Neurological disorders -I

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MICROCEPHALY

Definition

Microcephaly is head circumference that measures more than three standard deviations below the mean for age and sex.

This condition is relatively common, particularly among developmentally delayed children.

- there are many causes of microcephaly,
- abnormalities in neuronal migration during fetal development, including heterotopias of neuronal cells and cytoarchitectural derangements, are often found

- Microcephaly may be subdivided into 2 main groups:
- primary (genetic)microcephaly and secondary (nongenetic) microcephaly.
- A precise diagnosis is important for genetic counseling and for prediction for future pregnancies

Primary Microcephaly

- Primary microcephaly refers to a group of conditions that usually have no associated malformations
- follow a mendelian pattern of inheritance or are associated with a specific genetic syndrome.

- Affected infants are usually identified at birth because of a small head circumference.
- The more common types include familial and autosomal dominant microcephaly and a series of chromosomal syndromes.

- Primary microcephaly is also associated with at least 7 gene loci, and 7 single etiologic genes have been identified.

- It is known as autosomal recessive primary microcephaly and has autosomal inheritance.

- Many X-linked causes of microcephaly are caused by gene mutations that lead to severe structural brain malformations such as
- lissencephaly,
- holoprosencephaly,
- polymicrogyria,
- cobblestone dysplasia,
- neuronal heterotopia,
- pontocerebellar hypoplasia; these should be sought on MRI.

Secondary microcephaly

- Secondary microcephaly results from a large number of noxious agents that can affect a fetus in utero or an infant during periods of rapid brain growth, particularly the 1st 2 yr of life.

Acquired microcephaly can be seen in conditions such as

- Rett,
- Seckel,
- Angelman syndromes
- encephalopathy syndromes associated with severe seizure disorders.

A-PRIMARY (GENETIC)

1-Familial (autosomal recessive)

- Incidence 1 in 40,000 live births
- Typical appearance with slanted forehead, prominent nose and ears; severe mental retardation
- prominent seizures;
- surface convolutional markings of the brain, poorly differentiated and disorganized cytoarchitecture

2-Autosomal dominant

- Nondistinctive facies, upslanting palpebral fissures, mild forehead slanting, and prominent ears
- Normal linear growth,
- seizures readily controlled,
- mild or borderline mental retardation

Syndromes

Down (trisomy 21)

- Incidence 1 in 800 live births
- Abnormal rounding of occipital and frontal lobes and a small cerebellum; narrow superior temporal gyrus,
- propensity for Alzheimer neurofibrillary alterations, ultrastructure abnormalities of cerebral cortex

Edward (trisomy 18)

- Incidence 1 in 6,500 live births
- Low birth weight, microstomia, micrognathia, low-set malformed ears, prominent occiput, rocker-bottom feet, flexion deformities of fingers, congenital heart disease, increased gyri, heterotopias of neurons

Cri-du-chat (5 p-)

- Incidence 1 in 50,000 live births
- Round facies, prominent epicanthic folds, low-set ears, hypertelorism, characteristic cry
- No specific neuropathology

B-SECONDARY (NONGENETIC)

1-Congenital Infections

A-Cytomegalovirus

- Small for dates,
- petechial rash,
- hepatosplenomegaly,
- chorioretinitis,
- deafness,
- mental retardation,
- seizures,
- Central nervous system calcification and microgyria

B-Rubella

- Growth retardation,
- purpura,
- thrombocytopenia,
- hepatosplenomegaly,
- congenital heart disease,
- chorioretinitis,
- cataracts,
- Deafness
- Perivascular necrotic areas, polymicrogyria, heterotopias, subependymal cavitations

C-Toxoplasmosis

- Purpura, hepatosplenomegaly, jaundice, convulsions, hydrocephalus, chorioretinitis, cerebral calcification

2-Drugs

Fetal alcohol

- Growth retardation, ptosis, absent philtrum and hypoplastic upper lip, congenital heart disease, feeding problems, neuroglial heterotopia, disorganization of neurons

Fetal hydantoin

- Growth delay, hypoplasia of distal phalanges, inner epicanthic folds, broad nasal ridge, anteverted nostrils

3-Other Causes

- Radiation most severe with exposure before 15th wk of gestation
- Meningitis/encephalitis Cerebral infarcts, cystic cavitation, diffuse loss of neurons
- Malnutrition Controversial cause of microcephaly

- Metabolic Maternal diabetes mellitus and maternal hyperphenylalaninemia
- Hyperthermia Significant fever during 1st 4-6 wk has been reported to cause microcephaly, seizures, and facial anomalies
- Hypoxic–ischemic encephalopathy :Initially diffuse cerebral edema; late stages characterized by cerebral atrophy and abnormal signals on MRI

CLINICAL MANIFESTATIONS AND DIAGNOSIS

- A thorough family history should be taken, seeking additional cases of microcephaly or disorders affecting the nervous system.
- It is important to measure a patient's head circumference at birth to diagnose microcephaly as early as possible.
- A very small head circumference implies a process that began early in embryonic or fetal development.

- An insult to the brain that occurs later in life, particularly beyond the age of 2 yr, is less likely to produce severe microcephaly.
- Serial head circumference measurements are more meaningful than a single determination, particularly when the abnormality is minimal.
- The head circumference of each parent and sibling should be recorded.

- Laboratory investigation of a microcephalic child is determined by the history and physical examination. If the cause of the microcephaly is unknown, the mother's serum phenylalanine level should be determined.

- High phenylalanine serum levels in an asymptomatic mother can produce marked brain damage in an otherwise normal nonphenylketonuric infant.

- A karyotype and/or array comparative genomic hybridization study is obtained if a chromosomal syndrome is suspected or if the child has abnormal facies, short stature, and additional congenital anomalies.

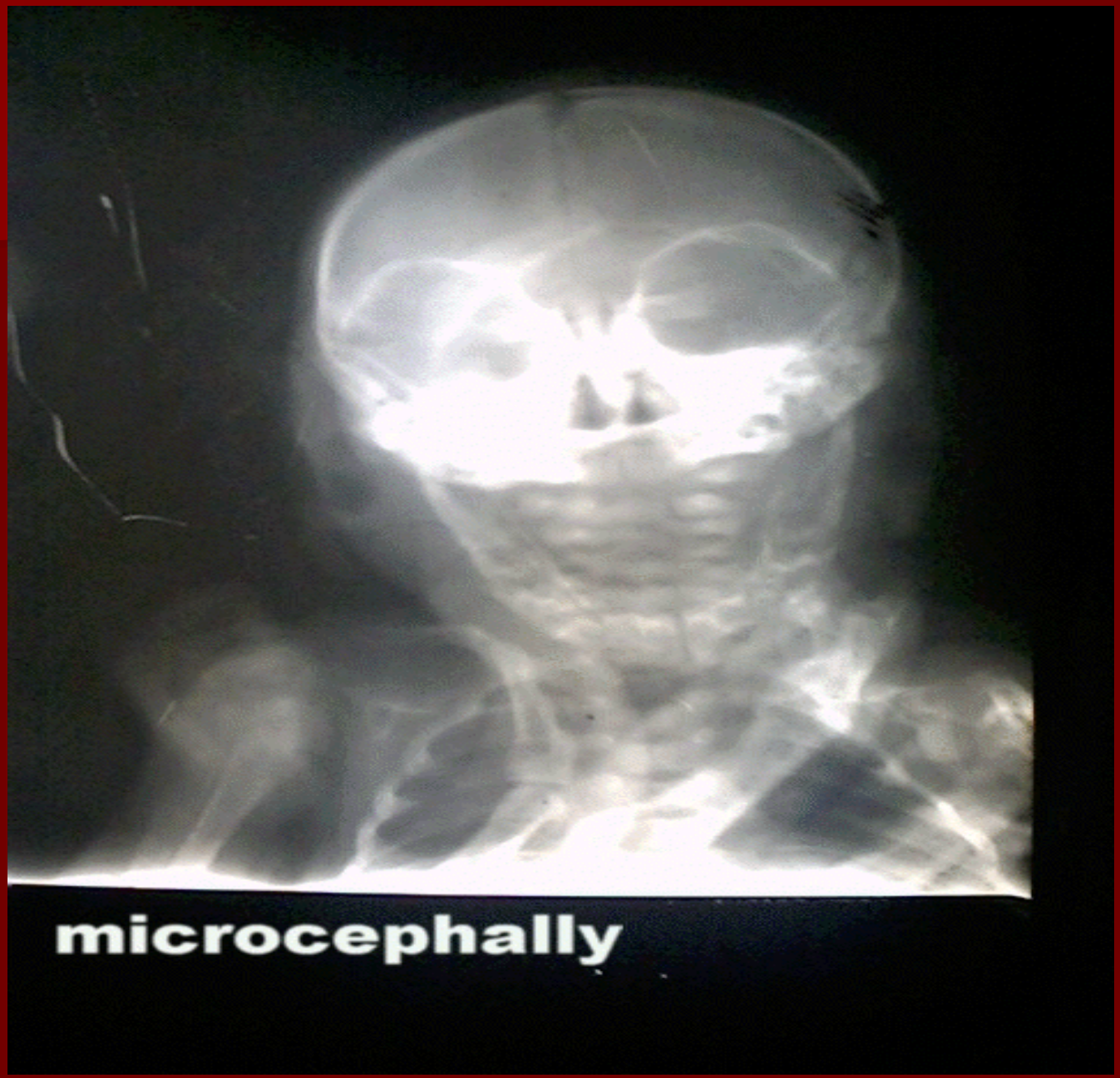
- MRI is useful in identifying structural abnormalities of the brain such as lissencephaly, pachygyria, and polymicrogyria, and CT scanning is useful to detect intracerebral calcification.

