

lead to paralysis ← motor mov. of eye → لا يستطيع التحريك ← لا يستطيع التحريك

أعراض ناتجة عن قلة الدم

Cerebrovascular disease

* 20% of the tumor in children → nervous system tumors
* malformation
* congenital
* degenerative.

ENAS ABU EWAIDA

from embolism for example

- Can be classified into ischemic (impairment of blood supply) or hemorrhagic (rupture of a vessel because of HTN or vascular anomalies) etiologies.

infarction
↑ ischemic changes
[CVD]

- Ultimately infarction (tissue death) in either etiologies.
- Stroke (when symptoms last for more than 24h) versus TIE (transient ischemic event/ patient gets better in less than 24h).
- The 3rd leading cause of death (1. ischemic heart diseases 2. cancer).

impairment of blood supply
Ischemia/hypoxia: → impairment of O₂

- Ischemia is more serious since not only the O₂ is low but also nutrients and waste removal.

toxins this lead to tissue injury etc

Global (the entire NS is affected) or focal.

منطقة محددة

Manifestation related to the region affected.

embolus / thrombosis
obstruction in specific point

Embolism more common than thrombosis.

- NS and kidneys are highly affected (brain uses 20% of O₂).

Brain

severe anemia
respiratory distress
hypotension
NS damage
Loglabal.

② Hemorrhagic → بليدي دم في منطقة معينة مكرة الدنيا

no obstruction.
due to ↑ BP.
form hematoma [compression of surrounding nerve tissue]
+ ischemic changes

① Hypoxia and ischemia

The size of the lesion determined by:

بعضه جسم الضور على

- ① Duration: the longer the duration, the more the damage.
- ② Magnitude (the diameter of the blood vessel) and rapidity of the reduction.

reversible
كل ما كانت اذية قصيرة كل ما كان الضرر اقل

anastomosis

- Collaterals: From C. of Willis/external carotid/ophthalmic.

sudden obstruction.
gradual obt.
lateral anastomosis of BS.
may this collateral become retrograde

Cortical/leptomeningeal. BV to meninges

- Deep parts lack collaterals.
- In occlusion, these collaterals evolve and can compensate.
- Excitotoxicity (a phenomenon that describes the toxic actions of excitatory neurotransmitters):

ischemic NS neuron

chemicals

nt Cg glutamate

lead to open Na⁺ channel [↑ Na⁺ inside the cell] → cell injury.

trigger high num. of metabolic activities

irreversible cell injury → permanent cell death
 ① rupture in cell mem
 ② damage in mitochondria
 ③ in nucleus
 ④ X protein synthesis mechanism

الخلايا التي لا يمكن إصلاحها
 irreversible injury..

lead to cell death

- Release of glutamate NT.
- Damage neurons by excessive influx of Ca^{++} → cell death

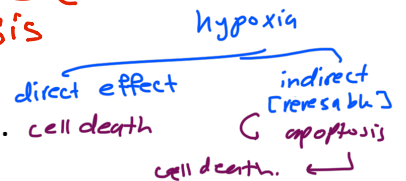


• Penumbra (the area surrounding an ischemic event such as thrombotic or embolic stroke): → apoptosis

منطقة في الدماغ التي
 complete impairment
 [loss of BS]
 irreversible damage

- Area of "at risk" brain tissue.
- Can be rescued by antiapoptotic interventions.

apoptosis من خلايا



ischemia يتسبب cell death
 apoptosis مباشر أو غير مباشر
 ② ③ ④

Focal cerebral ischemia

① Embolism

Most frequent.

Sources:

- atherosclerosis
- Most commonly cardiac thrombi from the left side of the heart. stasis in the atrium / fibrillation ... etc
- Atheroma plaque within the carotid. the thrombus is fragile structure so may move and called embolism.
- Paradoxical: in congenital anomalies when there is connection between the right and left sides, the embolus can move from the left side to anywhere. from deep veins, more in middle age women
- Cardiac surgery.
- Tumor, Fat (especially after lower limb fracture), and air.

lead to obstruction

fragile
 brain
 middle cerebral from the carotid A

Most frequently the middle cerebral artery.

② Thrombotic occlusion focal / not global [generalized]

Most commonly acute plaque changes in the bifurcation (why here? exposure to subendothelial collagen erosion of the surface [microsis of endothelial tissue, rupture, intraback hemorrhage] lead to complete obst.)

