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Sarcoidosis - An Auto Immune Disease

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Abstract: ***Sarcoidosis is a multisystem inflammatory disease that mostly affects the lungs and lymph nodes, but it can also affect the heart, nervous system, skin, and eyes. It is characterized by non-caseating granulomas. Its symptoms can range from minor respiratory problems to serious side effects like cardiac arrhythmias and neurological disorders. Although the precise cause is unknown, genetics, environmental exposure, and immune dysregulation are being taken into consideration. Clinical evaluation, imaging, laboratory results, and tissue biopsy are usually used to make the diagnosis while ruling out similar conditions. Corticosteroids are the mainstay of treatment, with immunosuppressive medications used for more resistant cases, in order to control symptoms and prevent organ damage. One particularly complicated variation that poses particular difficulties for diagnosis and treatment is neurosarcoidosis.***

Keywords: Sarcoidosis, granuloma formation, neurosarcoidosis, multisystem disease, immune response

1. Introduction

1.1. Sarcoidosis:(1)

Sarcoidosis is a rare condition that causes small patches of swollen tissue, called granulomas, to develop in the organs of the body. It often affects the lungs and lymph nodes and can also affect your skin. The symptoms of sarcoidosis depend on which organs are affected, but typically include tender bumps on the skin, shortness of breath, a persistent cough. A persistent cough, Chest pain, Dry cough, Coughing up blood, Fatigue, Fever, Joint ache or pain, Weight loss, Hair loss.

Other symptoms include Blurred vision, Eye pain, Burning, itching or dry eyes, Severe redness, Sensitivity to light, Fainting (syncope), Irregular heartbeats, Arrhythmias, Rapid or fluttering heartbeat (palpitations).

The exact cause of sarcoidosis is unknown, but it may be triggered by Infections with bacteria or viruses, Contact with dust or chemicals, and Certain genes.

Sarcoidosis is more common in: African Americans and White people of Scandinavian heritage.

Most cases are diagnosed between the ages of 25 and 40.

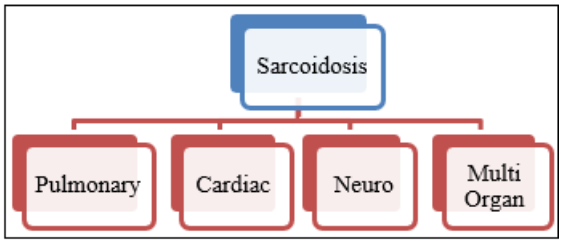
There's no specific cure for sarcoidosis, though it often goes away on its own.

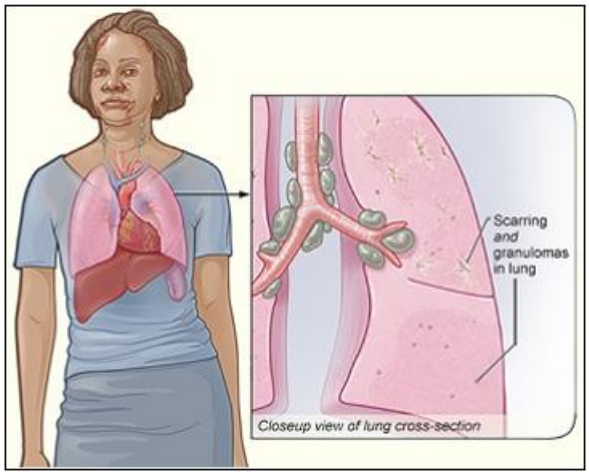
Treatment usually involves managing symptoms and preventing organ damage.

Medications to treat sarcoidosis include:
a) Corticosteroids,
b) Immunosuppressants,
c) Anti-tumor necrosis factor-alpha antibodies (anti-TNF-alpha antibodies),
d) Nonsteroidal Anti-Inflammatory Drugs (NSAIDs).

1.2. Types:

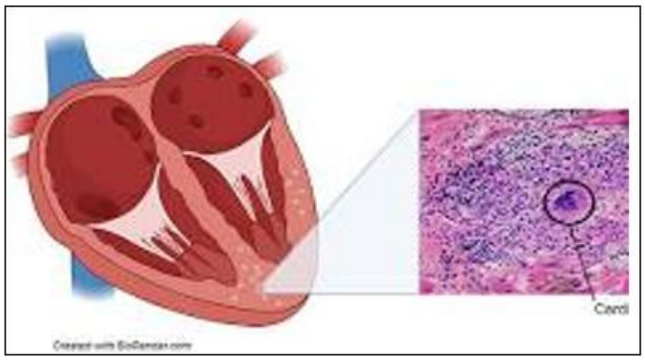
a) Pulmonary Sarcoidosis: (2)
Pulmonary sarcoidosis is an inflammatory disease that causes tiny clumps of cells, called granulomas, to form in your lungs and lymph nodes. The lymph nodes are part of your immune system, which helps fight infections.