Additional studies include

- a fasting plasma and urine amino acid analysis;
- serum ammonia determination;
- toxoplasmosis, rubella, cytomegalovirus, and herpes simplex (TORCH) titers as well as HIV testing of the mother and child;
- a urine sample for the culture of cytomegalovirus.
- Single-gene mutations as a cause of both primary microcephaly and syndromic microcephaly are being increasingly identified.

Clinical picture(General)

- Slanted forehead, prominent nose and ears.
- Severe mental retardation.
- Seizures
- Serial measurement of head detects arrest or limited head growth.


microcephally

Differential Diagnosis

- Cranniostenosis

Treatment

- Supportive: for seizures and social handicaps
- Advice parents about recurrence risk in future pregnancy

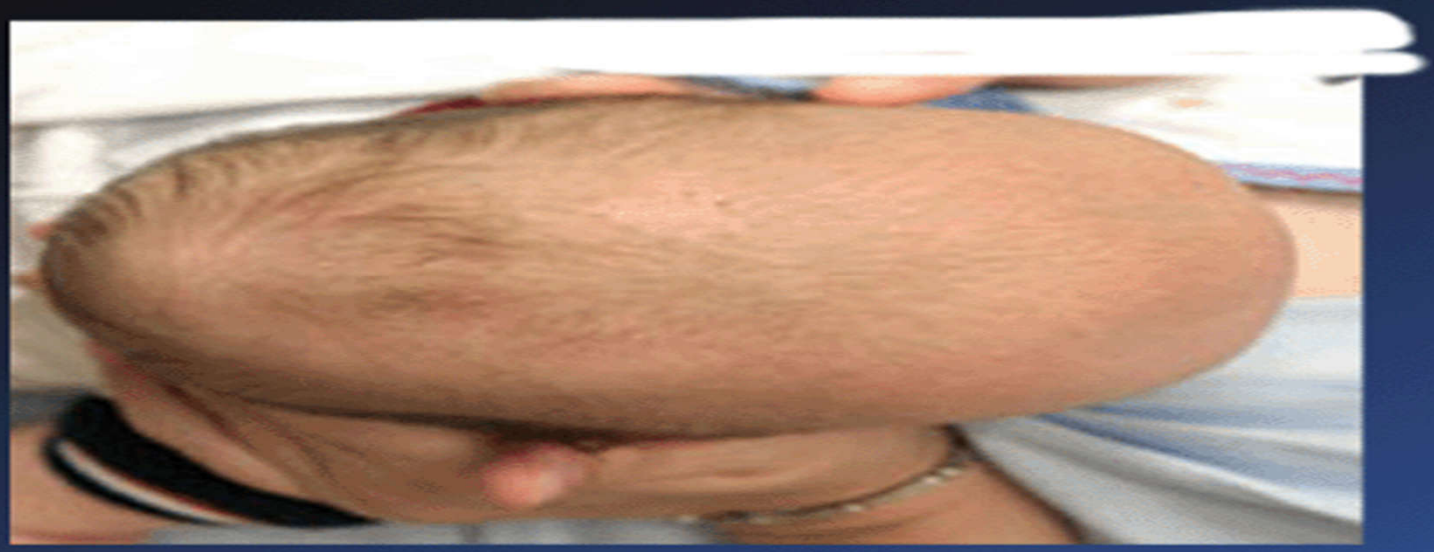
CRANIOSTENOSIS

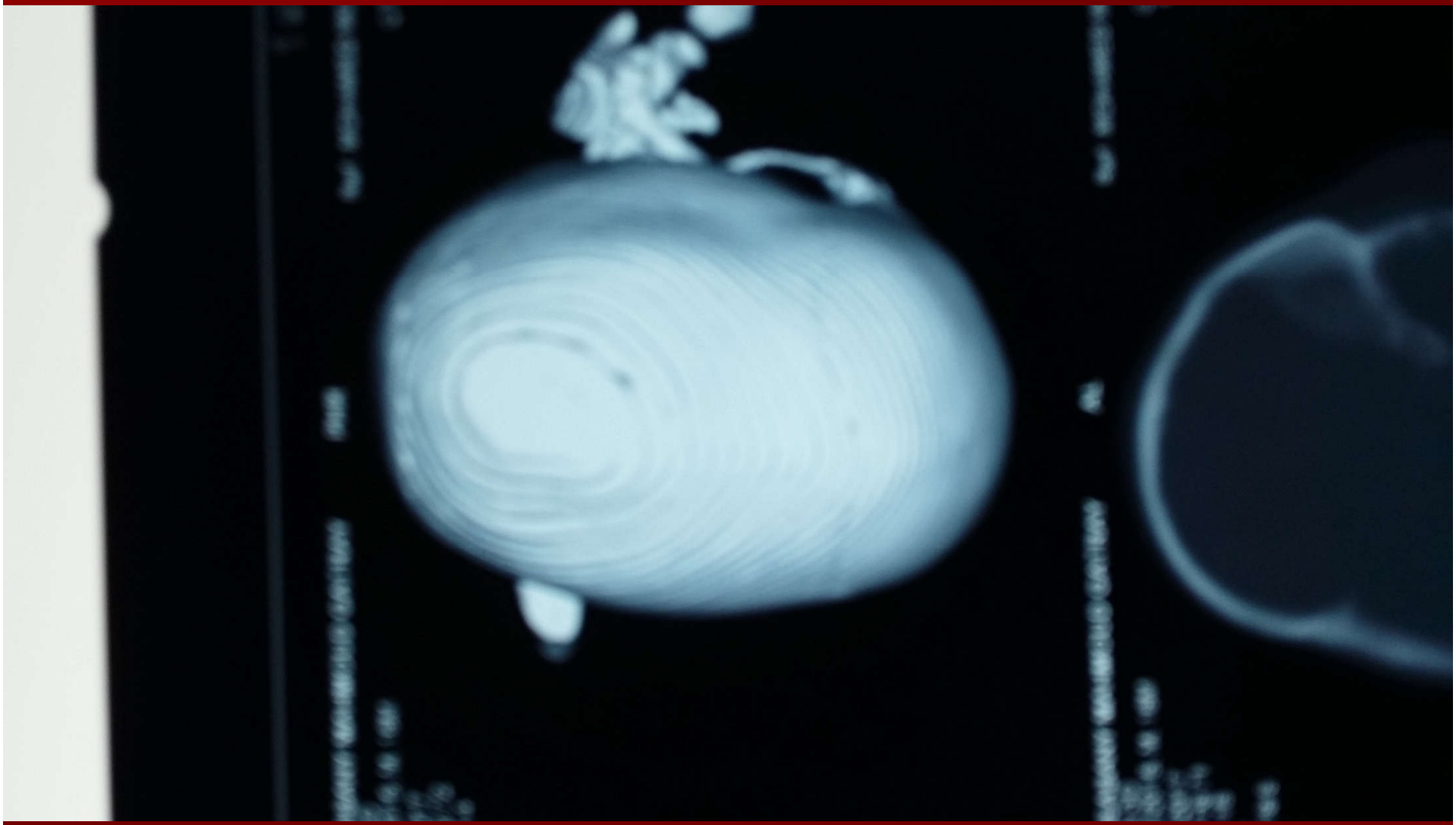
Definition:

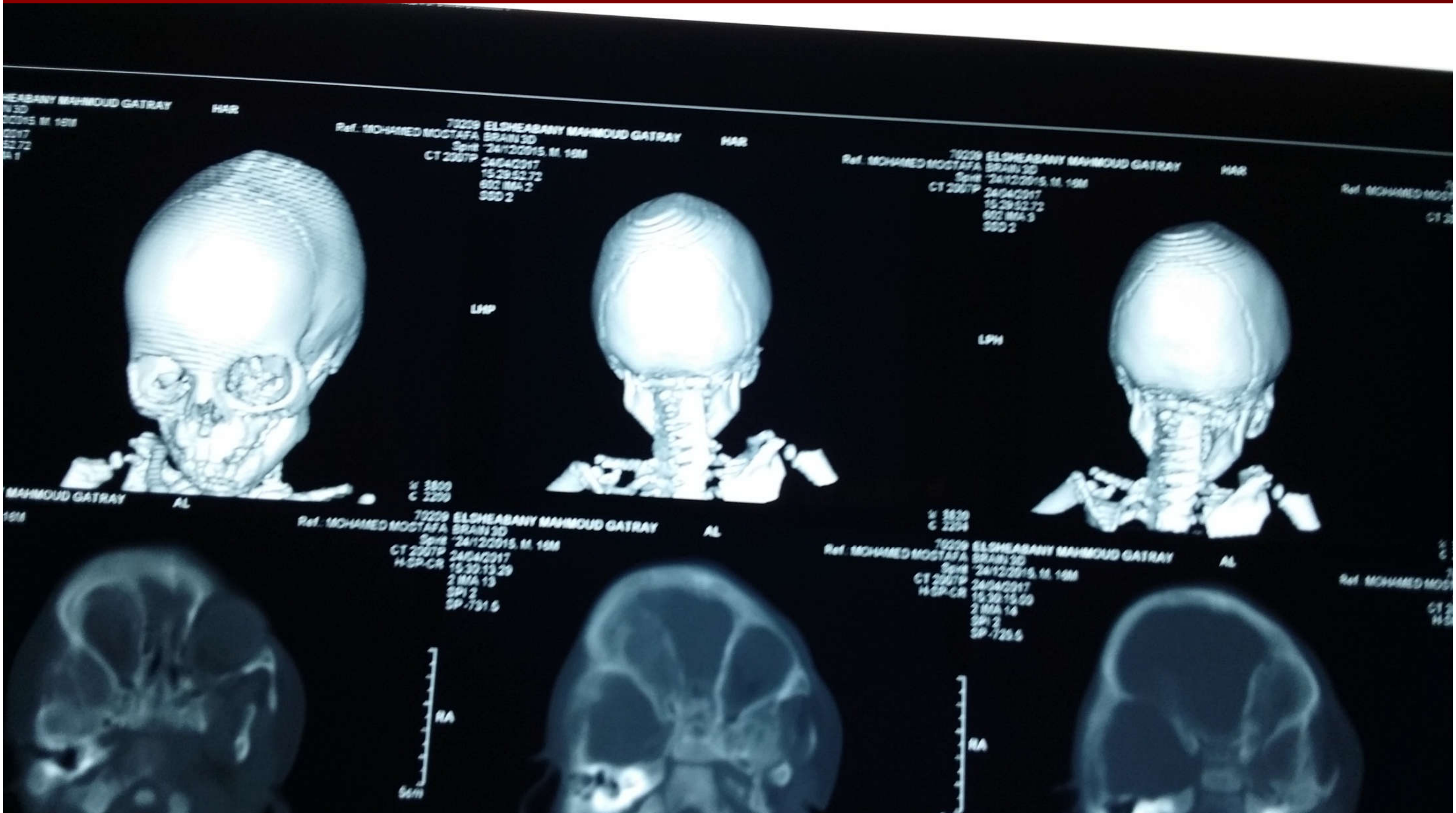
- Craniostenosis is premature closure of one or more of skull suture. It may be isolated craniostenosis or syndromic craniostenosis.

Clinical picture

- Skull Deformity
  - Scaphocephaly : long and narrow skull due to closure of sagittal suture.
  - Brachycephaly: The skull is short anteroposteriorly and extends laterally and superiorly.
  - Other deformities: according to the closed suture.
- Bony ridges over closed sutures.
- Convulsions may occur
- Signs of increased intracranial pressure
- It may be associated with some syndromes and include fusion of fingers and toes.



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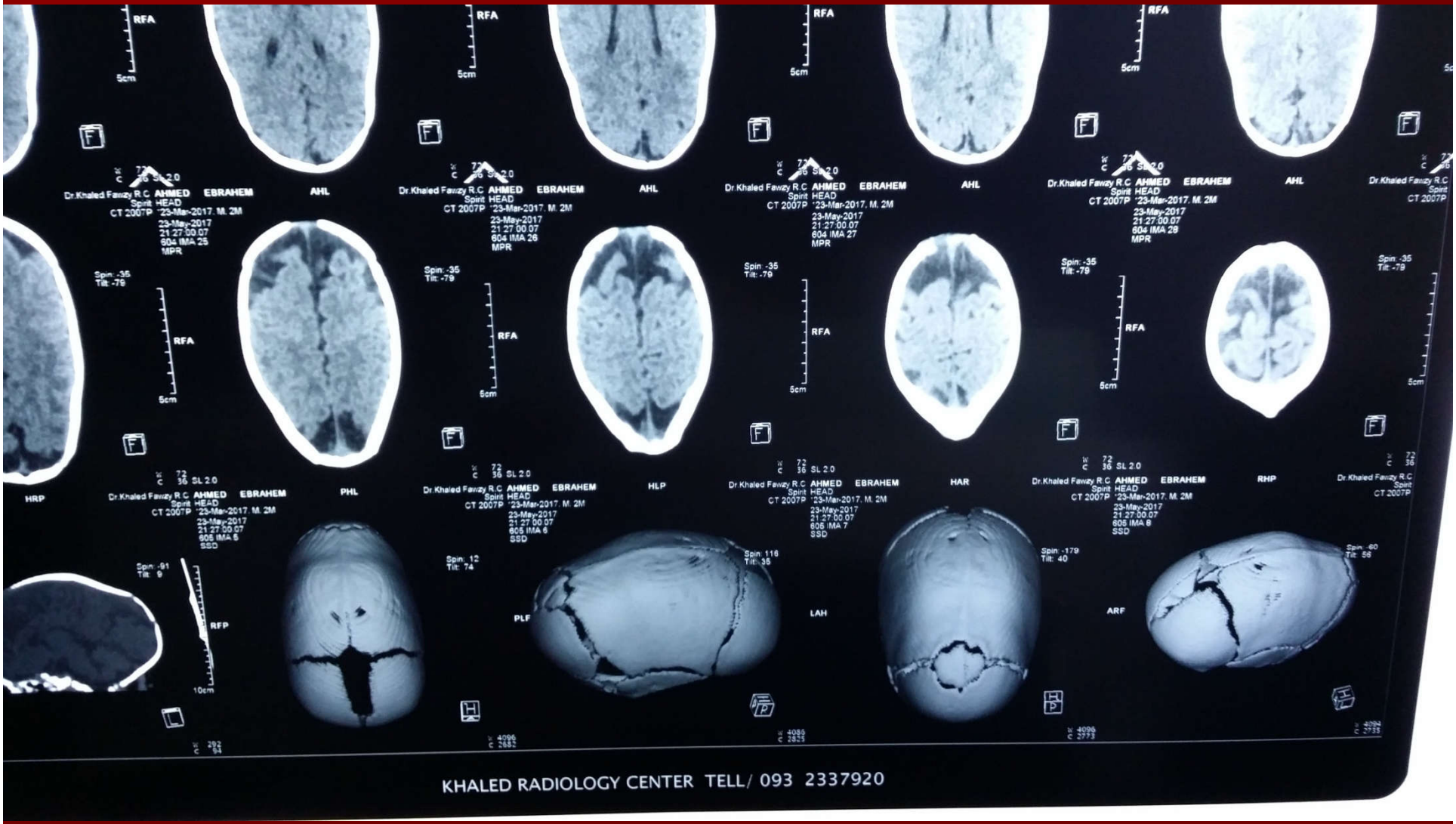
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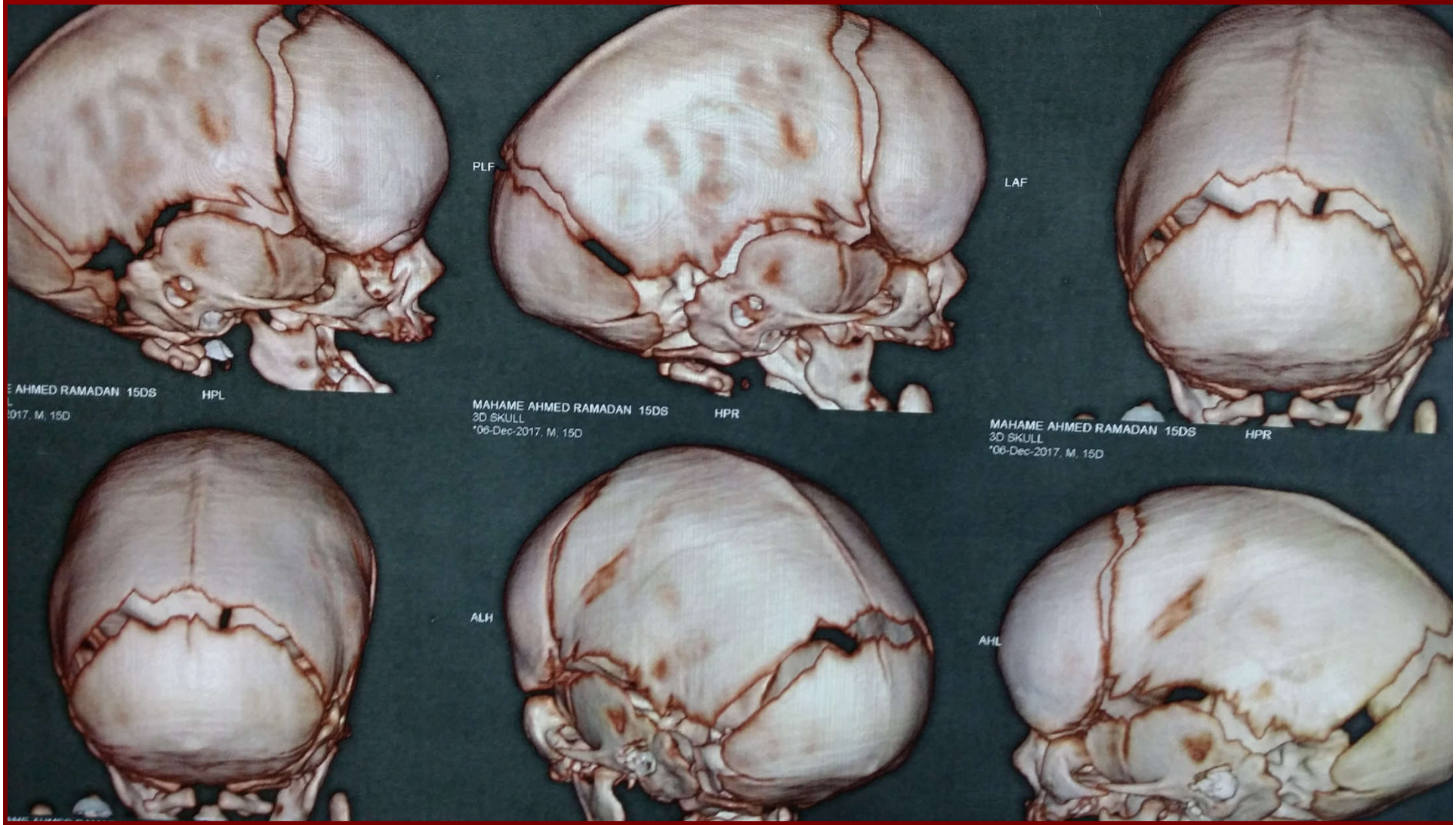
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ALH
AHL