Laminar flow at bifurcation is disturbed and there is turbulence causing mechanical injury to the endothelial cells leading to these events).

③ Inflammatory process

Syphilis and TB.

Vasculitis. accompanied by thrombus formation

④ Other

Hypercoagulability.

Dissecting aneurysm.

* Critical stenosis: obstruction of human 70% [stable angina] 90% depend infarction in any time [unstable angina]

* Atherosclerosis / cell injury followed by attempt to repair [infi. cell, macrophag. ECM ... etc]

✓ Drug abuse. [heroin, cocaine]
↳ damage in BV → Ischemia.

Focal cerebral ischemia

Non-hemorrhagic type.

Starts as non-hemorrhagic (pale/anemic).

Secondary hemorrhage.

hemorrhagic changes → necrotic tissue (BS) → Paly [no blood, Anemic]

- Due to reperfusion after thrombolysis.
- Leading to hemorrhagic infarct.
- Petechial (dot-like) morphology. small hemorrhagic area. not hematoma

* Gross morphology

- 1 First 6 hours. no changes
- 2 By 48 hours. yellow discoloration.
- 3 2-10 days. 2ry hemorrhagic changes
- 4 10 days-3 week. forming cavity by remove the necrotic area.

In the first 6h, ^① no changes are seen macroscopically then it turns to a ^② yellowish color and the landmarks of the tissue start to get lost. If a ^③ secondary hemorrhage happens, we see petechial hemorrhage and the repair starts around the affected area.

granulation tissue → new blood vessels & inflammatory cells

* Microscopic

Acute infarct

- 6-12 hours.

Eosinophilic neuronal necrosis: the dead neuron starts turning red instead of basophilic. disintegration of the nucleus

Edema. لا حيز فيها ^{lymphatic v. ما في} [the CNS lack of lymphatic system so there is fluid imbalance] عظمى في edema

Indistinct gray/white matter. due to edema, necrosis [اح قشر الكبد - ع. بين]

Disintegration of the glial cells, fibers and endothelium

Cell death
cell degeneration

* hematoma: - accumulation of blood
↳ due to BV rupture.

* infarction → tissue edema [injury]
hemorrhagic ^{يزداد الحجم ويكثف}
may be: - [dot like]

← لكفاءة في منطقتي (تؤثر على باينغ BV, ECM) tissue
... ATP

كل ما عايشه أكثر
كثرة الشكل المتغير

تعمل حاجة بوفرة

يعلن

* Pyramidal cell

- 48 hours acute infarct

Neutrophilic emigration.

→ disintegrated chromatin, cytoplasm [eosinophilic]
necrosis (آفة نخرية) [تلف النسيج]

Subacute (evolving) infarct

48-72 hours. → 1st inf. cell

Phagocytes and microglia (remove dead tissue).

Reactive astrocytes.

New blood vessels (as early as 1 week after the Insult).

* Blood vessels with the surrounding inflammatory cells is called granulation tissue. *→ in the infected area.*

Astrocytes at the edge develop a network of cytoplasmic extensions, this is known as **gliosis** (proliferation of glial cells surrounding the injured area).

Healed infarct (after several months):

- Dense meshwork of glial fibers ^{cells extension.}
- New capillaries.
- Perivascular connective tissue
- Chronologic morphologic changes. ^{من ناكبة متتالية}
- A cavity could form in the infarcted area ^{infarction.} (surrounded by blood vessels and glial tissue).

ductus PBP $\rightarrow$ BV rupture
Hemorrhagic infarction/ Hemorrhagic type (hematoma)

- The same with blood extravasation added.
 - Accumulation of blood causing compression on surrounding tissue
 - Extensive if under anticoagulant.
- ۱۵۲۸

Venous infarction: Thrombosis of the sinuses. (The previous are related to arteries).

infarction ۱) in spleen ۲) نظر خونی = تجویفات / granulation tissue
 ↳ we don't see nerve or neuron but we see glial cell

