Cerebral Calcifications as a differential diagnosis of psychiatric symptoms

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Introduction

- Radiological investigations are useful tools to exclude organic pathology in patients presenting with psychiatric symptoms.
- One of the possible radiological findings that can indicate presence of current or previous organic pathology contributing to the clinical psychiatric presentation is the presence of cerebral calcifications which can occur in a wide range of conditions with different etiologies.
- Calcifications can occur as physiologic, dystrophic, congenital or vascular calcifications.
- For psychiatric patients who present with cerebral calcifications, the location of calcification and the clinical psychiatric and systemic presentations are important in establishing a final diagnosis (Mufaddel & Al Hassani, 2014).

Types of calcification based on location

- Based on their location, cerebral calcifications can be divided into:
- Extra-axial calcifications
- Intra-axial calcifications

Extra-axial calcifications

- Extra-axial cerebral calcifications are commonly caused by meningiomas, dural osteomas, calcifying tumours, and physiological calcifications (Celzo et al, 2013).
- Some rare conditions with multi-system involvement can also be associated with extra-axial calcifications such as that occurring in Gorlin-Goltz syndrome with characteristic falx-cerebri calcification (Mufaddel et al, 2014).

Structres involved in extra-axial calcification

- Falxcerebri,
- The pineal gland,
- Choroid plexus,
- Habenula,
- Dura and arachnoid,
- Tentorium cerebelli,
- Superior sagittal sinus,
- Petroclinoid and interclinoid ligaments,
- Arachnoid granulations

Frontal lobe meningioma

- Frontal meningiomas can compress the frontal lobes externally, leading to personality and intellectual changes.
- They are sometimes seen by psychiatrists before the diagnosis of meningioma is established due to the nature of their psychiatric symptoms (cases presenting with longstanding history of visual hallucinations and personality change.
- Headache may precede the psychiatric symptoms and others may later develop epilepsy.
- Symptoms may resemble depression, anxiety, hypomania, and schizophrenia.
- Surgical treatment was associated with improvement of symptoms

Gorling-Goltz syndrome

- Gorling-Goltz syndrome is an autosomal dominant syndrome with multiple and diverse clinical features that involve the nervous system, skin, eyes, endocrine system, and bones.
- Gorlin-Goltz syndrome is diagnosed by the presence of either two major criteria or one major and two minor criteria.

Major and minor criteria

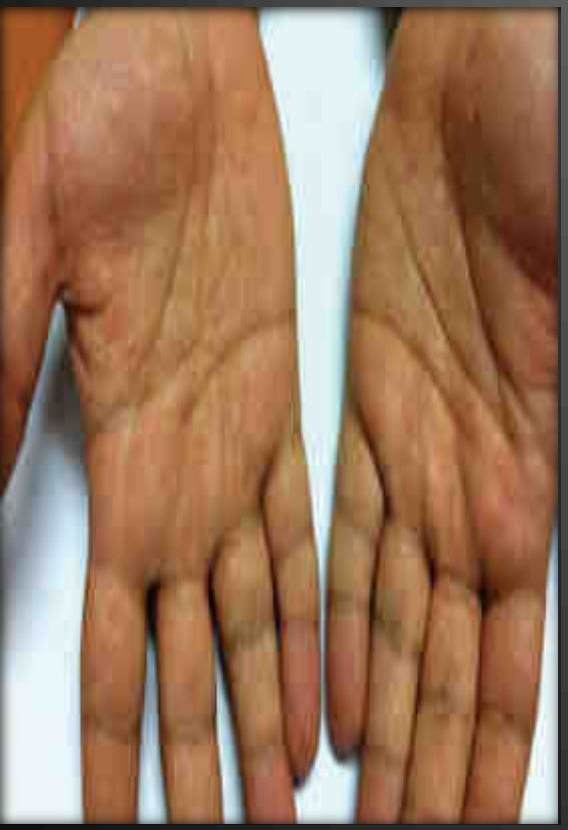
The major criteria:

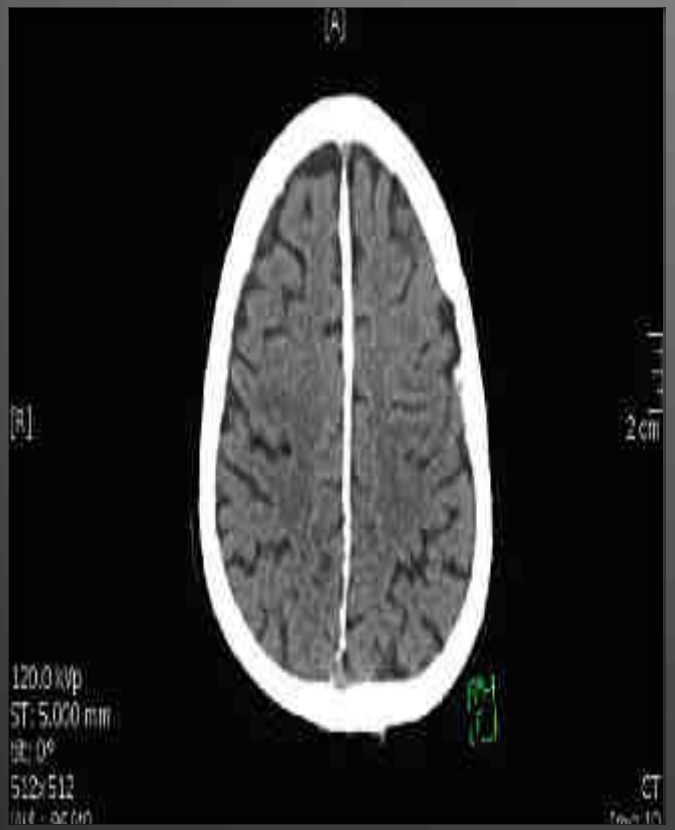
- Multiple (>2) basal cell carcinomas
- Odontogenic keratocysts of the jaws proven by histopathology.
- Three or more palmar or plantar pits.
- Bilamellar calcification of the falx cerebri.
- Bifid, fused or markedly splayed ribs.
- First-degree relatives with nevoid basal cell carcinoma.

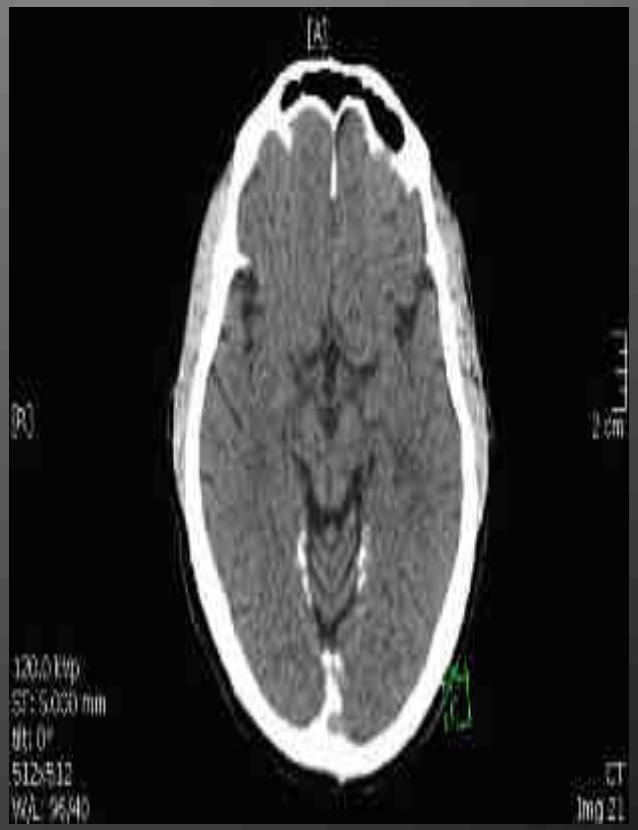
The minor criteria:

- Macrocephay
- Frontal bossing, cleft lip/palate, pectus, and syndactyly of digits.
- Sprengel deformity, pectus, and syndactyly of digits.
- Radiology abnormalities: bridging of sella turcica, hemivertebrae, and flame-shaped radiolucencies.
- Ovarian fibroma
- Medulloplastoma

A Case of Gorlin-Goltz Syndrome Presented with Psychiatric Features.