- The most prevalent genetic disorders associated with craniosynostosis include
- Crouzon,
- Apert,
- Carpenter,
- Chotzen,
- and Pfeiffer syndromes.

- Crouzon syndrome is characterized by premature craniosynostosis and is inherited as an autosomal dominant trait.
- The shape of the head depends on the timing and order of suture fusion
- most often is a compressed back-to-front diameter or brachycephaly resulting from bilateral closure of the coronal sutures.

- The orbits are underdeveloped, and ocular proptosis is prominent.
- Hypoplasia of the maxilla and orbital hypertelorism are typical facial features.


Crouzon syndrome with exophthalmos
Crouzon syndrome at the age of five

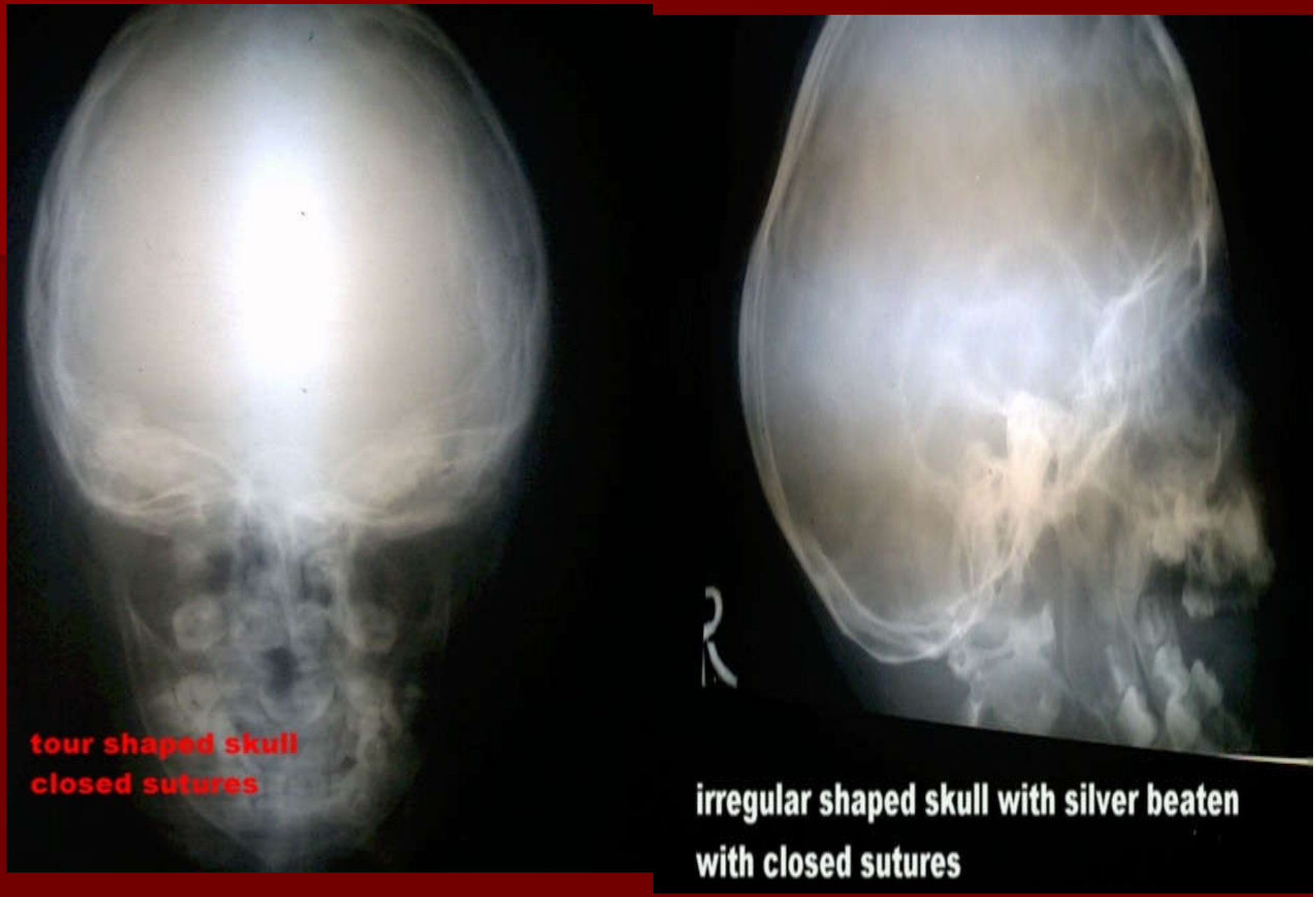
Investigations

- Skull X ray

  skull deformity, fusion of sutures, signs of increased intracranial tension(beaten silver appearance and wide sella turcica .(

- CT:

  manifestations of increased intracranial pressure may be seen


tour shaped skull
closed sutures
R
irregular shaped skull with silver beaten
with closed sutures

Treatment

- Early surgical craniectomy of the affected sutures is essential for management of increased intracranial pressure (ICP) with good results.

INCREASED INTRACRANIAL PRESSURE

Definition

- The intracranial pressure (ICP) exceeds the normal value. Normal value of ICP is less than 160mm of water .

Etiology

- The brain is positioned in a rigid bony skull. Increase of any of the contents inside the skull lead to increased the tension.