Diagnosis of Pulmonary Sarcoidosis: Chest X – Ray, High Resolution CT scan, Pulmonary Function Tests, Blood Test, Biopsy.

b) Cardiac Sarcoidosis: (3)
Cardiac sarcoidosis is a rare condition that occurs when tiny collections of immune cells, called granulomas, form in the heart tissue. These granulomas can interfere with the heart's normal functioning, resulting in abnormal heart rhythms, also known as arrhythmias. The clinical presentation is variable and includes congestive heart failure, sudden cardiac death, ventricular arrhythmia, or atrioventricular block. It is a rare condition with a poor prognosis. Cardiac involvement portends a poor prognosis and left ventricle ejection fraction is the most important predictor of mortality in cardiac sarcoidosis.



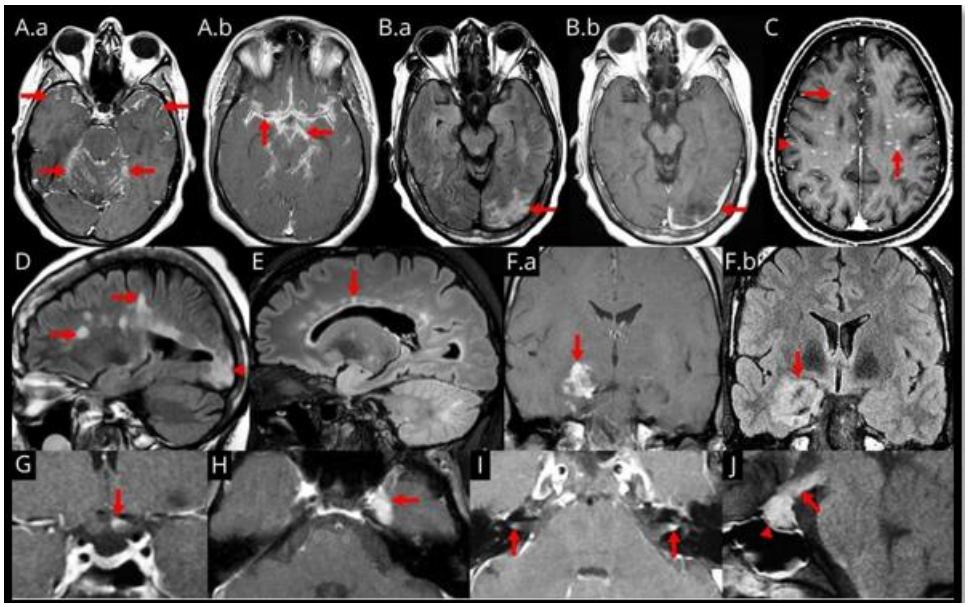
Diagnosis of Cardiac Sarcoidosis:

- Electrocardiogram (ECG) to measure the electrical activity of the heart.
- Echocardiogram to create images of the heart's structure and function.
- Holter monitor to record your heart rhythm over a 24-hour period.
- Cardiac MRI to produce detailed images of the heart.
- Positron emission tomography (PET) scan to identify areas of inflammation in the body.
- Endomyocardial biopsy, which involves taking a small tissue sample from the heart for examination under a microscope.

Cardiac sarcoidosis is more common in Japan. More than half of the people with sarcoidosis in Japan also have the condition in their hearts. However, cardiac sarcoidosis is less common than sarcoidosis in other organs.

c) Neurosarcoidosis: (4)

