Pathology

INFLAMMATION

LECTURE (6)

As a doctor you should know what can threaten your patient's life
you should know what makes your patient suffers from pain
THAT'S WHY YOU LEARN PATHOLOGY

Definition: BLUE Examples:GREEN Important: RED Extra explanation:GRAY Disease names: **UNDERLINE**.

Lecture(6) Outlines

- Definition of granulomatous inflammation
- Morphology of granulomas
- Cells found in granuloma
- Types of granulomas
- Common causes of Granulomatous Inflammation
- Pathogenesis of granuloma formation
- Clinical cases

Definition of granulomatous inflammation

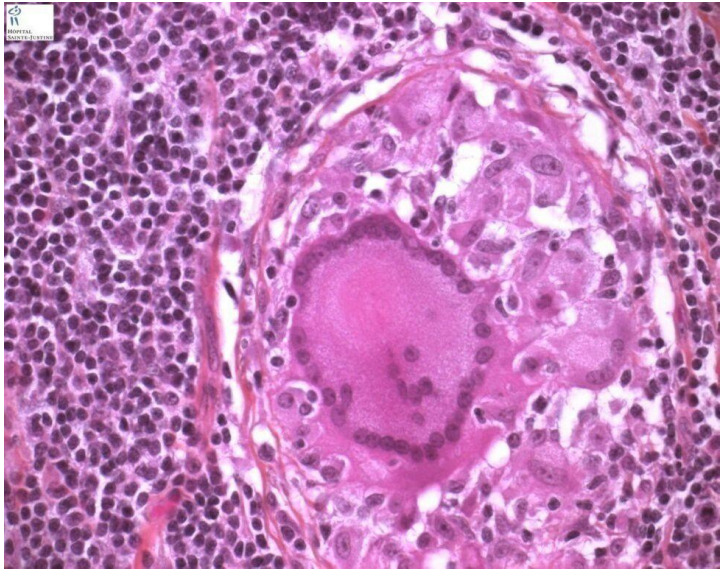
- **Granulomatous Inflammation**: a special pattern of chronic inflammation characterized by aggregation[1] of activated macrophages with scattered lymphocytes.

Another definition: a form of chronic inflammation characterized by the formation of granulomas.

Granuloma: Nodular collection of epithelioid macrophages surrounded by a rim[3] of lymphocytes.
Epithelioid[2] **macrophages**: squamous cell-like appearance.

Why is recognizing granulomatous pattern important?
Because of the limited number of conditions (some of them are life-threatening) that can cause it.

In other words:
If you recognize the granulomatous pattern, you can exclude a lot of conditions and etiologies. Thus, focusing on a limited number of conditions that can cause it.



1- مجموعات
2- The suffix -oid usually means “looks like” , so epithelioid means “epithelial like” , and so on :)
3- إطار أو حواف محيطة به

Morphology (structure/form)

- Activated macrophages in granulomas have pink, granular cytoplasm with unclear cell boundaries; these are called **epithelioid cells**.
- The aggregation of these cells are surrounded by a rim[1] of lymphocytes.
- Multinucleated giant cells are found in granulomas.
- Older granulomas may have a rim of fibroblasts and connective tissue.
- In granulomas associated with certain infectious organisms (mostly tubercle bacillus), a combination of hypoxia and free radical injury **leads to a central zone of caseous necrosis**.
- It appears as eosinophilic amorphous, structureless, granular debris[4], with complete loss of cellular details.
- The granulomas associated with Crohn disease, sarcoidosis, and foreign body reactions tend to not have a caseous necrotic centers (non-caseating).