1-Infections

- Meningitis
- Cerebral abscess
- Tuberculoma

2-Fluid

- Intracranial hemorrhage
- Hydrocephalus
- Cerebral edema: after trauma or hypoxia or infection

3-Mass

- Leukemia
- Other brain tumors

4-Pseudotumor Cerebri(benign increase ICP)

- Hypervitaminosis A and vitamin A deficiency.
- Tetracycline therapy
- Metabolic disorders like galactosemia.
- infections

Clinical picture

- **In infants (before closure of fontanelle and sutures)**
  - **Irritability, lethargy and morning vomiting**
  - **Large sized head**
  - **Tense bulging anterior fontanel**
  - **Distended scalp veins**

In older children (After closure of fontenelles and sutures)

- **Irritability, lethargy and morning vomiting**
- **Headache**
- **Diplpia, papilledema and visual disturbance**
- **Sixth nerve paralysis**
- **Coma and disturbed conscious level**
- **Bradycardia, hypertension and irregular respiration**

Investigations

- Radiological

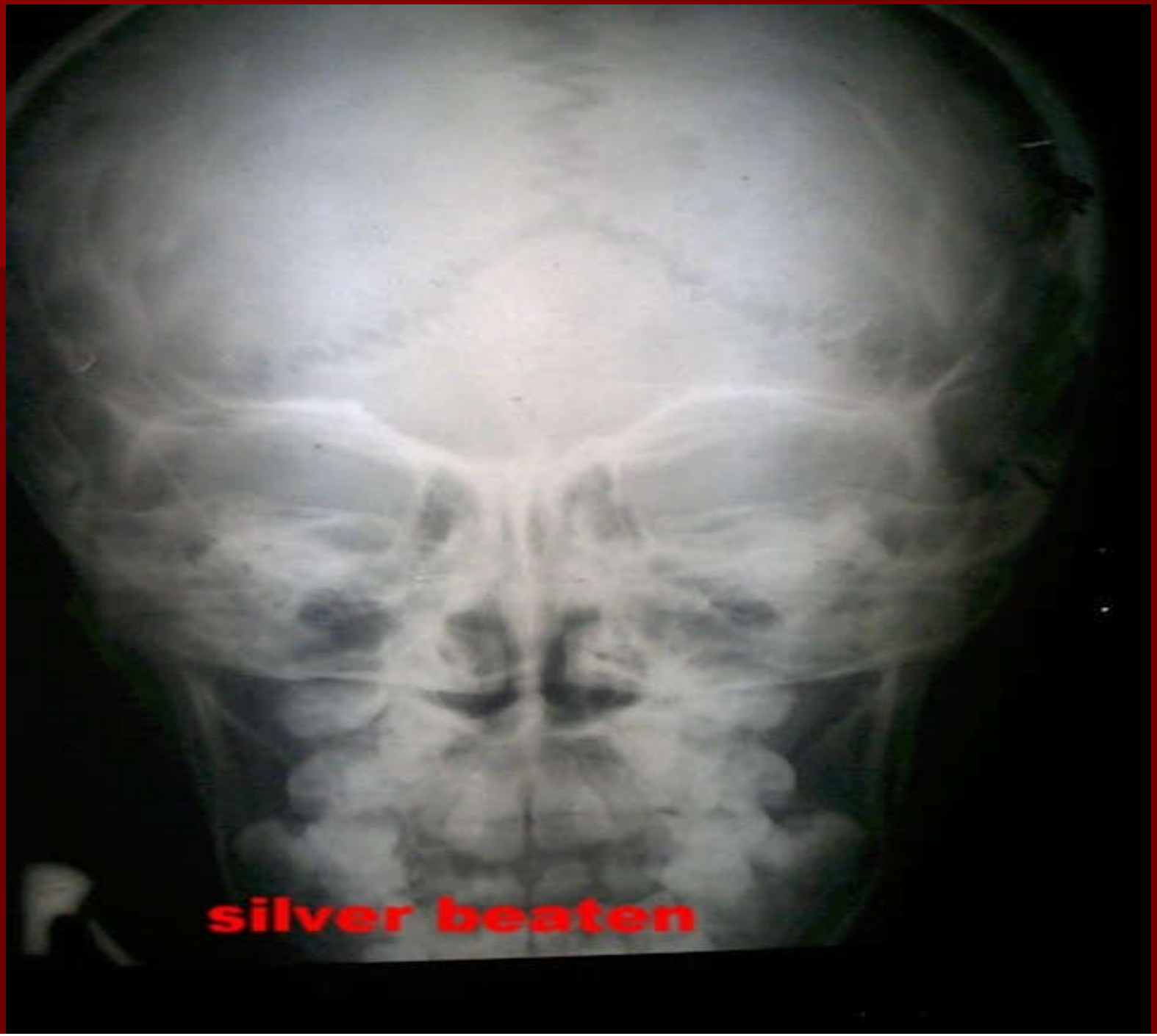
  1-Skull X ray

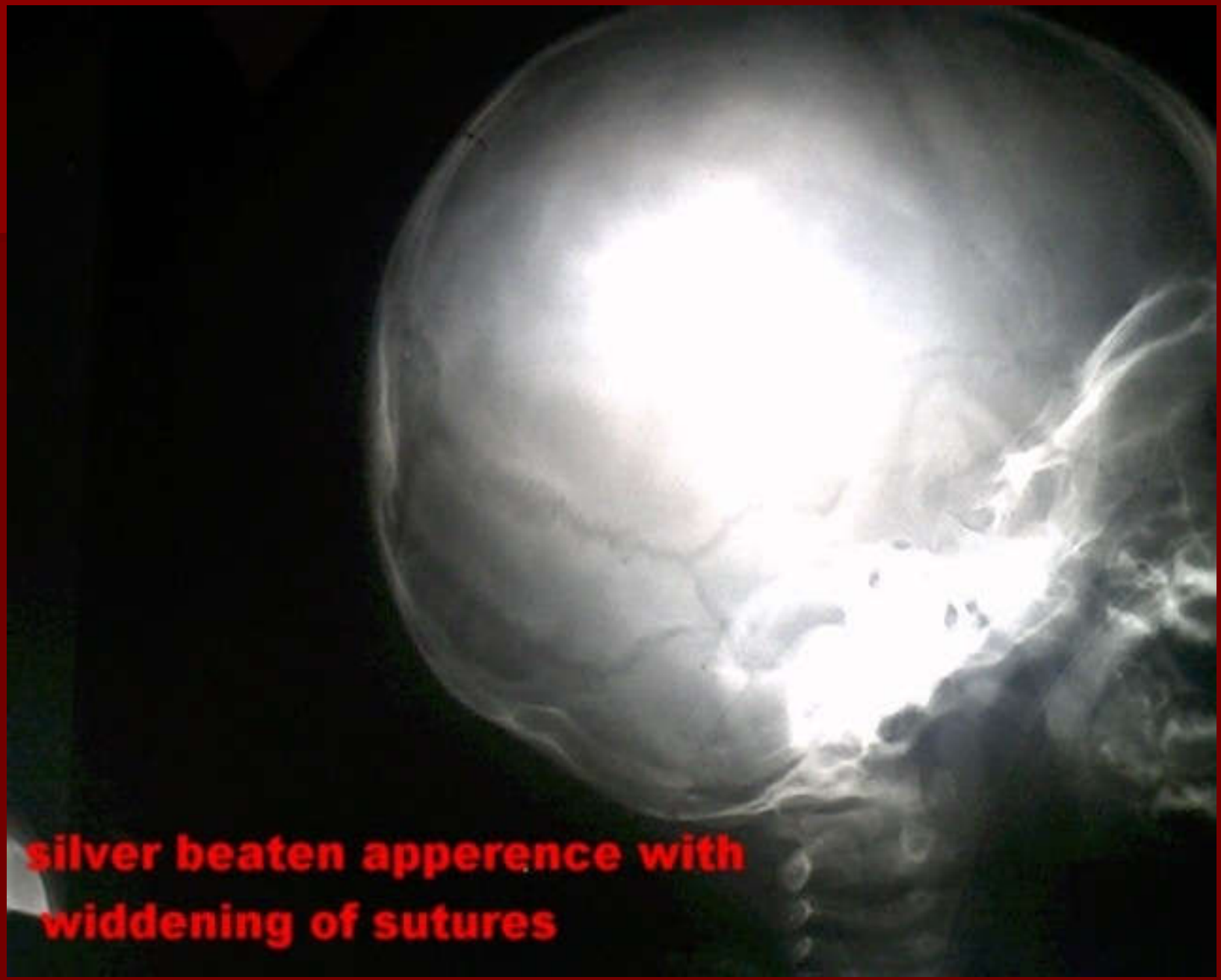
  wide separated sutures, beaten silver appearance and wide sella turcica

  2-CT or MRI: to find cause as hydrocephalus, abscess or mass.

- Laboratory

According to suspected etiology


silver beaten


silver beaten apperence with
widdening of sutures

Treatment

- Treatment of the etiology
- Reduction of increased ICP:

  a- Mannitol IV infusion

  b-Acetazolamide (10-30 mg/kg/24 hr) & corticosteroids have been used in cases of pseudotumour cerebri.