Lacunar infarcts

- Occlusion of small vessels as a result of arteriolosclerosis/hypertension. *one or two layers of smooth muscle*
- Less than 15 mm. *as a result of arteriosclerosis + BP*
- Single or multiple.
- Involves putamen, globus pallidus, thalamus, internal capsule, deep white matter, caudate nucleus and pons.
- Tissue loss surrounded by gliosis. *granulation tissue*

via infarct

Global cerebral hypoxia/ischemia

- Cardiac arrest, shock, and severe hypotension. *generalized ischemia*
- CO poisoning, anemia. *generalized hypoxia*
- Transient postischemic confusional state with complete recovery. *less than 24 hour*
- Or irreversible damage; "diffuse hypoxic/ischemic encephalopathy". *less than 24 hour, irreversible of diffuse ischemia, encephalopathy*
- Border zone (watershed) infarcts: *diffuse*
 - Border between arterial territories.
 - Result in wedge shaped infarct.
 - With secondary hemorrhage.
 - Often bilateral. *wedge shaped area*
 - Commonly after cardiac arrest resuscitation.

Ischemia لا يوجد (الحدود) في [wedge shaped infarct]

Morphology

- Edematous and swollen brain because of malfunction in the Na⁺ channels. *generalized edema, ant. cerebral and middle cerebral*
- Poor gray-white demarcation.
- Irreversible injury:

6-12 hours; dead red neuron.

24h-2 weeks, subacute changes; necrosis, macrophages, vascular proliferation and gliosis.

After 2 weeks; removal of necrotic tissue and gliosis.

replaced by or leaving some brown spaces

Intracranial hemorrhage

Epidural and subdural; mostly trauma related.

Subarachnoid and intraparenchymal; related to cerebrovascular disease.

Intraparenchymal hemorrhage

- Sudden onset of symptoms.
- Versus secondary hemorrhage.
- Middle/late adult life.
- Ganglionic (in the inner part of the brain, near the basal ganglia inside the white matter) versus lobar hemorrhage (more superficial).

* Hypertension is the most commonly associated factor with ganglionic intraparenchymal hemorrhage.

- 50-60% Putamen.

• Cerebral amyloid angiopathy is the risk factor most commonly associated with lobar hemorrhage.

• Effects of HT on blood vessels? HTN leads to weakening of tunica media leading to impaired blood supply, degeneration of blood vessel wall and smooth muscle loss.

* Amyloidosis: accumulation of a certain protein.

[lobar: most superficial] + cortex
Effect of HTN on small blood vessels:

Hyaline arteriosclerosis as a result of plasma proteins' accumulation.

homogenous eosinophilic material
→ damage → hemorrhage.

Subarachnoid hemorrhage

The most common cause is rupture of saccular "berry" aneurysm in a cerebral artery.

