Multicentric Castleman's disease (MCD) is a rare lymphoproliferative disorder driven by interleukin (IL-6) overproduction. Symptoms include fatigue, night sweats, loss of appetite, weight loss, hypoproteinemia, and general lymphadenopathy; severe cases can lead to death. MCD can be classified into 3 cell histologies: hyaline vascular, plasma, and mixed, with the mixed cell type most common. MCD patients are further classified based on their human immunodeficiency virus (HIV) status; HIV-positive patients develop MCD due to IL-6 secretion stimulated by human herpes virus-8 (HHV-8), however, the mechanisms underlying IL-6 overproduction in HIV-negative patients are not well understood.

Treatment options are limited and often focus on the management of symptoms. The rarity of the disease, heterogeneous presentation, lack of robust agnostic, and lack of both clinical guidelines and epidemiology studies, make incidence and prevalence is unknown.

OBJECTIVE
To characterize the clinical characteristics of MCD, estimate the incidence and prevalence of MCD, and document outcomes by examining patient records from 2 US MCD referral centers.

METHODS
MCD patient records were collected from the Mayo Clinic (Rochester, MN, United States) and the Fred Hutchinson Cancer Research Center (FHCRC, Seattle, WA, United States).

Eligible patients met the following criteria: age ≥ 18 years, a clinically and pathologically confirmed MCD diagnosis (either active or new diagnosis) between January 2000 and December 2009, and medical records available for data extraction.

Data were collected using a standardized data abstraction form and were stored in a central, encrypted online database; data validation programs were designed to minimize data entry errors.

Catchment areas for each center were defined by mapping patient ZIP codes using mapping software (ArcGIS, ESRI, Redland, CA, United States), consulting with the principal investigator, and examining case distribution within a 4-hour driving distance from the center (Figure 1).

Clinical, demographic, and healthcare utilisation information (including symptoms, comorbidities, hospitalisations, patient visits, mode of presentation, treatment, and systemic drug therapy, were extracted from patient records.

RESULTS

Demographic Characteristics
- Baseline demographic and disease characteristics are summarized in Table 1.

- MCD patients (N = 59) were evenly distributed between the 2 centers; 39 patients were from FHCRC, and 20 were from the Mayo Clinic.
- The majority of patients were male (61%) and Caucasian (68%), and the mean age was 52 years.
- Among patients whose employment status was known (n = 42), 48% were working full- or part-time, and 30% were disabled or retired.
- Of the 41 patients with education data available, 44% of patients had up to a high school education.
- Characteristics of patients within the catchment area were similar to those found in surrounding areas; those patients residing outside of the catchment area were more likely to have graduate or professional degrees and lower-recorded healthcare utilisation.

Clinical History
- Of the 33 patients with information regarding physician care prior to the study, 43% were treated by a hematologist, 39% by a primary care physician (PCP), and 21% by a rheumatology specialist.
- Among patients with documented histological information (n = 39), 49% of MCD cases were of the plasma cell subtype, 35% were hyaline vascular, and 15% were mixed (Table 1).
- In patients with known HIV status (n = 41), 5% were HIV positive; in patients with known HHV-8 status (n = 41), 17% were HHV-8 positive (Table 1).
- Patients with MCD symptoms prior to the study (n = 33) frequently reported fatigue (49%), fever (39%), and night sweats (39%; Table 2).
- Of the 37 patients with laboratory data available, 10% had abnormal liver function tests, 10% had abnormal kidney tests, 10% had abnormal blood cell counts, and 10% had abnormal blood chemistry.
- Of the 35 patients with laboratory data available, 10% had abnormal liver function tests, 10% had abnormal kidney tests, 10% had abnormal blood cell counts, and 10% had abnormal blood chemistry.

CONCLUSIONS

This is the first multicentre report to provide an MCD prevalence estimate based on known cases: 2.4 per million adults and 0.7 per million adults for the FHCRC and the Mayo Clinic catchment areas, respectively.

- Both prevalence estimates are likely underestimates due to under-diagnosis of MCD in some geographic areas.
- The MCD prevalence in North America is probably closer to the FHCRC and Mayo catchment estimates, with a mid-range between 1.7 and 3.4 per million adults.
- The results of this study need to be validated by replication in additional treatment centres in order to provide a more accurate assessment of the MCD population, and to determine true prevalence and incidence.

REFERENCES

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