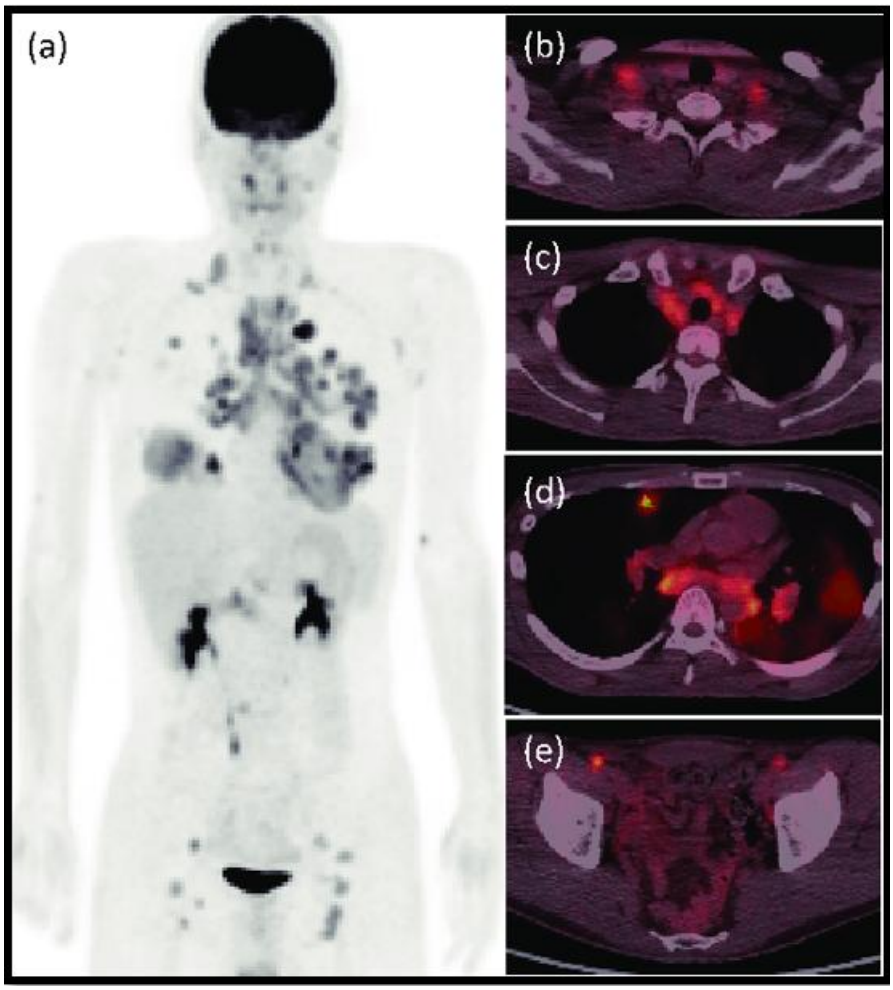
Neurosarcoidosis results from sarcoid granulomas within the nervous system. Pathologically, lymphocytes and mononuclear phagocytes surround a noncaseating epithelioid cell granuloma. Symptoms result from the location of where the granulomas lie in the nervous system.



Diagnosis of Neurosarcoidosis: Medical History & physical examination, Blood Tests, Lumbar Puncture, Imaging Test.

d) Multi Organ Sarcoidosis: (5–7)

A multi-organ disease, sarcoidosis may affect a range of systems, including the nervous system, musculoskeletal system, lymph glands, lungs, skin, liver, spleen, eyes, heart, brain, and kidneys. In some cases, inflamed granulomas may interfere with the functioning of an organ. The disease is not contagious.



Diagnosis of Multi Organ Sarcoidosis: Chest X – Ray, High – Resolution CT scan, Pulmonary Function Test, Biopsy, Blood Tests.

1.3. Diagnosis: (6)

Diagnosing sarcoidosis can be a bit of a puzzle because there's no single definitive test. Doctors typically rely on a combination of factors to come to a diagnosis. Here's a breakdown of the diagnostic process:

a) Considering your symptoms:

- Sarcoidosis can affect many organs, so doctors first consider your symptoms and how long you've been experiencing them.
- Common symptoms include fatigue, weight loss, fever, night sweats, swollen lymph nodes, skin lesions, eye problems, shortness of breath, cough, chest pain, heart rhythm problems, and fainting.

b) Physical examination:

- Your doctor will perform a physical exam to check for signs of sarcoidosis, such as enlarged lymph nodes or abnormal lung sounds.

c) Imaging tests:

- Chest X-ray, high-resolution CT scan, and MRI scans can be used to look for granulomas, which are collections of immune cells that are a hallmark of sarcoidosis.
- These scans can also reveal inflammation in your lungs, heart, or other organs.

d) Blood tests:

- Blood tests can't diagnose sarcoidosis definitively, but they can help assess your overall health and rule out other conditions.
- Blood tests may check your blood counts, kidney and liver function, and levels of calcium in your blood.

e) Biopsy:

- In some cases, a biopsy may be necessary to confirm the diagnosis of sarcoidosis.
- This involves taking a small tissue sample from the affected organ, such as the lungs, lymph nodes, skin, or even the nervous system, for examination under a microscope.

f) Ruling out other causes:

- An essential part of the diagnosis is excluding other diseases that can cause similar symptoms.
- Your doctor will consider infections, lung diseases like tuberculosis, and other causes of granulomas.