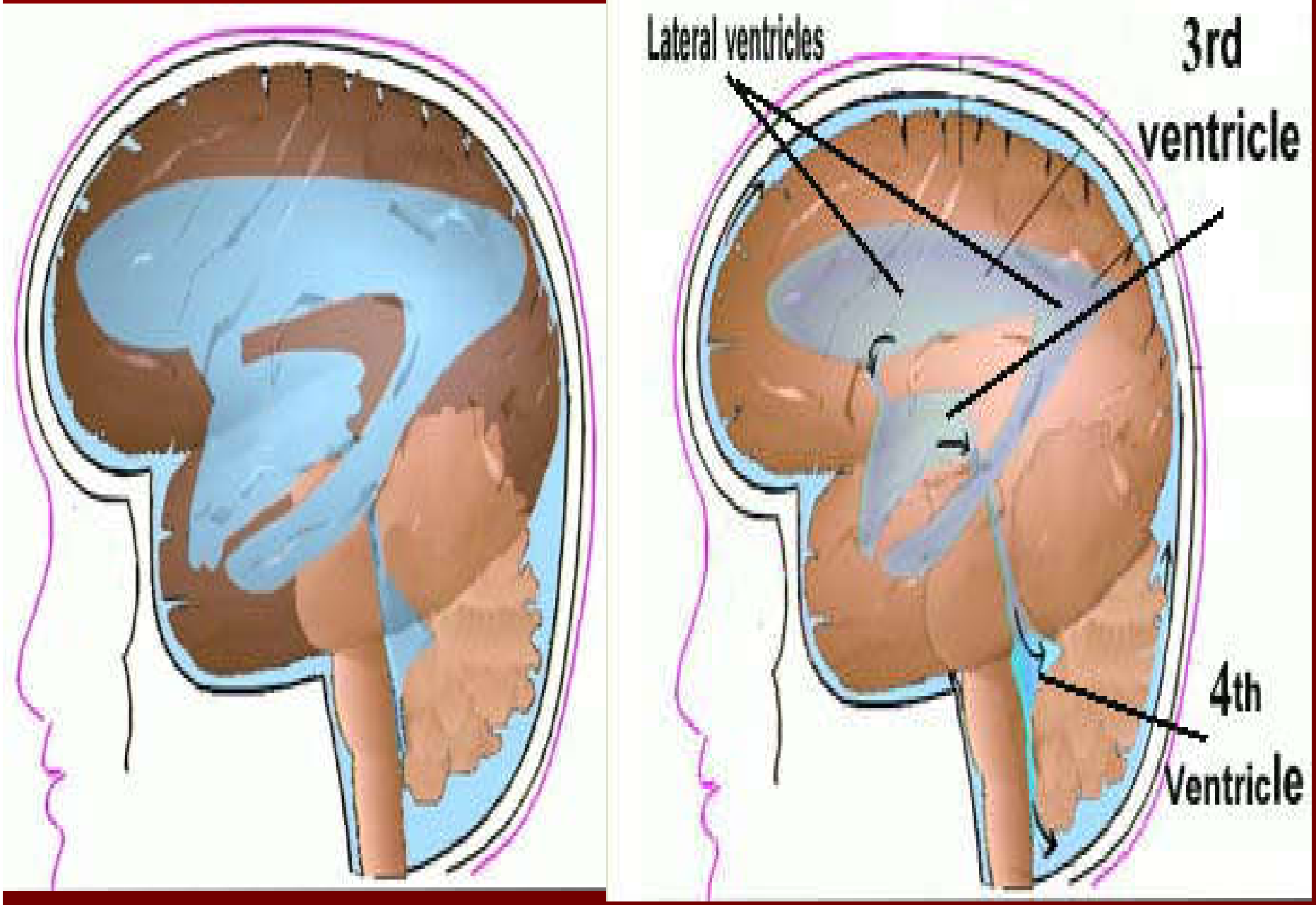
HYDROCEPAHLUS

Definition

- Accumulation of CSF within the head that result from impaired circulation and absorption of CSF or rarely from increased production by a choroid plexus papilloma.

CSF Circulation

- CSF is formed mainly in the ventricular system by the choroid plexus which is located in the lateral, third and fourth ventricles)
- CSF flows from the lateral ventricles to the third ventricle through foramina of Monro.
- CSF then flows from third ventricle to fourth ventricle through the narrow aqueduct of Sylvius.
- CSF then leaves fourth ventricle to the subarachnoid space through foramina of Luschka and foramen of Magendie.
- CSF is absorbed mainly by the arachnoid villi and to a much less extent by the lymphatic channels and by the choroid plexus itself.


Lateral ventricles
3rd
ventricle
4th
Ventricle

- Hydrocephalus results from obstruction within the ventricular system is called *obstructive or noncommunication hydrocephalus*.

- Hydrocephalus results from obstruction within the subarachnoid space or malfunction of the arachnoid villi is called non *obstructive or communicating hydrocephalus*.

Etiology:

1-Obstructive or noncommunicating hydrocephalus

A-Congenital

- Aqueductal stenosis: X linked recessive disease.
- Chiari malformation type II; it results from elongation of fourth ventricle and kinking of brainstem, with displacement of the inferior vermis, pons and medulla into the cervical canal. Hydrocephalus and myelomeningocele are present
- Malformation of vein of Galen
- Dandy-Walker syndrome; cystic dilatation of fourth ventricle and cerebellar atrophy.

B-Acquired

- Aqueductal gliosis; from neonatal meningitis or intracranial hemorrhage especially in preterm infants.

- Posterior fossa tumor, cysts or abscess.

2-Nonobstructive or communicating hydrocephalus

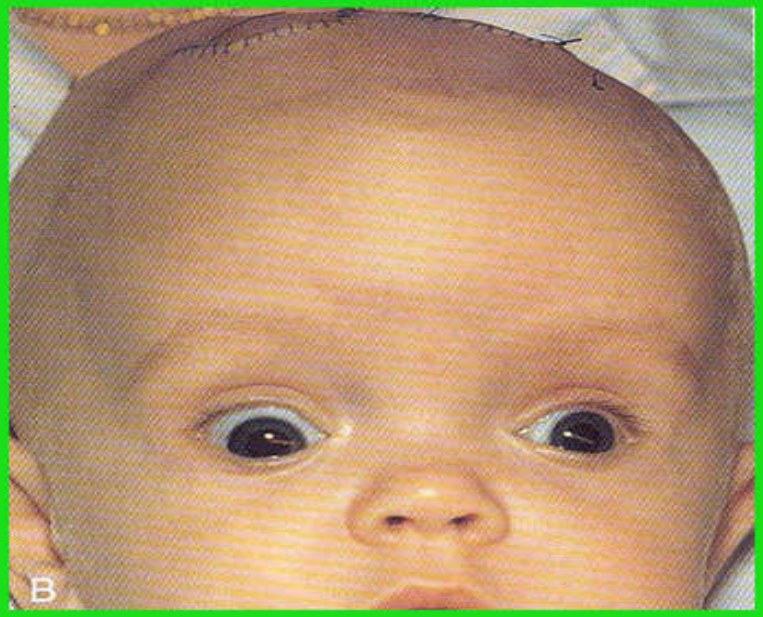
- Subarachnoid hemorrhage especially in preterm infants
- Pneumococcal and tuberculous meningitis
- Intrauterine intracranial infections as toxoplasmosis and cytomegalovirus
- Leukemic infiltrates.

Clinical picture

- **Infants and before closure of the fontanelle**.
  - Skull:
    - **Large size and progressive increased in size with repeated measurements**
    - **Separation of sutures**
    - **Fontanelles are widely opened. Anterior fontanel is tense and bulging.**
    - **Scalp skin is stretched and thin with dilated veins.**
    - **McEwen sign: cracked pot percussion note of the skull due to separation of sutures**
    - **Bruit is auscultated in cases vein of Galen malformation.**
    - **Transillumination is positive with massive ventricular dilatation.**

