

Ongoing symptoms and reduced health measures in unicentric Castleman disease patients despite perceived-to-be curative surgical excision

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Unicentric Castleman disease (UCD) is one of several subtypes of Castleman disease that share characteristic histopathology. While UCD involves one region of enlarged lymph nodes (LN) and milder symptoms, idiopathic multicentric CD (iMCD) involves multiple regions of enlarged lymph nodes and cytokine-driven organ dysfunction. UCD symptoms can occur due to compression of neighboring structures or inflammatory cytokine production. Complete excision of the enlarged LN is reported in the literature to be curative in 84-96% of UCD patients. However, many UCD patients describe persistence or worsening of symptoms post excision despite normal laboratory values and absence of measurable disease. To better characterize and describe the experience of individuals diagnosed with UCD, we administered surveys to UCD patients to capture information about general quality of life (QOL), specific health measures, and ongoing UCD symptoms.

All patients enrolled in the ACCELERATE Natural History registry who either self-reported a UCD diagnosis or were suspected to have a UCD diagnosis were invited to participate in the Rand36-item Short Form survey, the EQ-5D-5L, the MCD Symptom Score survey, all of which are validated instruments, as well as an additional form regarding ongoing symptoms. Among the 107 UCD patients invited to participate, 51 (48%) responded. Descriptive analyses were conducted on all 51 respondents with a self-reported UCD diagnosis. Subsequently, a subset consisting of 25 respondents, who had been reviewed by a panel of physicians that confirmed a UCD diagnosis (confirmed subcohort, CS), was analyzed.

Mean (SD) EQ-5D-5L health index score (100 being perfect health, 0 being worst health imaginable) of the 51 patients was 67.6 (19.9), compared to a representative sample of the US population whose score was 80.4. Patients reported having poor health over the prior 4 weeks, with low scores indicating high levels of fatigue (38.8) and poor general health (47.7). These are notable and comparable to scores for fatigue (52.2) and general health (57.0) among a separate cohort of patients with diabetes, hypertension, coronary heart disease, and/or depression.

Strikingly, 57% of patients reported continuation of symptoms post-LN excision, with an additional 16% being unsure. Only 29% reported complete symptom resolution, with the remainder reporting partial resolution (29%), stable disease (20%), worsening disease (12%), or unsure (10%). Nearly all 51 respondents underwent their LN-excision >1 year prior (93%). Fatigue (61%) and night sweats (39%) were most commonly reported in patients with continued symptoms. In fact, 27 patients (53%) reported ongoing symptoms on the day of survey completion with 93% of those patients reporting fatigue that day. Of note, sub-group analyses of the CS revealed similar findings, with a potential trend towards slightly better overall health with mean (SD) health index score 72.6 (14.5), fatigue (44%) and night sweats (36%), and ongoing symptoms reported in 40%. Of the patients in the CS, all

had a complete resection, with 3 demonstrating subsequent lymphadenopathy in new regions ranging from 6 months to 5 years after their initial excision.

Overall, these data suggest that UCD patients who have had resection of disease continue to experience symptoms that affect QOL. Patients reported lower QOL than a representative national average, as well as health measures comparable to a separate cohort of individuals with chronic health conditions. Of note, the full cohort of self-reported individuals consistently reported lower scores compared to the subset of patients with confirmed UCD (not statistically tested). Of the 26 non-confirmed cases, 8 did not achieve criteria to meet UCD and 18 have not yet been reviewed by our physician panel. A different undiagnosed disorder may be the root cause of symptoms in a portion of these patients and others may be experiencing symptoms due to a co-occurring disorder. These results may be confounded by reporting bias and may not be representative of the full UCD population. Nevertheless, these data suggest that perceived-to-be curative excision does not result in symptom-free outcomes in a substantial proportion of patients and that symptom management may be required beyond excision. Future work is needed to correlate these findings with clinical, laboratory, and experimental data to further elucidate mechanisms and treatment options.