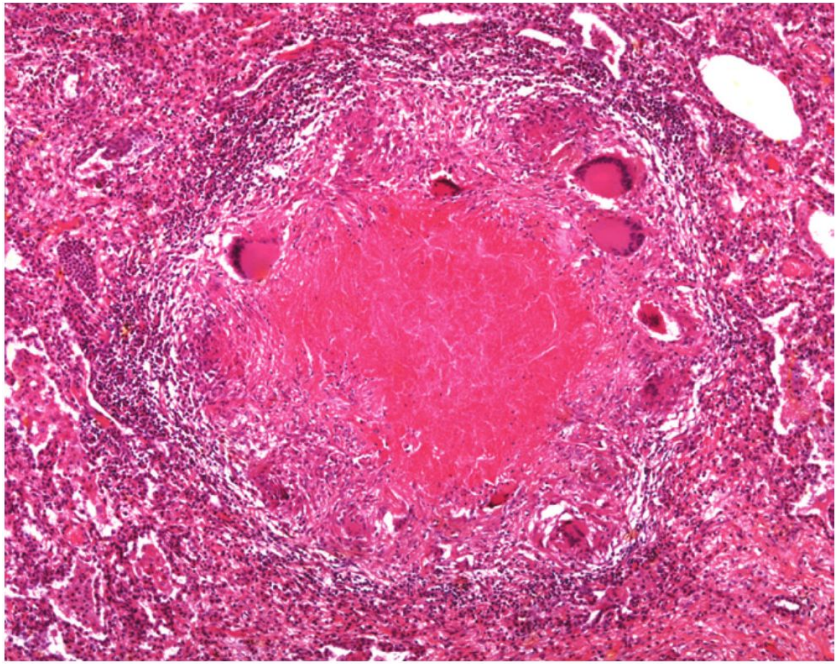
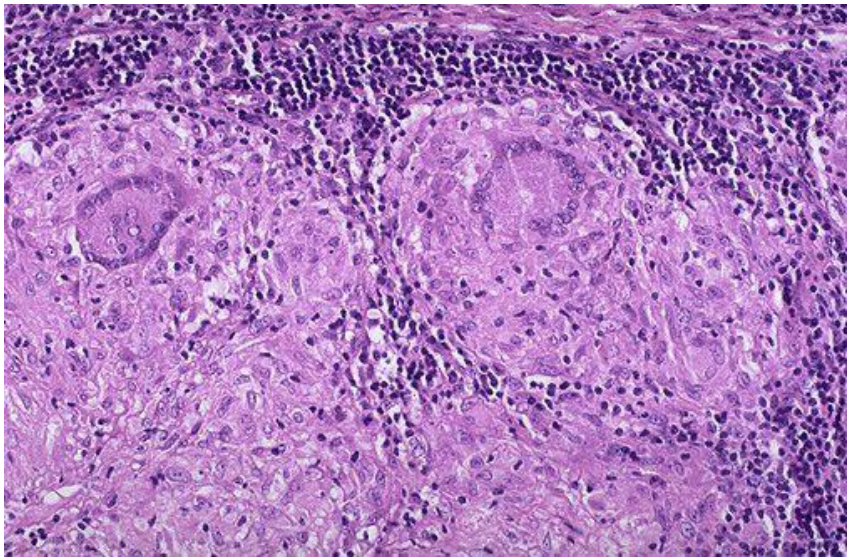
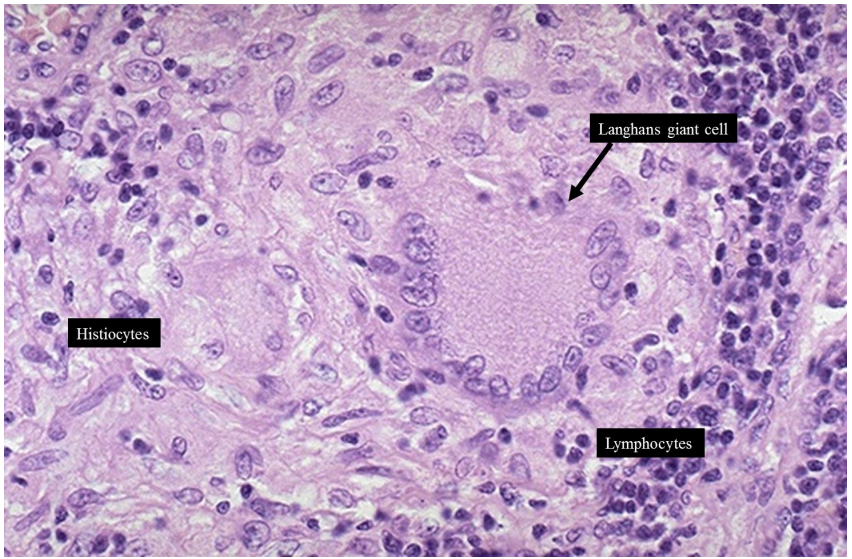


Figure 2–23 A typical granuloma resulting from infection with *Mycobacterium tuberculosis* showing central area of caseous necrosis, activated epithelioid macrophages, giant cells, and a peripheral accumulation of lymphocytes.