Mufddel A, AlSabosi M, Salih B, AlHassani G., Osman OT. A Case of Gorlin-Goltz Syndrome Presented with Psychiatric Features. Behav Neurol. 2014; 2014: 830874.)

Intra-axial calcifications

Etiology:

- neoplasm,
- vascular causes,
- infections,
- congenital disorders,
- endocrine/ metabolic causes.
- idiopathic (Fahr's disease).

Anatomical location:

- Basal ganglia
- Cerebellum

Brain tumors

Tumors that are commonly associated with intracranial calcifications include

- astrocytomas,
- craniopharyngiomas,
- meningiomas,
- pineal gland tumors,
- oligodendrogliomas,
- and ependymomas.

(*Makariou & Patsalides, 2009; Celzo et al, 2013*).

Brain tumors

- In some cases psychiatric symptoms **can be the first presenting symptoms** of brain tumours in the absence of neurological signs. (e.g. incidental MRI findings of **thalamic tumor** have been reported in patients presenting only with psychiatric symptoms).
- Patients may present with **mood change, psychotic symptoms, panic attacks, personality changes, or memory problems**. (*Moise & Madhusoodanan ,2006*).
- In other cases, **neurological signs can be minimal and the psychiatric symptoms are more prominent** (e.g., **parietal lobe tumors** which can present with **depression accompanied by minimal neurological findings**. (*Madhusoodanan et al, 2004*).

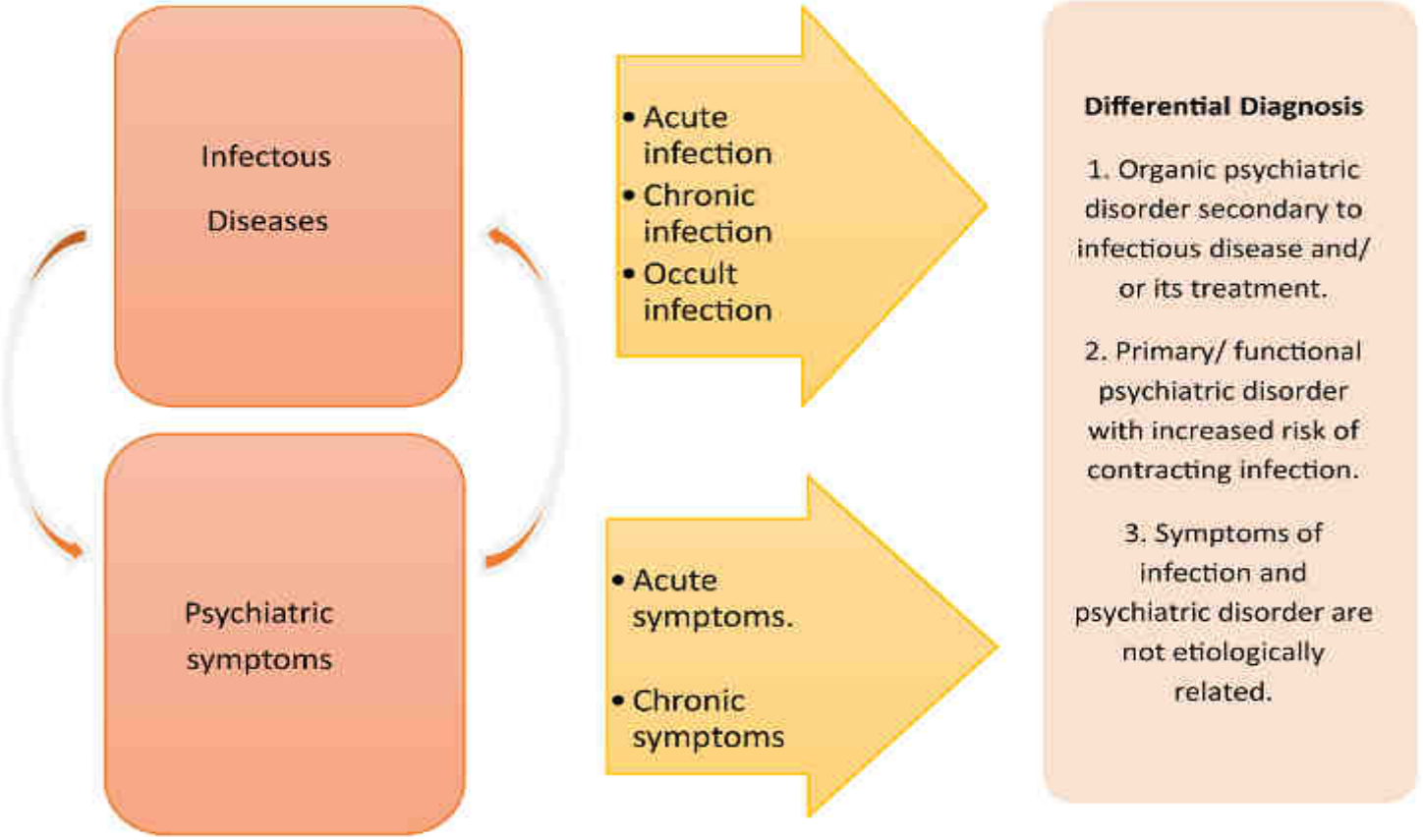
Vascular Disorders:

- **Etiology**: atherosclerosis, aneurysm, arteriovenous malformation or cavernous malformation.
- Atherosclerotic calcifications: **larger volumes of calcification** are associated with **lower cognitive scores** and **smaller total brain volumes** (Bos et al, 2012).
- Vascular disorders are associated with developing **neurodegenerative conditions** such as Alzheimer's disease, multiple sclerosis and Huntington's.
- Cerebrovascular disease may also lead to **vascular type of dementia** which is the **second commonest cause of dementia.**

Infections

- Both acquired and congenital infections can be associated with cerebral calcifications as well as psychiatric symptoms (e.g. mood symptoms secondary to brucellosis or toxoplasmosis).
- Late-onset neuropsychiatric complications, occurring several years following the infection, have also been reported such as in the case of subacute sclerosing panencephalitis due to measles.
- Some Infectious diseases are thought to have possible etiological role for major psychiatric disorders (e.g. Influenza virus and HSV-1),
- *Mufaddel A., Omer A., Omer O. Psychiatric aspects of infectious diseases. OJPsych 2014*

Co-existing psychiatric symptoms and infectious diseases.



Mufaddel A., Omer A., Omer O. Psychiatric aspects of infectious diseases. OJPsych 2014).

Infections

- The most common **acquired intracranial infections** that are typically associated with intracranial calcifications include: cysticercosis, tuberculosis, HIV and cryptococcus infections (*Makariou & Patsalides, 2009*).
- **Congenial toxoplasmosis** usually presents with the **classic triad of chorioretinitis, hydrocephalus, and intracranial calcifications.**
- Sequelae of congenital toxoplasmosis include **mental retardation, psychomotor abnormalities, seizures, deafness, microcephalus, and hydrocephalus** (*Robert-Gangneux & Dardé, 2012*).
- Other infectious diseases: CMV, Rubella, Neonatal herpes simplex encephalitis.