The specific tests used will depend on your individual symptoms and which organs are suspected to be involved. There's no set order for the tests, and some may be done simultaneously. A positive biopsy is not always required for diagnosis, but it can be helpful for confirmation.

1.4. Treatment: (7)

Treatment	First Line	Corticosteroids
		Pulmonary Radiology
	Second Line	Methotrexet
		Leflunomide
		Azathioprine
	Third Line	Infliximb
		Adalimumab
		Cyclophosphamoide
	Other Treatment	Supplimental Oxygen
		Immuno Suppressant Medications
		TNF Inhibitors
		Lung Transplantation

2. Literature Review

2.1 Neurosarcoidosis: (8) (4)

2.1.1 Neurological Involvement: (9)

Although the etiology is unknown, sarcoidosis is a systemic disease that results in the formation of granulomas. Classically, the granulomas in sarcoidosis are non-caseating granulomas, which may be found throughout lymph nodes and organs, including the brain and nervous system. About 5% to 10% of patients with sarcoidosis will have neurologic complications.

Patients who have active disease and systemic characteristics are more likely to develop Neurosarcoidosis. Neurosarcoidosis is a difficult diagnosis that is typically made via exclusion. A non-caseating granuloma can occasionally be discovered by a biopsy of a muscle or nerve. The disease Neurosarcoidosis has no known cure. For most individuals, corticosteroids must be taken on a long-term basis.

Neurological complications in sarcoidosis, a multisystem disease, have been documented since its recognition by Winckler in 1905. Most commonly, facial, and optic neuropathies are seen, with an incidence of 3.5%-7.7%. Recent case series show that around half of patients have isolated cranial neuropathies, with peripheral nerve and muscle involvement accounting for 10% - 70% of these series.