1- طوق (يعني محاط بالليمفوسايتس من كل الجهات)
2- متعدد الأنوية
3- عديم الشكل
4- بقايا

Some pictures of granulomatous inflammation





Cells found in granuloma:

Epithelioid cells: are activated macrophages that resemble an essential characteristic of granuloma and are surrounded by a rim of lymphocyte.

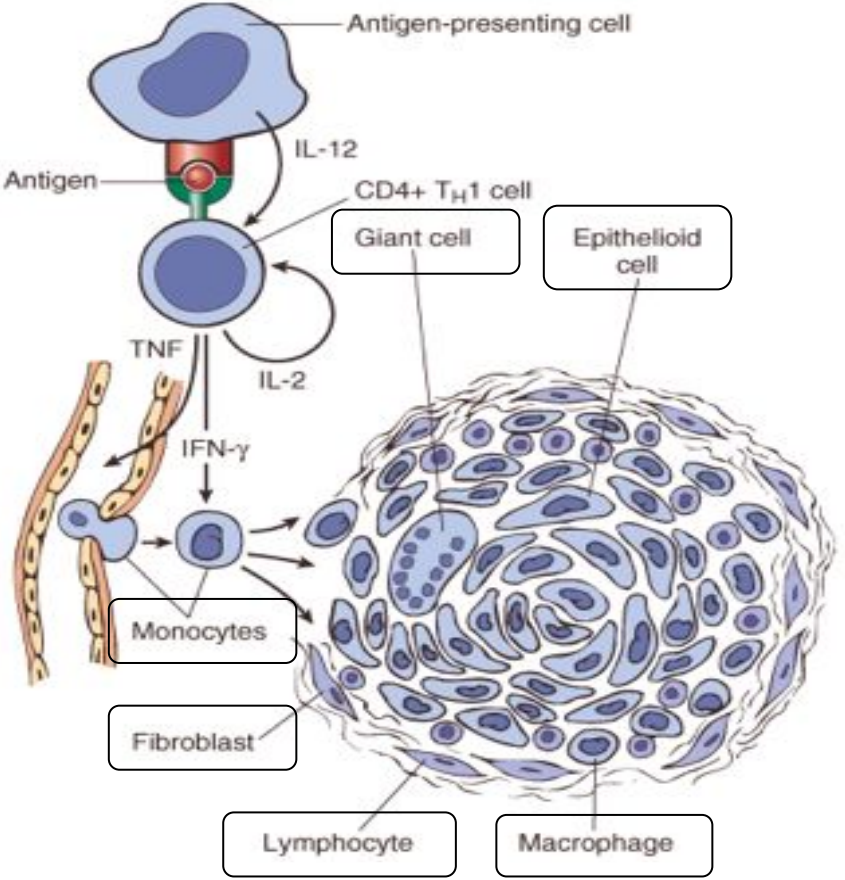
Giant cells(Langhans cells): multinucleated cells form from the cytoplasmic fusion of macrophages.

Fibroblasts: older granuloma may have a rim of fibroblasts and connective tissue.

Lymphocytes: mediate cellular immune response.

Macrophages: phagocytose the injurious agent

Monocytes.



Types of granuloma

foreign body granuloma (non-immune)

- Aroused by relatively immobile foreign bodies.
- Foreign body granuloma forms when material such as, suture , are large enough to block phagocytosis.

Foreign bodies:

- Graft material.
- Talc (Associated with intravenous drug abuse)

- These materials **don't** provoke any specific inflammatory immune response.
- Can be identified in the center of the granuloma, by polarized light (appears refractile)

immune granuloma

- Caused by insoluble particles, typically microbes, that are capable of inducing a cell-mediated immune response.