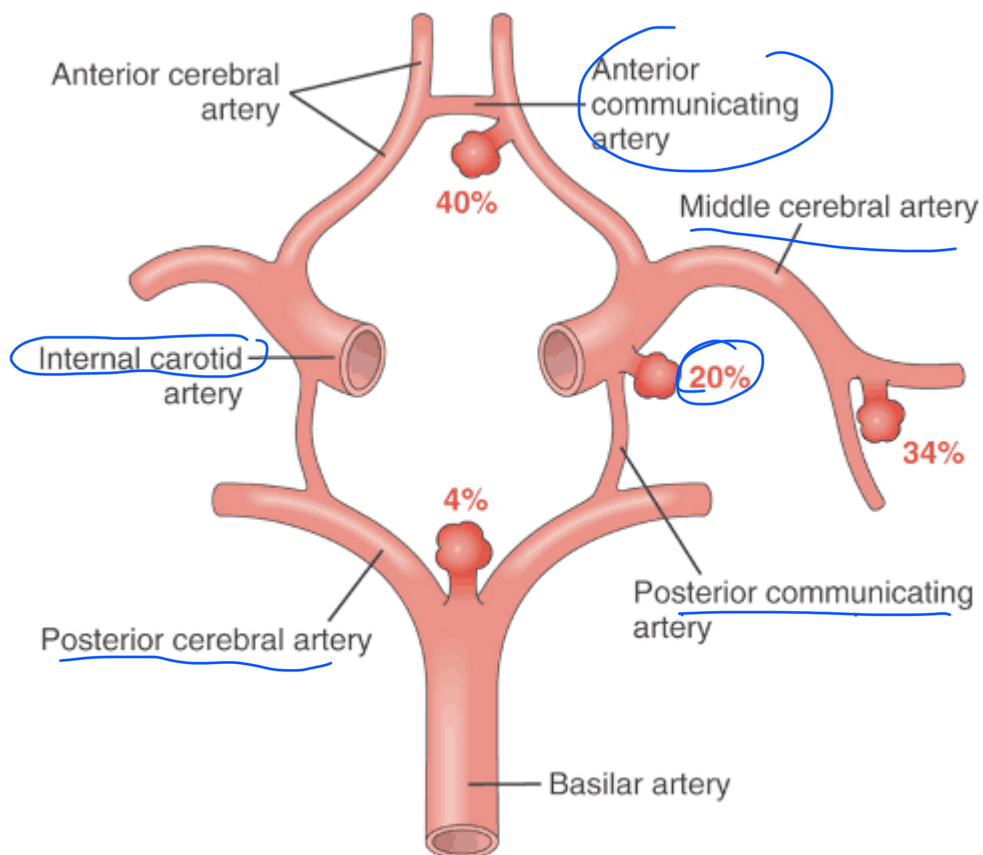
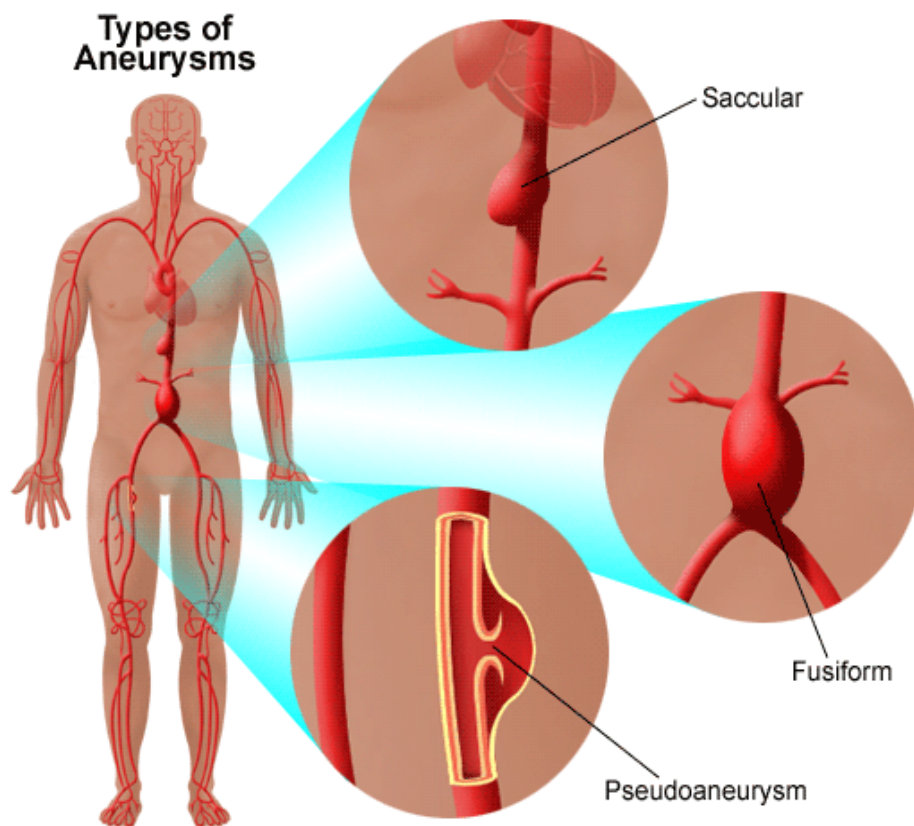
Saccular aneurysm:

2% of the population.

90% found near major arterial branch points in the anterior circulation.

* this lead to weakening of the BV
→ due to hypertension + age

stroke/hemorrhage



on protruding
Fusiform: the entire wall/ saccular: a part of the wall (asymmetrical).