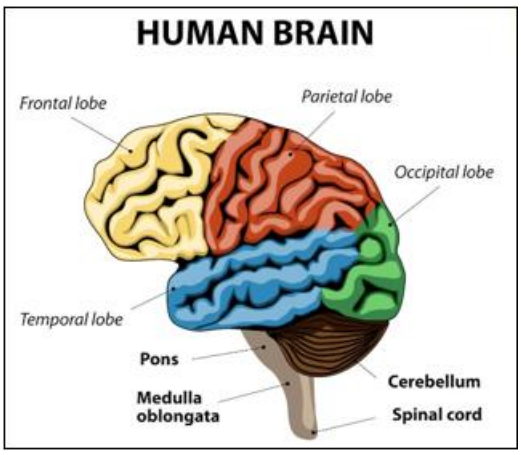


Figure: Normal Human Brain

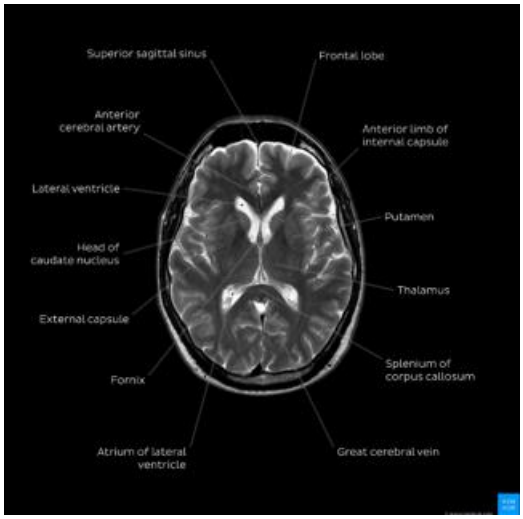


Figure: MRI of Normal Brain

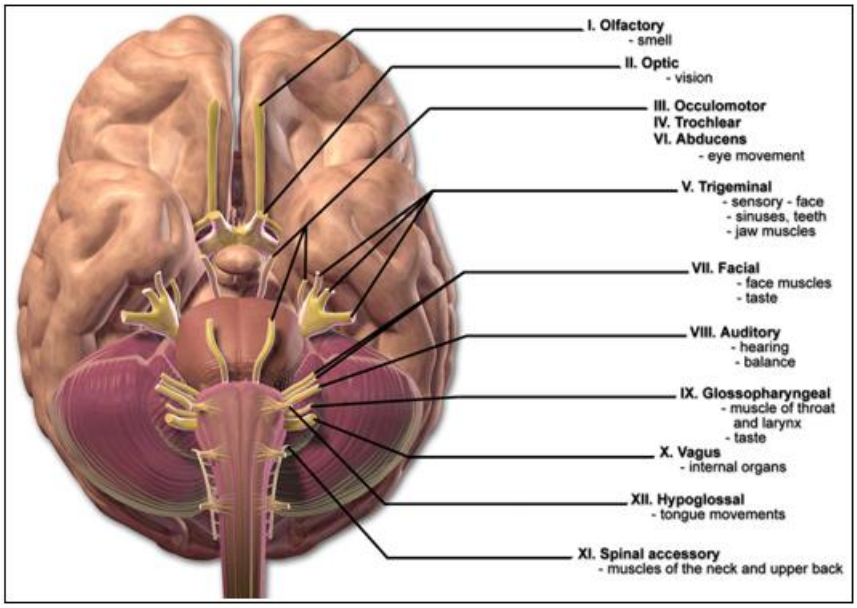


Figure: Sarcoid Brain

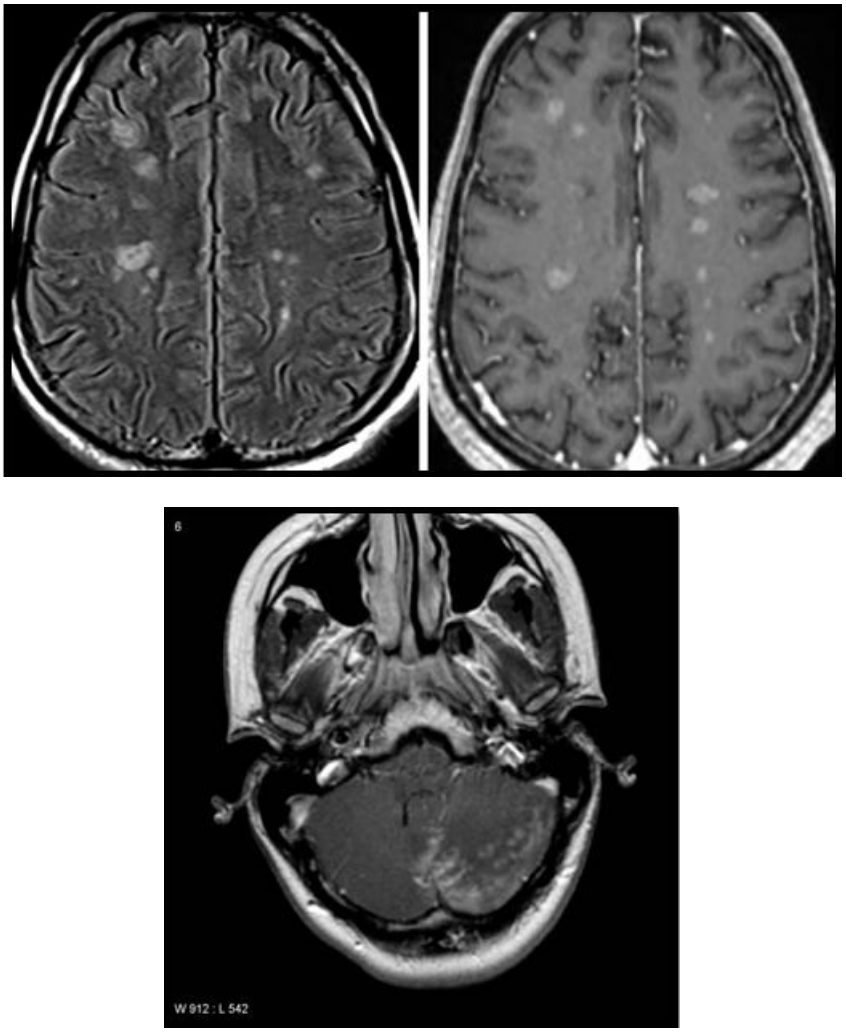
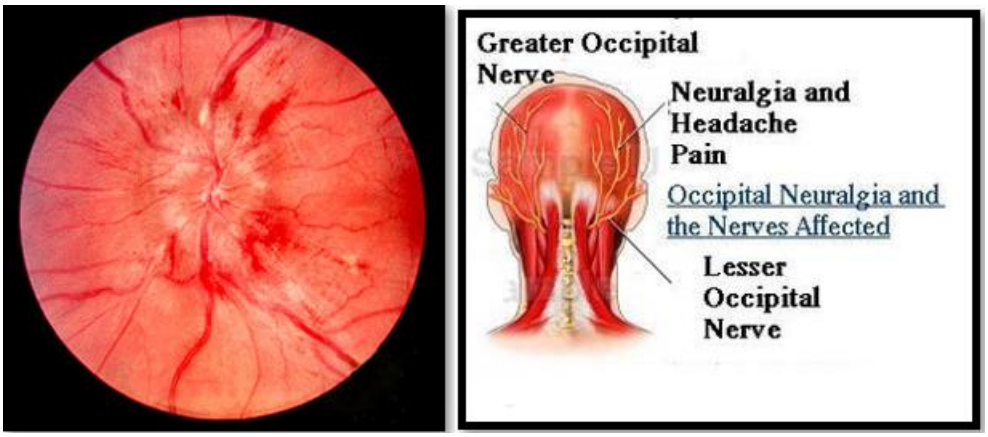