Such as :

- tuberculosis, leprosy, Actinomycosis,Cat scratch disease (caused by bacteria) .

- Schistosomiasis, Leishmaniasis (caused by parasites) .

- Histoplasmosis, Blastomycosis (caused by fungi).

- Berylliosis (caused by Metal/Dust)

Extra (immune granuloma)

Fungi

- **Histoplasmosis**
- **Blastomycosis**

Metal/Dust

- **Berylliosis**

Unknown

- **Sarcoidosis**:

Noncaseating granuloma (no caseous Necrosis)

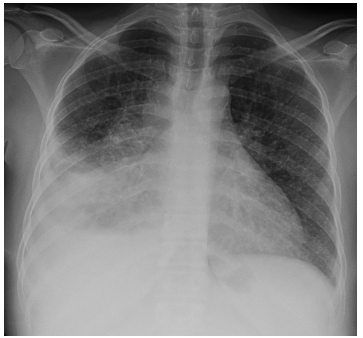
- **Chron`s disease**

Parasites

Schistosomiasis > البلهارسيا

Leishmaniasis > داء الليشمانية

Bacteria



Tuberculosis (TB)

Leprosy

Extra: Examples of diseases w/ Granulomatous inflammation

Table 2–8 Examples of Diseases with Granulomatous Inflammation

Disease	Cause	Tissue Reaction
Tuberculosis	*Mycobacterium tuberculosis*	Caseating granuloma (tubercle): focus of activated macrophages (epithelioid cells), rimmed by fibroblasts, lymphocytes, histiocytes, occasional Langhans giant cells; central necrosis with amorphous granular debris; acid-fast bacilli
Leprosy	*Mycobacterium leprae*	Acid-fast bacilli in macrophages; noncaseating granulomas
Syphilis	*Treponema pallidum*	Gumma: microscopic to grossly visible lesion, enclosing wall of histiocytes; plasma cell infiltrate; central cells are necrotic without loss of cellular outline
Cat-scratch disease	Gram-negative bacillus	Rounded or stellate granuloma containing central granular debris and neutrophils; giant cells uncommon
Sarcoidosis	Unknown etiology	Noncaseating granulomas with abundant activated macrophages
Crohn disease	Immune reaction against intestinal bacteria, self antigens	Occasional noncaseating granulomas in the wall of the intestine, with dense chronic inflammatory infiltrate

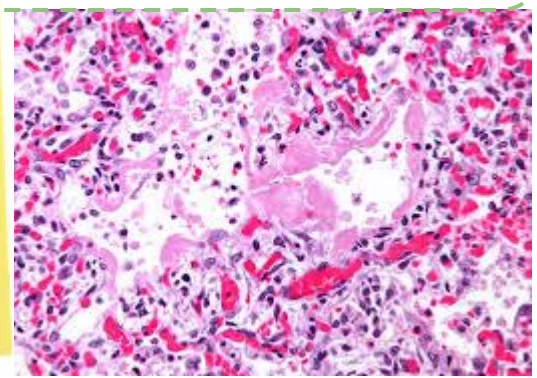
Clinical case (1/5)

Acute interstitial Pneumonia.

It's an inflammatory condition that effects the **alveoli** (الحويصلات الهوائية).

Symptoms: cough, fever, high ESR, malaise, vomiting, and high neutrophils count in the blood.
Diagnosis: bacterial inflammation in the lung. (acute pneumonia)

Acute interstitial pneumonitis occurs most frequently among people older than forty years old.



Clinical case (2/5)

Viral infection.

Symptoms: fever, malaise, and weakness

Viral infection are usually associated with leukocytosis[1].
Neutrophils are usually elevated in bacterial infection but not viral.

Diagnosis: Viral Infection

1. **Leukocytosis** means high number of leukocytes (up to 60%).

