on T1-WI with enhancement after contrast administration. On the right posterior lobe of the cerebellum a meningioma is observed as a heterogeneous mass on T1-WI that enhance after gadolinium administration.

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**Fig. 40:** Bilateral vestibular schwannomas with cystic degeneration on the left side on T1-WI and T2-WI.

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Fig. 41: T2-FLAIR, T1-WI and T1 after contrast administration demonstrate múltiple cranial meningiomas.

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**Fig. 42:** T2-FLAIR, T1-WI and T1 after contrast administration demonstrate intraventricular meningiomas.

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**Fig. 43:** Coronal and sagittal MR images after contrast administration demonstrate homogeneous enhancement of cranial meningiomas.

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**Fig. 44:** Sagital MRI demonstrate multiple foci of intramedullary enhancement in cervical region suggestive of ependymomas.

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**Fig. 45:** Sagital MRI demonstrate multiple foci of intramedullary enhancement in lumbar region suggestive of ependymomas. There is also observed a intramedullary spinal lesion in the cone which is hyperintense on T2-WI and enhances intensely after contrast administration. In the clinical setting it is suggestive of an ependymoma.
**Fig. 46:** Sagittal MRI showing multiple peripheral schwannomas

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Fig. 47: Coronal MRI showing left schwannoma in cervical region.

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Fig. 50: MRI shows an asymmetry in the signal intensity of a patient with an endolymphatic sac tumor.
Fig. 49: MRI images shows a solid hemangioblatoma in a patient with von Hippel lindau disease.

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Conclusion

Phakomatosis are a heterogeneous group of diseases that affect primarily the central nervous system, although other organs may also be involved. Its clinical expression is very heterogeneous so it is important to know its main features in order to obtain a correct radiological diagnosis and subsequent management.
References