Pathogenesis

- A developmental anomaly.
 - Absence of smooth muscle and elastic lamina.
 - The majority are sporadic: cigarette and HT. hypertension.
 - Genetic factors.
- arterial system
elasticity
risk factor

Morphology

- Shape and size: less than 3 cm.
 - Atheroma, thrombus.
 - Prior hemorrhage.
 - Bleeding into the subarachnoid or brain substance.
 - Absence of smooth muscle and elastic lamina: thickened hyalinized intima and a covering of adventitia.
- berry or wide Base .. etc.
hemorrhage
thick, hyaline
fibrosis
thick

Vascular malformations

4 groups:

1 AV malformations:

- Risk of hemorrhage.
 - KRAS mutation.
- abnormal BV and if there is HTN may be ruptured

2 Cavernous malformations:

- Risk of hemorrhage

3 Capillary telangiectasias.

4 Venous angiomas.

Morphology

AV malformations:

- Warm like.
 - Pulsatile shunting (because of its arterial relation).
 - Subarachnoid or brain.
- connection between artery and vein..

neoplastic :- new formation, independent due to genetic changes

- Prior hemorrhage.
- Duplication and fragmentation of elastic lamina.
- Thickening and replacement of media by hyalinized CT. [smooth muscle loss]
- Separated by gliosis.

Cavernous malformation:

- No brain parenchyma. no Septa, no gliosis
- Most often cerebellum and pons.
- Low flow velocity.
- Old hemorrhage.
- not pulsating → there is no direct connection with arterial system

Vascular dementia

- Multiple infarcts over years. [classic dementia]
- Dementia, gait abnormality (when a person is unable to walk in the usual way). [loss of Brain material [neurons]]
- Caused by: [severe]

1. Atherosclerosis.

2. Thrombosis/embolus from the carotid or heart.

3. Arteriolosclerosis from chronic HT.

Dementia: impaired ability to remember, think, or make decisions that interferes with doing everyday activities.

Done ✓

Prognosis, treatment, benign, malignant, CNS, tumor, prognosis, treatment

Surgical removal maybe [mainly] surround normal + tumor tissue

- Brain inside Skull

- SC inside vertebral column

lipoma in the optic chiasma / nervous system

parts of CNS vision, pituitary gland

nervous system, lung, liver, Bone ← metastasis

Tumors

Overview

مع ان در CNS هدف از metastasis

The majority are primary.

20% of all cancers of childhood.

70% of childhood CNS tumors arise in the posterior fossa.

↑ cerebellum

A comparable number of supratentorial tumors in adults. 70%.

در دکتان لبیب فضویت در NS مرصوبت ار surgery قد نیاز در prognosis صلبا

Different concept of benign and malignant. Their biologic behavior isn't the same with other tumors because the area is critical hence even benign may prove fatal. may Benign Brain tumor → ↑ ICP may be lethal ...

توما بیتون ایچج بیشیل حتی ترتیب مشا شکت ار الکینون من الاصلیة الحقة + تقیل حجم ار ماس

Mostly not amenable for complete resection. Even if a surgery is possible, surgeons do a gross total resection not microscopic (like in

↑ removal without cause any problem.

tumors in other organs) to protect vital centers. ex Benign tumor around the resp. control

lead to cardiac or resp arrest ← or Cardiac

1. SC / Skull ← ع-جج فایز ار SC / Skull rare metastasis outside + local invasion outside of the skull.

بیب ضابطه ار ماس Bone Structure → vertebrae skull

2. there is no lymphatic which the way of metastasis

Cerebrospinal dissemination in the CNS.

la CSF in subarachnoid space, and other spaces of CNS [dissemination in all part of CNS..]

Grading: 4 grades based on biologic behavior, gross appearance, IHC, molecular profile (genetic mtations).

Grade 1 is the least aggressive, the malignant behavior starts at grade 2, and grade 4 is the most aggressive.

Benign

grade 3, 4, 2 → malignant.

بیکس درجه حقه ار tumor ...

Grade: the description of a tumor based on how abnormal the tumor cells and the tumor tissue look under a microscope/ level of differentiation. The higher the grade, the more aggressive. Grade 1/2/3.

High grade tumors/ poorly-differentiated tumors have higher mitotic activity and are more likely for metastasis or recurrence.

بیکس درجه ار tumor ...

Stage: describes the size of a tumor and how far it has spread from where it originated. TNM system.

* الخلية العصبية هي / neuron ...
... there is supporting, helper cells.

Gliomas → from glial cells. [morphology, functionally ...]

The **most common** of primary tumors.

Derived from **multipotent progenitor cell**.

Within **particular age groups**.

more obvious in glioma.
دلائل أكثر وضوحاً في أورام الدماغ

Predilection for **specific regions**.
[there is no tumor called medullary Blastoma outside of post. fossa]

① **Astrocytoma; grade II-IV** malignancy.