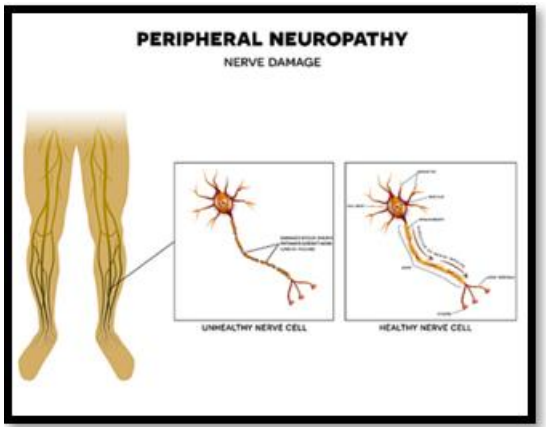
Figure: MRI Images of Brain with Sarcoid Patches

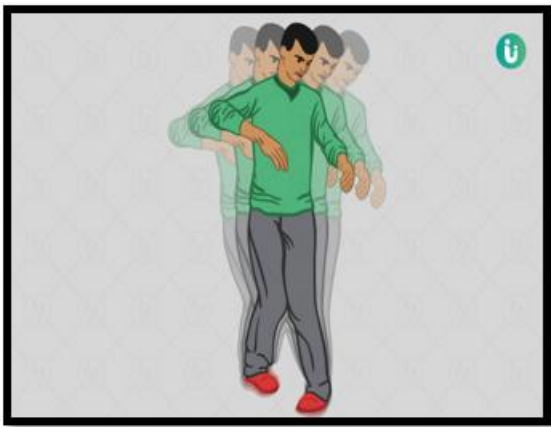
2.2 Etiology: (4)

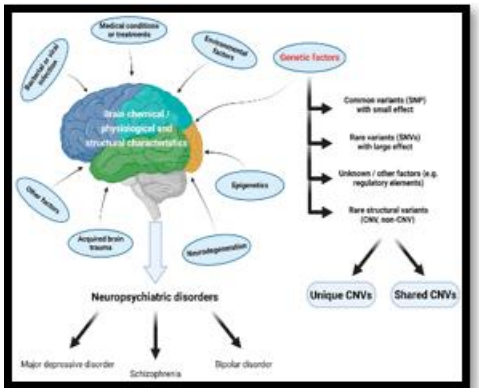
Sarcoidosis is thought to be caused by an overactive immune response, while the exact Etiology is unknown. Th1 cells activate macrophages by inducing the release of IFN-gamma and IL-2. Granuloma development is the result of the inflammatory reaction that macrophages have triggered.