Congenital Disorders:

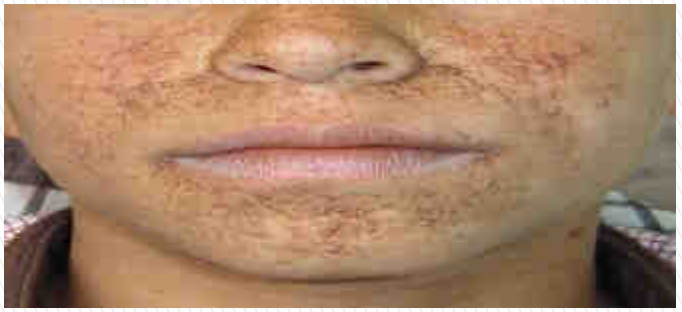
Cerebral calcification in congenital disorders is frequently seen in:

- Sturge-Weber syndrome,
- tuberous sclerosis,
- neurofibromatosis,
- intracranial lipoma,
- Cockayne and
- Gorlin syndromes

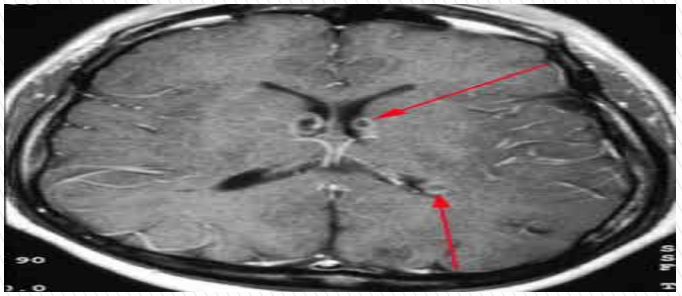
Tuberous sclerosis

- TS is an autosomal dominant condition that presents with a triad of:
  - Epilepsy
  - Low Intelligence
  - Adenoma Sebaceum
- Cognitive impairment is often **severe** and **learning disability** occurs in **38%-64%** of cases.

Adenoma sepaceum



Cerebral hamartoma



Bilateral renal masses & bilateral renal cysts

Webb DW, Fryer AE, Osborne JP. On the incidence of fits and mental retardation in tuberous sclerosis.J Med Genet. 1991;28:395-7.

TS and autism spectrum disorders

- TS is **one of the few established medical causes of autism** spectrum disorder.
- Epidemiological studies have shown that individuals with tuberous sclerosis complex were found to have:
  - **Mental retardation (50-60%).**
  - **Autistic-like pervasive developmental disorders (43-86%).**
- On the other hand, **children with autism have tuberous sclerosis** complex existing in **1%** of cases.

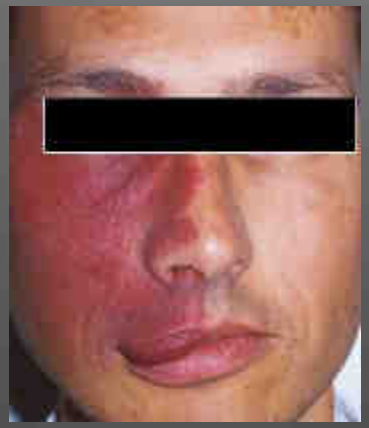
Harrison JE, Bolton PF. Annotation: tuberous sclerosis. J Child Psychol Psychiatry 1997; 38: 603-614.

Other psychiatric symptoms in TS

- Other psychiatric symptoms include :
- **Psychosis,**
- **Anxiety and**
- **Depression.**
- **Childhood-onset mood disorders** were also reported in some cases

Sturge-Weber Syndrome (encephalo-facial-angiomatosis)

- Is a congenital disorder with exceptional familial occurrence.
- Capillary malformations involving the skin, eye and the brain.
- Skin involvement presents with port-wine naevus involving one side of the face in the distribution of a fifth nerve division.
- Brain involvement presents with lepto-meningeal angioma which tends to involve the parietal and occipital lobes.
- Eye involvement may lead to glaucoma.



