

# Information on

# CASTLEMAN DISEASE

## What is Castleman Disease?

Castleman disease (CD) is a rare disease of lymph nodes and related tissues that results from the overgrowth of the cells in the body's lymphatic system. Although Castleman Disease is not considered a cancer, it can develop into lymphoma. There are two main types of Castleman Disease: Unicentric, which is localized and affects only a single lymph node region, and Multicentric, which is widespread and affects multiple lymph nodes and lymphatic tissues and which can severely weaken the immune system. Multicentric Castleman Disease can be further classified as either HHV-8 -positive or HHV-8-negative.

## Key Statistics and Risk Factors

Approximately 200 new cases of Castleman Disease are diagnosed each year in the U.S. Unicentric Castleman Disease is more common than Multicentric, and can affect children as well as adults. It occurs most frequently in younger females. Multicentric Castleman Disease is more likely to occur in people infected with HIV and in older adults.

Most patients with Castleman Disease do not have any known risk factors. The only known risk factor for Castleman Disease is infection with HIV, the virus that causes AIDS. Multicentric Castleman Disease is much more common in people who are HIV positive. Those who have developed AIDS are more prone to

develop Multicentric Castleman Disease because they tend to have weakened immune systems.

## Signs and Symptoms

Castleman Disease can cause a variety of symptoms, although some people might not have any symptoms at all. Multicentric Castleman Disease usually includes widespread chronic swelling of the lymph nodes and sometimes enlargement of the liver and spleen.

Many people with Unicentric Castleman Disease experience no symptoms. When symptoms are present, they are usually due to compression of vital structures, such as the trachea, blood vessels or nerves, caused by enlarged lymph nodes.

## What are the symptoms of Castleman Disease?

Symptoms of Unicentric Castleman Disease may include:

- A feeling of fullness or pressure in the chest or abdomen that can make breathing or eating difficult
- An enlarged lump under the skin in the neck, groin or armpit
- Fatigue
- Fullness in the face
- Weight loss
- Cough
- Anemia

Multicentric Castleman Disease usually includes widespread, chronic swelling of the lymph nodes.

The enlarged nodes can be in the chest or abdomen, groin or the underarm area. When present on the sides of the neck, they can often be seen or felt as lumps under the skin.

Multicentric Castleman Disease can also affect lymphoid tissue of internal organs, such as the liver or spleen, causing them to enlarge. Enlarged organs might be seen or felt as masses under either side of the rib cage. They can cause a sense of fullness or pain in the abdomen and can interfere with eating.

**Symptoms of Multicentric Castleman Disease may include:**

- Weakness and fatigue
- Night sweats
- Recurrent fever
- Shortness of breath
- Nausea and vomiting
- Loss of appetite
- Weight loss
- Enlarged lymph nodes, usually around the neck, collarbone, underarm and groin areas
- Enlarged liver or spleen

**Diagnosing Castleman Disease**

If symptoms or physical exam indicate that a patient might have a lymph node condition, the physician will get a thorough medical history, including details about symptoms, possible risk factors and other medical conditions. The physician will look for infection in the part of the body near the swollen lymph nodes, since infection is the most common cause of swollen lymph nodes.

The physician will likely order blood work if there is a suspicion of Castleman Disease, some other type of immune system condition, or serious infection. Imaging studies will be performed to look for enlarged lymph nodes or organs that might be causing symptoms. PET scans are helpful for identifying small collections of fast-growing cells that might not be visible with other imaging studies.

Castleman Disease can only be diagnosed through biopsy (removing an enlarged lymph node) and examination under the microscope.

**Treatment**

In most cases of Unicentric Castleman Disease, the preferred treatment is surgical removal of the mass. Adjuvant therapy, such as steroids and/or rituximab before surgery, can be useful to shrink a bulky tumor. Unicentric Castleman Disease patients generally do well once the affected lymph node is removed.

Surgery is not usually an option in the case of Multicentric Castleman Disease because of the number of lymph nodes involved. Treatment generally includes medications and other therapies to control abnormal cell growth. Specific treatment depends on the extent of the disease and on whether there is associated HIV or HHV-8 infection or both.

**Therapy options for HHV-8 positive Multicentric Castleman Disease include:**




- Rituximab, which depletes the reservoir of HHV-8 positive cells and significantly reduces the risk of lymphoma
- Etoposide, a chemotherapeutic agent, for more severely afflicted patients
- Maintenance therapy with valganciclovir, an anti-viral agent

**Therapy options for HHV-8 negative Multicentric Castleman Disease include:**

- Siltuximab or Rituximab. Siltuximab is a monoclonal antibody to the human IL-6 receptor. It is designed to attack a specific target, such as a substance on the surface of lymphocytes, the cells in which Castleman Disease begins.
- Immunosuppressants, immunomodulators, biologics, and cytotoxic chemotherapies, including cyclosporine, sirolimus, bortezomib, thalidomide, anakinra,  $\alpha$ -interferon, cyclophosphamide and etoposide
- Autologous stem cell transplantation

**Prognosis**

Unicentric Castleman Disease has an excellent prognosis. It usually does not progress to lymphoma, and surgically removing the tumor cures 90–95% of cases.



The outlook for patients with Multicentric Castleman Disease varies, depending on the specific nature of their disease.

### The Future

The introduction of rituximab has been a major advance in HHV-8 positive Multicentric Castleman Disease. Therapy with IL-6-targeting monoclonals, such as siltuximab, has been an important innovation in HHV-8 negative Multicentric Castleman Disease. However, anti-IL-6 monoclonals are not effective for all patients.

The Myeloma Institute participates with the Castleman Disease Collaborative Network to accelerate research and explore the causes of Multicentric Castleman Disease. The network includes a community of more than 200 researchers worldwide. Maximizing patient volume for historical studies is crucial for improving diagnostic criteria and patient care.

The Myeloma Institute is the leading research and treatment center in the world for Castleman Disease. Clinical trials at the Myeloma Institute offer an excellent opportunity for state-of-the-art treatments that might otherwise not be available.

This information about Castleman Disease and other patient education materials are available at [www.myeloma.uams.edu](http://www.myeloma.uams.edu)



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