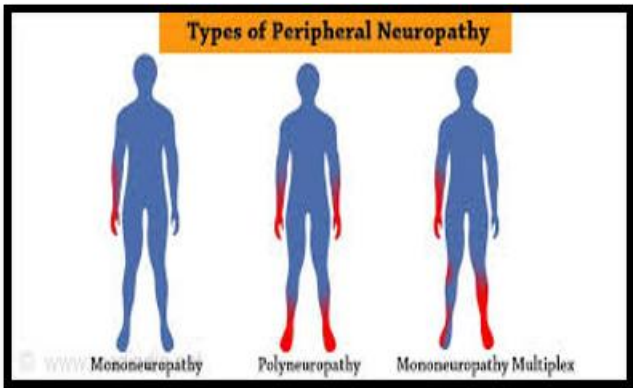
The most common neurological abnormalities reported include the following_Papilledema, Cranial Neuropathies, Peripheral neuropathy, Myopathy and Mononeuropathy, Neuropsychiatric Disturbances, Ataxia, Hydrocephalus.

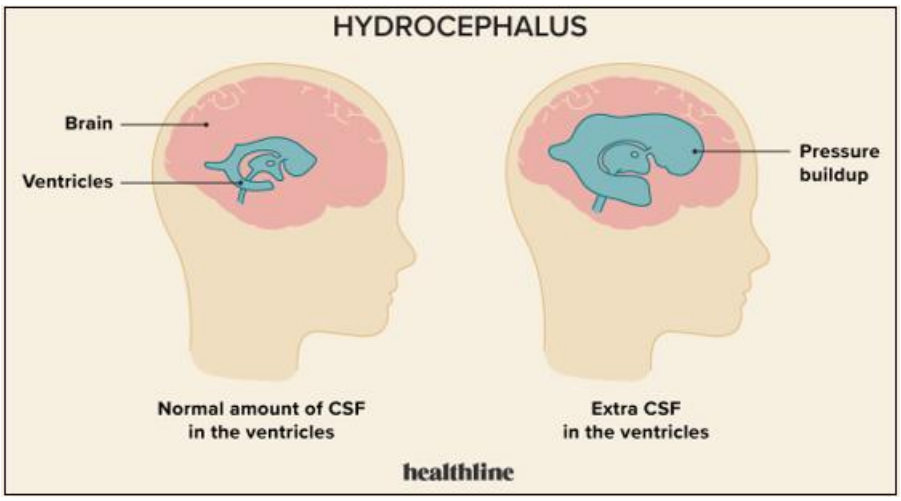



PERIPHERAL NEUROPATHY
NERVE DAMAGE
UNHEALTHY NERVE CELL
HEALTHY NERVE CELL

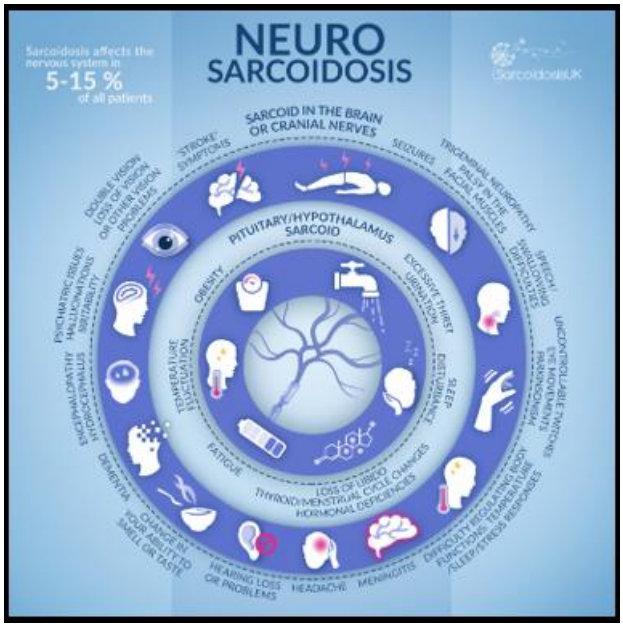



Genetic factors
Neuropsychiatric disorders
Unique CNVs
Shared CNVs
Major depressive disorder
Schizophrenia
Bipolar disorder


Types of Peripheral Neuropathy
Mononeuropathy
Polyneuropathy
Mononeuropathy Multiplex


HYDROCEPHALUS
Brain
Ventricles
Pressure buildup
Normal amount of CSF in the ventricles
Extra CSF in the ventricles
healthline

2.3 Symptoms:



If the condition is affecting the pituitary gland, symptoms may include Changes in menstrual periods, Fatigue, Excessive Thirst, Excessive Urination.