Clinical case (3/5)

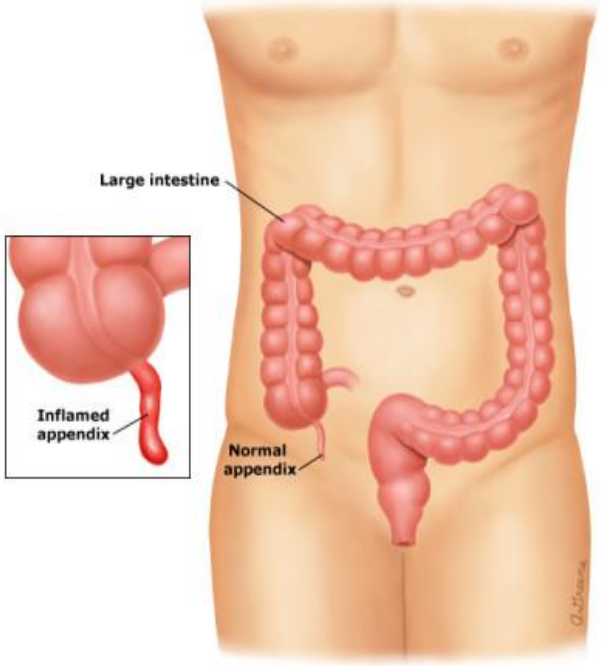
Acute Appendicitis.

Inflammation of the appendix (الزائدة الدودية).

Symptoms: Abdominal pain in the right side.

Examination: The surgeon found that his appendix was swollen, with vascular conjunction (cause of redness), and inflammatory. e

Diagnosis: acute appendicitis.



Clinical case (4/5)

Mycobacterium Tuberculosis

Case: A 20 year old patient, with exudate in his pleural cavity. His CBC showed increased neutrophils.

Diagnosis: We should think of an inflammatory condition, and namely, a bacterial infection.
TB could be our suspect :)

Remember: In acute inflammation of the lung, the alveoli are intact, and the normal architecture of the lung is preserved. There is exudate but the architecture is preserved. On the other hand, in chronic inflammation of the lungs, we see lots of fibrosis and lymphoid follicles and proliferation of type 3 monocytes to compensate the cells that have been destroyed.

Pathogenesis: Alveolar fibrosis→ hypoxia→ pulmonary failure → death

Why are some cells destroyed?
Because fibrosis obstructs the gas exchange and some cells die.

Clinical case (5/5)

Alcoholic hepatitis.

Case: A 35 year old man. He had a swelling somewhere in his body and it was transudate. You take a biopsy from his liver (because you suspected liver steatosis) and you woah you find fatty change.

Diagnosis: Alcoholic hepatitis. In conclusion, the liver protein synthesis is reduced.

Pathogenesis: The chronic inflammation leaves fibrosis, and in some cases it causes a disease; eg: alcohol induced liver damage.
At the beginning, there will be fatty change, but after some time, there will be chronic alcoholic hepatitis.
As a result, there will be fibrosis, which leads to hepatic cirrhosis. The liver cells will be in nodules and it will be surrounded by fibrosis leading to death.

1. **Transudate** is extravascular fluid with low protein content and a low specific gravity.

Pathogenesis of granuloma formation (Ex: TB)

Granulomatous Inflammation pathogenesis:

Neutrophils ordinarily remove agents that induce an acute inflammatory response.

However, there are circumstances in which reactive neutrophils **cannot** digest the substances that induce acute inflammation.

Pathogenesis of TB:

- **Cord factor:** it is a glycolipid molecule found in the cell wall of **Mycobacterium tuberculosis** and similar species.
- It protects mycobacterium tuberculosis from the defenses of the host.
- **Cord factor** presence increases the production of:

1. cytokines Interleukin-12 (IL-12)
2. IL-1β
3. IL-6
4. Tumor necrosis factor (TNF).

HOPEFULLY WE DID A GREAT JOB

ONLINE TEST

FOR ANY QUESTIONS AND SUGGESTIONS CONTACT US ...

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To make sure that all students are aware of any changes, please check out this link to know if there are any additions or changes.
The same link will be used for all of our work:
(Pathology Edit)

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DIFFICULTIES IN YOUR LIFE DON'T COME TO DESTROY YOU.. BEST OF LUCK