80% of **primary** brain tumors in **adults**.

SC, cerebellum

Usually in **cerebral hemispheres**.

May occur also in the cerebellum, brain stem and spinal cord. [rare]

4-6 decades (30s-50s).

Morphologic classification: H&E (anaplastic, glioblastoma,...).

Molecular classification: the cancer is accumulation of genetic mistakes...

[isocitrate dehydrogenase] **IDH mutant**: Better prognosis. there is changes in the tumor...

frequent in glioma • IDH wild type. normal gene...
tumor especially in Astrocytoma
IDH: isocitrate dehydrogenase.

Glioblastoma is grade **IV astrocytoma** (if other glial tumors show grade IV characteristics, we can also use the term glioblastoma).

Pathogenesis of Glioblastoma

Primary:

glioblastoma. primitive

- **De novo** development.
- In **older** individual **new onset**.
- Most are **wild type IDH**. normal gene
- **Gains** of chromosome **7**.
- **Loss** of chromosome **10**.
- **TERT** promoter mutations.
- **EGFR** amplification.

growth factor Receptor
2 type

other genetic alteration:-

* **TERT**:- telomerase reverse transcriptase. [enzyme make transcription..]
repetitive RNA → DNA sequ. of DNA. cell senility → cell death.
[telomerase] → cell death. → ...
[telomerase] جزء من DNA ...
... cell cycle ...

* هناك خلايا في الجسيم مثل BM/giant cell متلازمة يتوقف رايضا خلايا لهم مخوف في ار telomerase خلية التكاثر
 * rebuilding of telomerase يكتسب فاعلية immortality

Secondary:

- كان صلا grade 2 هار حيزه في ار mutation آتة لينا grade 2 خا صيته اشري راجع في التكاثر
- In **younger** patients, progression of **lower grade** astrocytoma.
 - Driver mutations of **IDH1 or IDH2**. *other mutation*
 - * **mutant + type...**

في بعض انواع tumor
 Most gliomas have **genetic aberrations** that lead to:

① **Evasion of senescence:** Telomeres/telomerase.

② **Escape normal growth control:** **CDKN2A** deletion.

③ **Activation of growth signaling:** **EGFR or PDGFR**.

④ **Evasion of apoptosis:** **TP53** mutation.

→ Program cell death → tumor
 X apoptosis ← mutation in TP53
 حالي منقطع tumor
 مبه في TP53 mutation

in normal state there is cyclin dependent Kinase (CDK) cell cycle (نقطة)
 CDF inhibitor
 cyclin dependent
 absent in many types of tumor

Morphology

Diffuse astrocytoma: **grade 2 astrocytoma**.

- Gross, size and texture: similar to surrounding tissue, gray/ white mater border is lost, the texture is harder.
- Microscopy: similar to origin but darker and irregular with an uneven distribution, aggregations around the neuron (satellitosis).
- IHC:** **GFAP** (glial fibrillary acidic protein/ +ve in glial cells tumor, -ve in neuron-derived tumors), **IDH1** (90%).

لكن عن انواع ابروتينات

Anaplastic astrocytoma: **grade 3 astrocytoma**.

- Microscopy: large, irregular nucleus, **hyperchromatic**, **higher mitotic activity**.

[origin] تغير في اصل

Anaplasia: a condition of cells with poor cellular differentiation, losing the morphological characteristics of mature cells.

Glioblastoma: **grade 4 astrocytoma**.

- Gross:** necrotic areas because the formation of new blood vessels is slower than the progression of the tumor, hemorrhagic areas.
- Microscopy:** **necrosis**, viable cells are arranged **parallel** to each other (**palisading**), **blood vessels proliferation** forming **vascular tufts**.

نوع السطح

light chromatin: [euchromatin active]
 مابين في خلايا ايفرغنيك ركن hyper chromatin له اخف
 La astrocytic cell [tumor cell of diffuse astrocytoma].

normal astrocyte ← قبل
 lumping مابين جفت خيوطها
 tumor نظر بال

* 2 hemisphere

* diffuse astrocytoma

متسلسلة بين الخلايا
في البنية الجذرية مابقية
نقطة mass

* in normal part
gray matter (يكون)
white " (مضاد)
دلتان بالخطوة (red)

there is + swelling [edema]

.. abnormal tissue tumor بغير