Infants and before closure of the fontanelle

- Eyes: deviate downwards giving sunset appearance. Optic atrophy may occur.
- Pyramidal tract lesions: brisk tendon reflexes, Spasticity, clonus and positive Babiniski sign .
- Abnormal midline lesions as meningocele and skin tuft may be present
- Irritability, lethargy, poor appetite and vomiting are common.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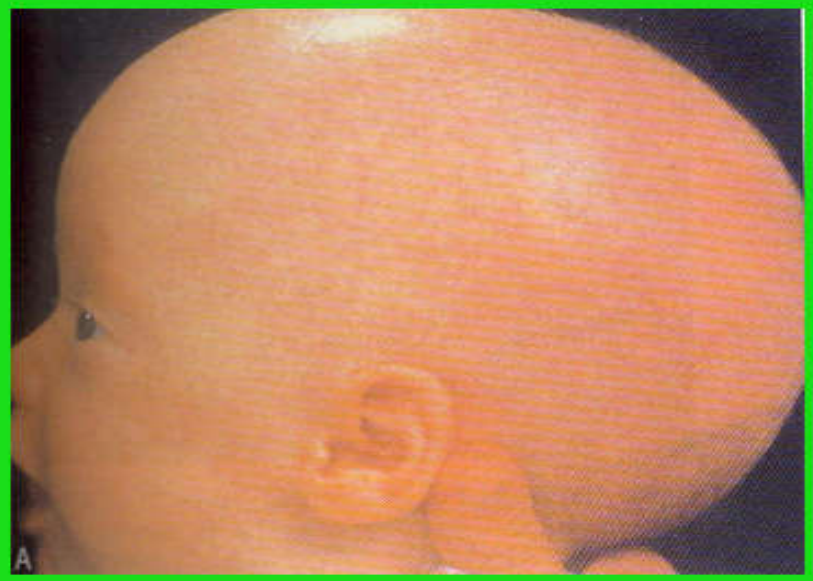
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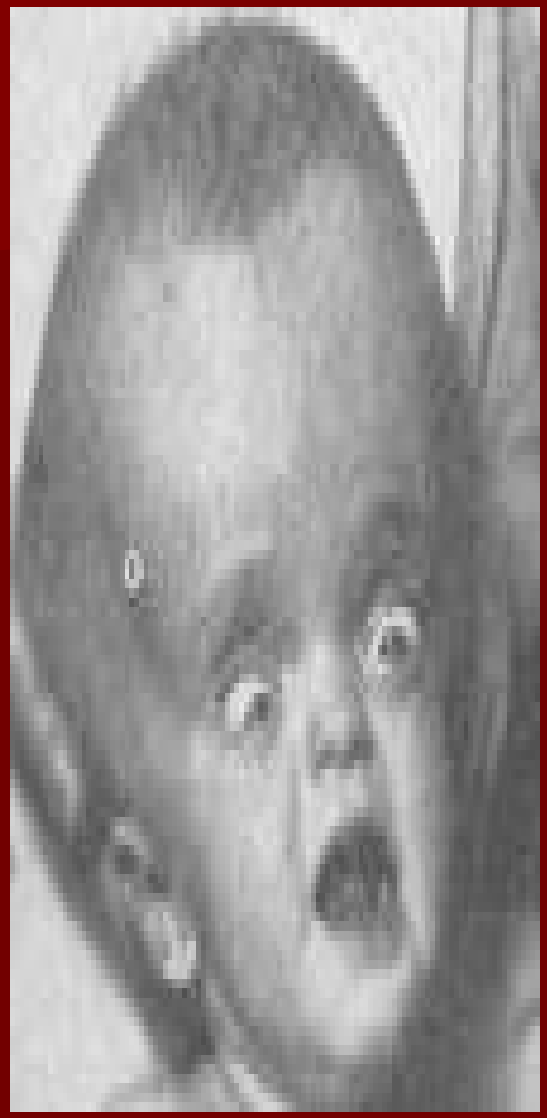
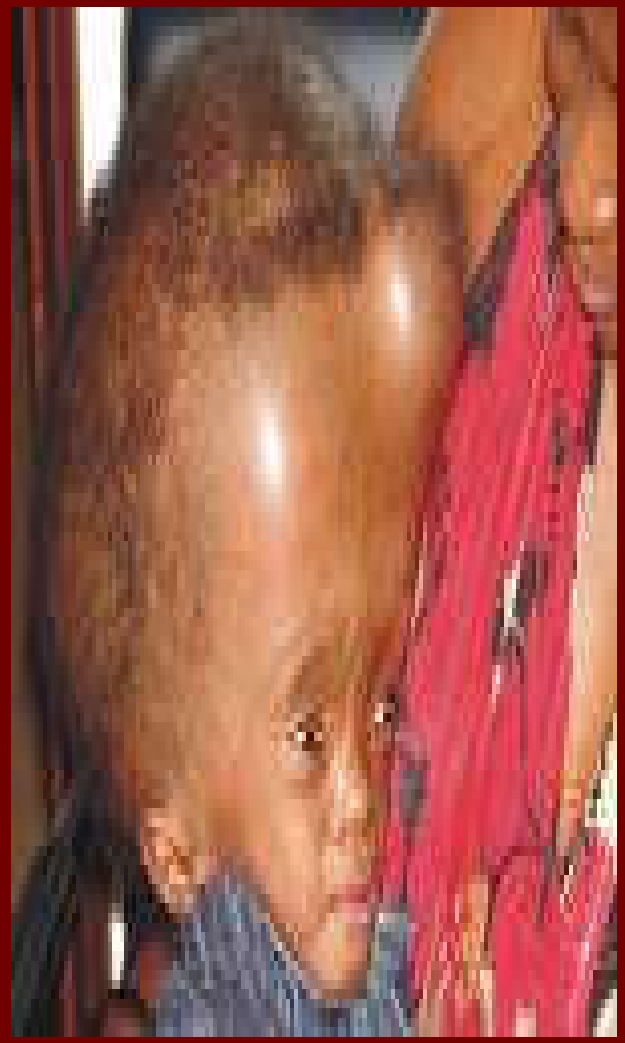
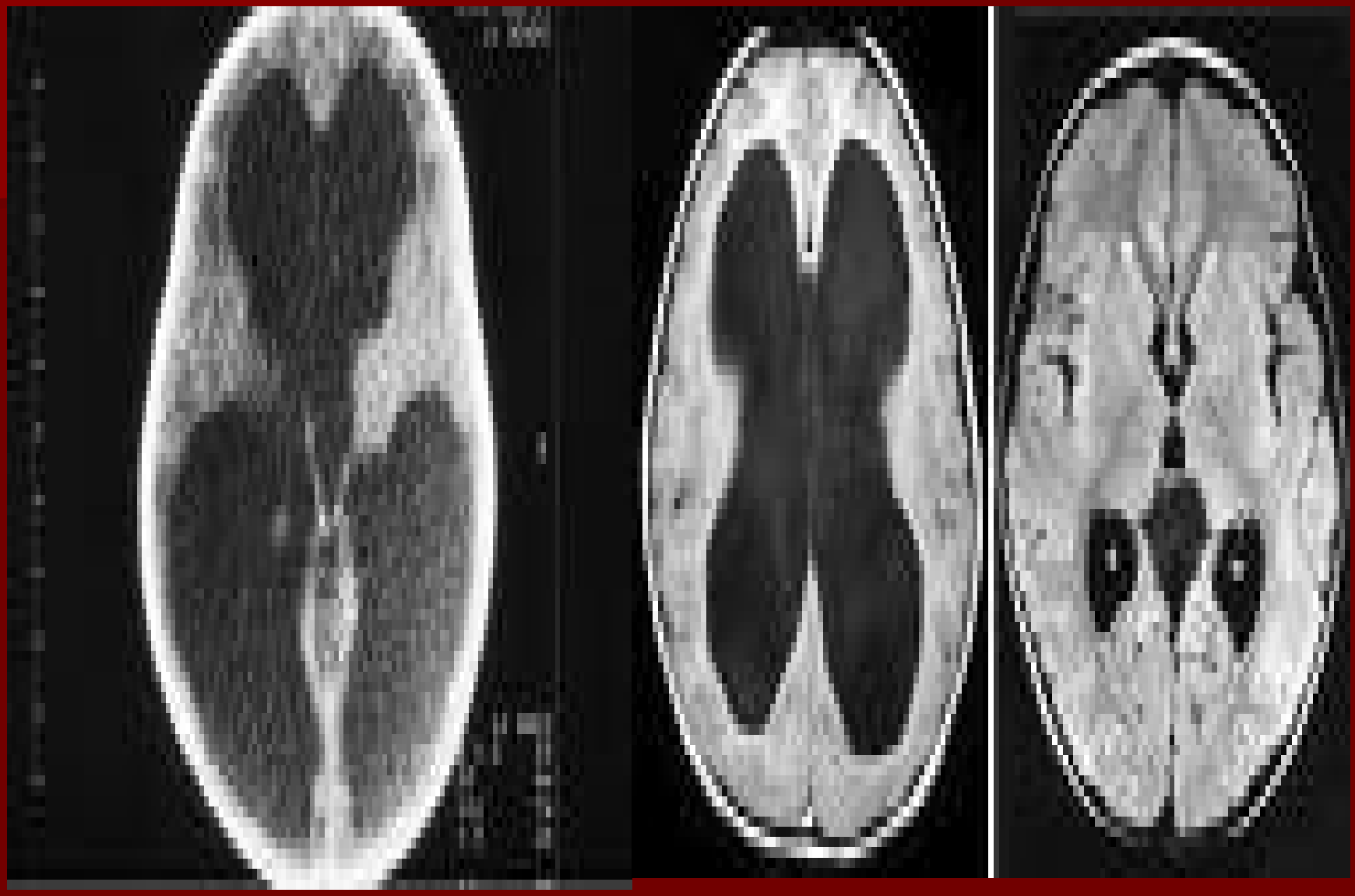



Older children

- Skull :
  - Increase in size is less prominent
  - Sutures are partially closed
- Headache is the most prominent feature
- Deterioration in school performance
- Irritability, lethargy, poor appetite and vomiting are common

Investigations

- **Radiological**
  - Skull X ray
    - Large size with separated sutures and wide fontanelles.
    - Wide sella turcica
    - May be erosion of posterior clenoids and beaten silver appearance.
  - Transcranial ultrasound; is useful for diagnosis
  - CT and MRI: to detect early hydrocephalus and etiology of hydrocephalus



Laboratory

- TORCH screen : may be positive in cases of intrauterine infections

Differential Diagnosis

Other causes of large head

1-Cranial (skull) causes

- Rickets
- Achondroplasia
- Cretinism
- Chronic hemolytic anemia
- Familial large head
- Metabolic and degenerative diseases as mucopolysaccharidosis.

