Multicentric Castleman Disease in HIV - 2 studies from Europe

Over the past two decades researchers in the UK have been collecting health-related information from HIV-positive people who developed Multicentric Castleman Disease (MCD). Some of these people participated in a clinical trial where they received intravenous infusions of an antibody (rituximab, Rituxan) designed to attack abnormal cells associated with MCD. The research team found that since the debut of potent combination anti-HIV therapy (commonly called ART or HAART) and the use of Rituxan, survival with HIV-related MCD has tremendously improved.

Study details

Researchers in London, UK, reviewed their database and assembled reports on cases of HIV-related MCD largely collected between the year 1997 and the present, with most cases occurring since the year 2000.

Our report focuses on 61 cases in which MCD was diagnosed mostly after a biopsy of the affected lymph node or tissue had been conducted.

The average profile of participants when they entered the study was as follows:

- 53 men, 8 women
- 42% had been taking ART for at least three months before MCD was diagnosed
- among participants who took ART, only 44% had an HIV viral load below the level of detection (400 or 50 copies/ml, depending on the year that they were tested)
- CD4+ cell count – 233 cells

Upon diagnosis of MCD, most participants began immediate therapy for this condition and began to take ART if they were not already taking it.

Results—Symptoms

All participants had one or more symptoms for between two weeks to two years before MCD was diagnosed.

Common symptoms and abnormal lab tests included the following:

- fever
- enlarged spleen
- many swollen lymph nodes
- cough
- rash
- obstruction of the nasal passages (as the lymph tissues at the back of the passages were swollen)
- Kaposi’s sarcoma (KS) skin lesions
- elevated levels of the protein albumin in the blood
- higher-than-normal levels of C-reactive protein (CRP) in the blood
- elevated levels of HHV-8 in the blood

At the time MCD was diagnosed, four participants were also diagnosed with lymphoma.

On average, participants were monitored for four years.

Results—Overall survival

The survival rates of participants at different points in time were as follows:
Two years after MCD diagnosis – 83%
Five years after MCD diagnosis – 77%

Such rates of survival are much greater than seen in the time before ART, when the average survival rate was about one year after a diagnosis of MCD.

**Effect of rituximab on survival**

Rituximab became available in 2003, so some participants received intravenous infusions of this therapy upon diagnosis of MCD. Later, starting in 2006, participants whom doctors thought had a poor chance of survival received both rituximab and chemotherapy consisting of the drug etoposide. Overall, 49 participants received rituximab with or without etoposide. The overall survival rates among rituximab users were as follows:

- Two years after MCD diagnosis – 94%
- Five years after MCD diagnosis – 90%

Rituximab made a significant difference in survival with a diagnosis of MCD. Before 2003, when it was not available, overall survival rates following a diagnosis of MCD were as follows:

- Two years after diagnosis – 42%
- Five years after diagnosis – 33%

**Deaths**

Four of the 49 patients who received rituximab died—three died within 10 days of initiating therapy for MCD. All four were already in the intensive care unit (ICU) at the time MCD was diagnosed, so they were clearly very ill. The fourth participant managed to survive and recover from MCD and was well for two subsequent years. However, he developed lymphoma and died from complications from this cancer.

Forty-six of the 49 participants completed their courses of rituximab therapy and all had their symptoms and fever resolve.

**Relapse**

Among 46 participants whose symptoms cleared, relapse occurred among eight participants about two years after recovery from their initial episode of MCD. All were retreated with rituximab and some also received chemo—all survived.

One participant experienced a third episode of MCD but recovered when retreated with rituximab.

The only factor that was linked to longer survival was having a low HIV viral load at the time MCD was diagnosed.

**Kaposi’s sarcoma**

Among HIV-positive people with KS, MCD and some forms of lymphoma can occur in the future, as these complications (MCD and some forms of lymphoma) are incited by HHV-8 infection.

In the present study, 24 people had KS lesions at the time MCD was first diagnosed. In nine of these 24 participants, KS lesions grew larger and/or more KS lesions appeared after they received rituximab. Doctors prescribed liposomal formulations of doxorubicin (Doxil, Caelyx) to successfully treat these lesions.

**Note well**

It is important to note that leading cancer specialists do not agree on what should be the ideal therapy for MCD. However, the results of the London study suggest that the use of rituximab with or without chemo is very useful in managing MCD.

**Back and forth**
In the setting of HIV infection, MCD takes on a “remitting and relapsing nature,” noted the London team. This means that although MCD can be put into remission and symptoms can be cleared, it can return. Regular medical monitoring is necessary to allow doctors to intervene early, before relapse becomes widespread.

**The French MCD study**

Researchers in Paris, France, reviewed their database of MCD treatment among HIV-positive people. A total of 48 participants received rituximab only and 65 received chemo only. Among participants who received rituximab, only one subsequently developed lymphoma. In contrast, 17 cases of lymphoma occurred among participants who did not receive rituximab.

Survival rates were greater among participants who received rituximab, as shown below:

Survival two years after MCD diagnosis:
- rituximab users – 93%
- did not use rituximab – 68%

Survival five years after MCD diagnosis:
- rituximab users – 90%
- did not use rituximab – 47%

Causes of death included complications from lymphoma and organ damage from MCD.

Although the French study, like its UK counterpart, was not a randomized, controlled clinical trial, results from both studies strongly suggest that the use of rituximab is very useful in treating MCD.

In the French study, death rates were greater than in the British study in part because participants were generally in worse health when they sought care. For instance, nearly 30% of the French participants needed to be hospitalized in an intensive care unit and their CD4+ counts were generally less than 200 cells.

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**REFERENCE:**


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