If the condition is affecting the brain or cranial nerves, symptoms may include Confusion, Disorientation, Hearing Loss, Dementia, Delirium, Dizziness, Vertigo, or abnormal sensation of movements, Vision Problems, such as double vision, Headache, Loss of sense of smell, Psychiatric Disturbances, Seizures, Speech Impairment.

If the condition is affecting peripheral nerves, this can cause symptoms such as Muscle Weakness, Numbness or tingling sensation, Loss of movement.

Causes and Risk Factors:

The cause of Neurosarcoidosis is unknown. Factors that may contribute to risk includes Infections, Immune System Disorders, Genetics, Environmental Factors.

2.4 Pathophysiology: (10)

Neurosarcoidosis is a manifestation of sarcoidosis, a multisystem granulomatous disease of unknown etiology. While the exact mechanisms leading to sarcoidosis and its neurological involvement are not fully understood, several key factors contribute to the pathophysiology of neurosarcoidosis:

Granuloma Formation:

- **Central to sarcoidosis:** The hallmark of sarcoidosis is the formation of non-caseating granulomas, clusters of immune cells that form in various organs, including the nervous system.
- **Immune dysregulation:** The exact trigger for granuloma formation is unknown, but it's believed to involve an abnormal immune response to an unidentified antigen.
- **Neuropathology:** In Neurosarcoidosis, granulomas can develop in the brain, spinal cord, meninges, or cranial nerves, leading to a variety of neurological symptoms.

Inflammatory Response:

- **Granuloma-associated inflammation:** Granulomas release inflammatory mediators, such as cytokines and chemokines, which contribute to tissue damage and neurological dysfunction.
- **Vascular involvement:** Inflammation can affect blood vessels, leading to reduced blood flow and oxygenation to brain tissue.

Neurological Manifestations:

- **Location and extent of granulomas:** The specific neurological symptoms depend on the location and extent of granulomatous involvement.
- **Cranial nerve involvement:** Granulomas affecting cranial nerves can cause a range of symptoms, including facial weakness, vision problems, hearing loss, and difficulty swallowing.
- **Meningitis:** Granulomatous inflammation of the meninges (leptomeningeal sarcoidosis) can lead to headaches, stiff neck, and other meningeal signs.
- **Parenchymal involvement:** Granulomas within the brain parenchyma can cause focal neurological deficits, seizures, or cognitive impairment.
- **Spinal cord involvement:** Rare but possible, granulomas in the spinal cord can result in weakness, sensory disturbances, or bowel and bladder dysfunction.

Immune-Mediated Damage:

- **Autoimmunity:** In some cases, neurosarcoidosis may involve an autoimmune component, where the body's immune system attacks its own tissues.
- **Demyelination:** Immune-mediated damage to the myelin sheath surrounding nerve fibres can contribute to neurological symptoms.

2.5 Epidemiology: (9)

Differences in illness prevalence have been recognized for decades; it has long been known that the incidence is highest in Nordic nations (11 – 24 per 10^5), and lowest in South-east Asian countries (0.85 in Korea, 2.17 in Taiwan, and 1.01 in Japan) (11) (12) (13) (14).African Americans in the United States have three times the incidence of European Americans, while Hispanic Americans have even lower rates.10 Recent investigations from the Swedish sarcoidosis registry have identified an annual incidence of 11 per 10^5 and a prevalence of 160 per 10^5, whereas three studies in the United States have found an annual incidence of 11 per 10^5 In the UK, the incidence was 14.5 per 10^5 during 1977 to 1983 on the Isle of Man, and lately.

The age of onset varies, with very few occurrences occurring in infants and the elderly, and a typical age of onset of 45 to 55 years, which is later in women than in males.

Overall, it is more prevalent in women than in men. Over time, the mortality rate is approximately 7% higher than in the general population, due mostly to the severity of the disease in those with respiratory, cardiac, and neurological involvement, but also to an increased risk of infection. Sarcoidosis patients are also more likely to have venous thromboembolism, cardiovascular disease, and haematological and skin cancers, as well as a higher

frequency of various autoimmune disorders, particularly thyroid disease, connective tissue diseases, and multiple sclerosis.

Sarcoidosis, an inflammatory condition, is distinguished by noncaseating epithelioid granulomas, which are formations of activated macrophages. The pathological hallmarks highlight the disease's inflammatory nature, with data indicating hereditary sensitivity to environmental variables like as infection and non-infectious exposures, which can result in disorders similar to sarcoidosis. (15)

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