2-Intracranial causes

- Subdural effusion or hemorrhage
- Brain tumors
- Brain cysts
- Chronic brain abscess
- Hydranencephaly
- Metabolic and degenerative diseases

Treatment

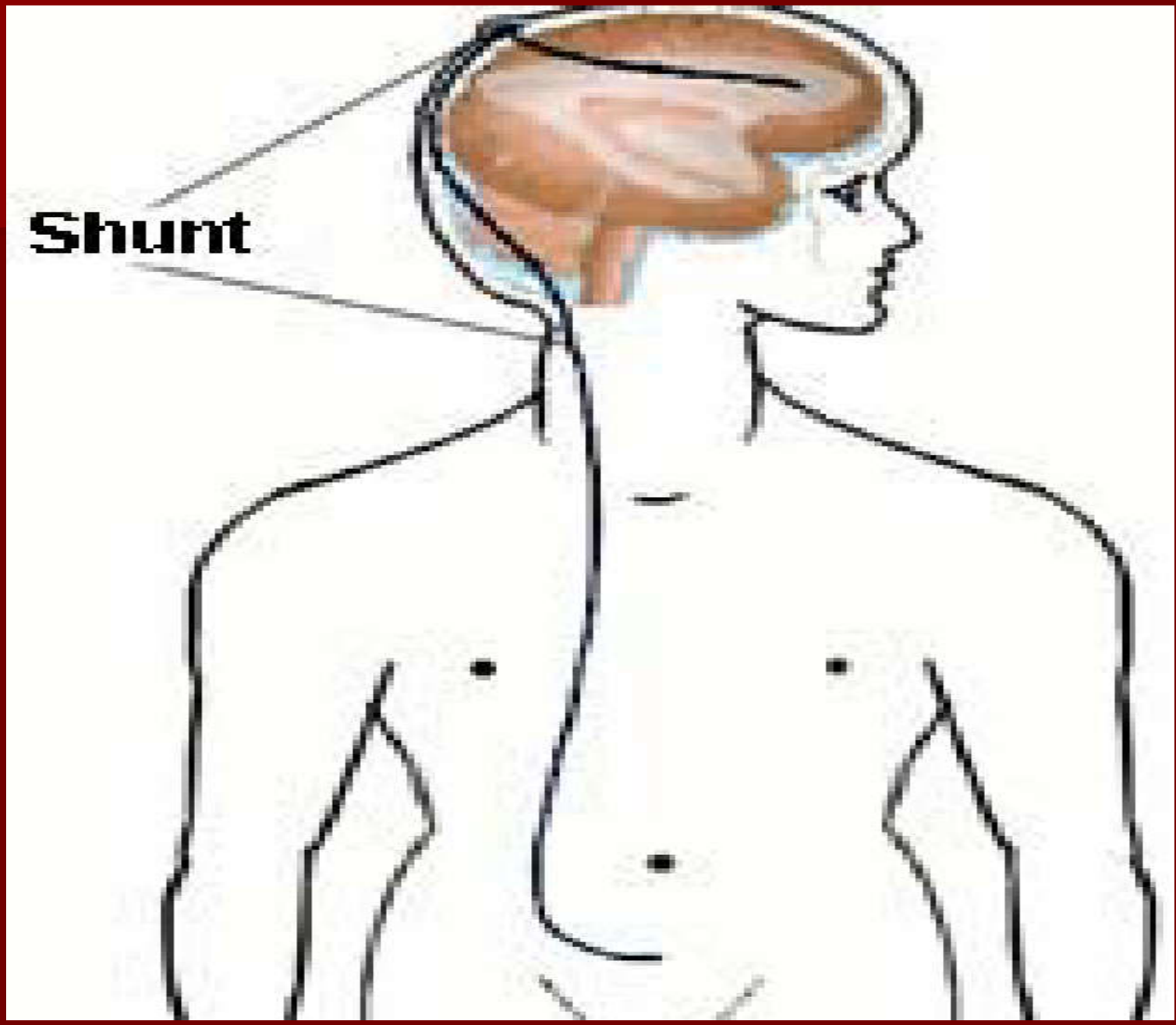
1-Medical

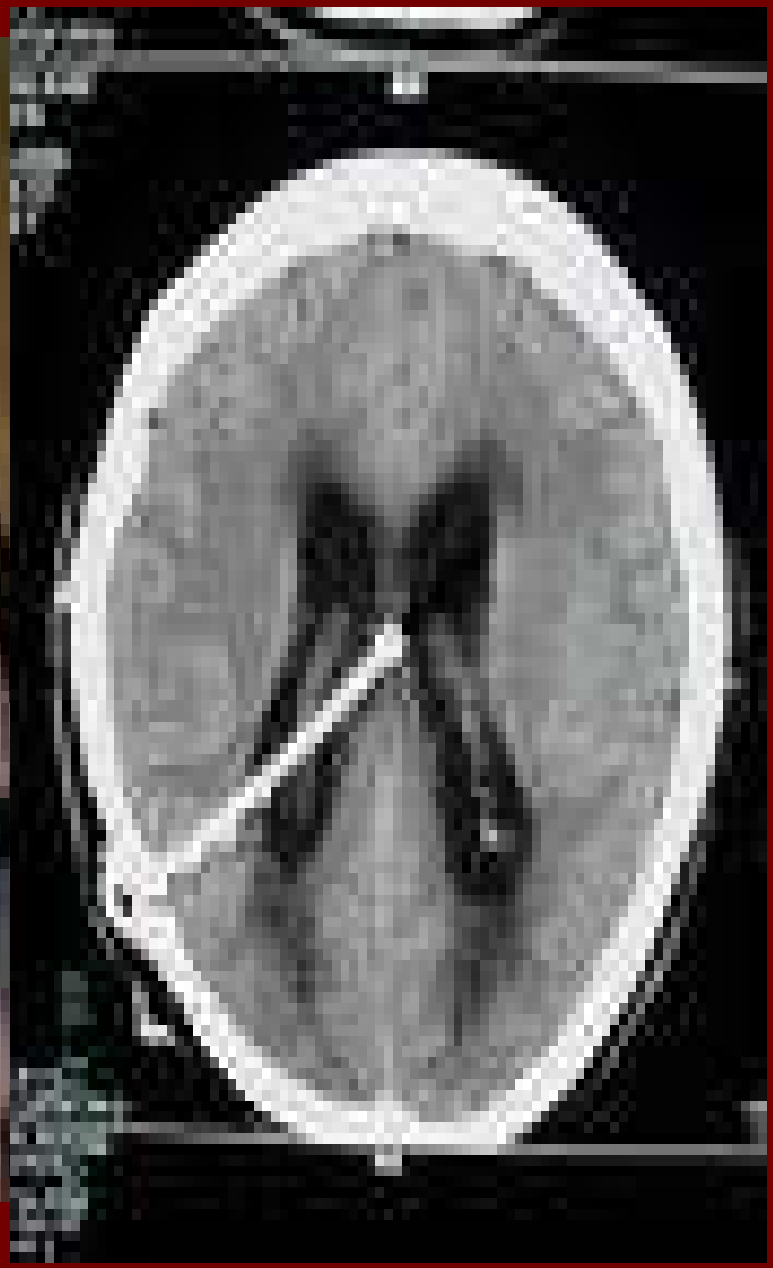
- Treatment of the cause
- Diuretics: Acetazolamide and furosemide to reduce CSF flow. It is only temporary treatment.

2-Surgical

- Extracranial shunt especially ventriculoperitoneal shunt to drain CSF from right lateral ventricle to peritoneal cavity.

- This is done by silicone rubber tube passing in the subcutaneous tissues. Shunt infection is the major complication.


Shunt




Thank you