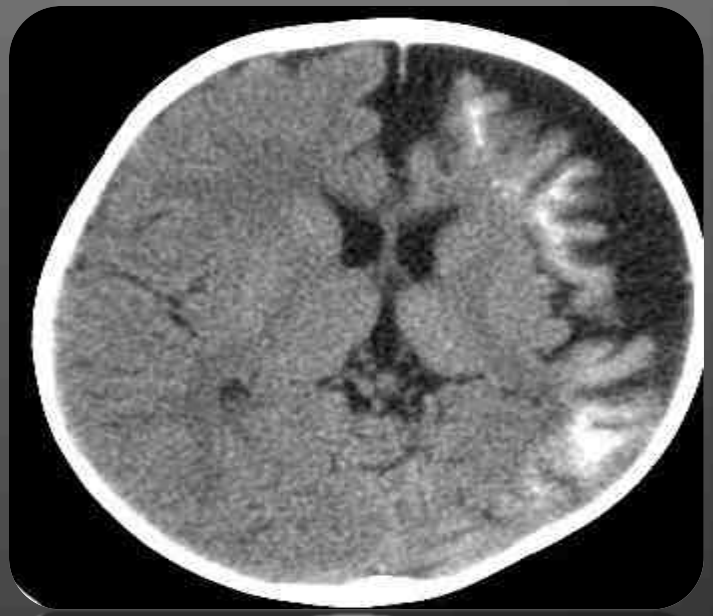
Right sided port-wine stain of the face and ipsilateral tissue hypertrophy.

Left-sided port-wine stain with conjunctival involvement. The patient also has left glaucoma.

Crosley CJ, Binet EF. Sturge-Weber Syndrome: presentation as a focal seizure disorder without nevus flammeus. ClinPediatr (Phila) 1978;17:606-9.

Neuropsychiatric features of Sturge-Weber syndrome

- Epilepsy
- Cognitive symptoms
- ADHD
- mood disorder (31%),
- disruptive behaviour (25%),
- adjustment disorder (25%).
- Substance-related disorders (67%).
- Headache
- Hemiparesis
- Visual field defects.



Sturge-Weber syndrome CT. Cerebral atrophy and calcification.

Taly AB, Nagaraja D, Das S, Shankar SK, Pratibha NG.Sturge-Weber-Dimitri disease without facial nevus.Neurology. 1987;37:1063-4.

Metabolic

- Basal ganglia and subcortical calcifications may occur in patients with chronic renal failure and secondary hyperparathyroidism.
- Calcification due to hypoparathyroidism typically involve the basal ganglia, thalami, and the cerebellum.
- Cerebral calcifications are more common pseudohypoparathyroidism than idiopathic hypopharatyroidism.
- Hypothyroidism can be associated with basal ganglia and cerebellar calcifications(Makariou & Patsalides, 2009).
- Psychiatric features in hypoparathyroidism include depression, anxiety, emotional lability, confusion, and psychosis (Hossain, 1970).

Familial Idiopathic Basal Ganglia Calcification (Fahr's disease):

- Fahr's disease is a rare neurodegenerative disorder which is characterized by the presence of symmetrical and bilateral calcification of the basal ganglia.
- Calcifications were also reported in other brain regions such as dentate nucleus, thalamus and cerebral cortex.
- Familial and non-familial cases of the disease have been reported, with predominantly autosomal-dominant fashion.
- Neuropsychiatric features and movement disorders are the common presenting clinical features (*Mufaddel & Al Hassani, 2014*).

Differential diagnosis of coexisting psychiatric symptoms and cerebral calcification

Psychiatric condition	Possible etiological conditions with cerebral calcification
Mood changes/ depression	**Intra-axial: t**emporal lobe tumors, parietal lobe tumors, thalamic lesions, craniopharyngioma , infections (brucellosis, toxoplasmosis, hypoparathyroidism, Fahr's disease, tuberous sclerosis. **Extra-axial calcifications:** Frontal lobe meningioma, Gorlin –Goltz syndrome
Psychotic symptoms	**H**ypoparathyroidism, Fahr's disease, Infections (influenza virus, HSV-1, congenital rubella, frontal lobe meningioma, Gorlin –Goltz syndrome
Personality changes	Extra-axial calcifications (Frontal lobe tumors such as meningioma)
Autism	Tuberous sclerosis, Infections (congenital rubella,
ADHD	Sturge-Weber syndrome, Neurofibromatosis
Mental retardation	Tuberous sclerosis, Sturge-Weber syndrome, Neurofibromatosis, Craniopharyngioma, Infections: Congenital toxoplasmosis, CMV
Dementia	Vascular lesions, Hypoparathyroidism

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Thank You