Introduction/Background

Castleman’s disease (CD), also known as giant lymph node hyperplasia or angiofollicular lymph node dysplasia, is a rare benign immunoproliferative disorder. CD is classified by histopathologic appearance (hyaline vascular, plasma cell or mix variant) as well as by the number of lymph nodes that are involved (unicentric and multicentric). We report the case of a 24-year-old female who was found to have unicentric anterior mediastinum CD. This article describes the clinical features, pathogenesis, diagnosis, and current treatment modalities for this uncommon disease.

Keywords: Castleman’s disease; Mediastinal mass, Lymph node hyperplasia; IL-6
Abbreviations: CD: Castleman’s disease; CT: Computerized Tomography; PET: Positron Emission Tomography

Case Presentation

A 24-year-old female presented with nonproductive cough for four weeks. She denied other systemic symptoms. Previous medical history was unremarkable and she was a non-smoker. Family history was contributory for ovarian cancer. Physical examination was unremarkable. Her blood work results were all within normal limits and a Human Immunodeficiency Virus test was negative.

A chest x-ray revealed mild left-ward deviation of the trachea and a contrast CT scan was obtained. A solid heterogeneous enhancing mass was found of approximately 3.5 cm is largest axial diameter localized inferior to the right thyroid lobe and extending into the anterior mediastinum, causing mass effect and left-ward deviation of the trachea (Figure 1). A positron emission tomography (PET)-CT scan was performed, and showed a soft tissue mass in the right neck Level IV compartment that extended into the superior mediastinum (Figure 2).
A subsequent core needle biopsy was performed. This showed lymph node tissue with paracortical hyperplasia, increased vascularity, focal hyalinization, reactive germinal center and groups of follicular dendritic cells. A mediastinal mass with these characteristics, based on histologic and imaging findings, was suggestive of hyaline-vascular Castleman’s disease. There was no histopathological evidence of lymphoma on the specimen (flow cytometric studies performed). Subsequently, a complete resection of the mass was performed. Histologic examination confirmed the diagnosis of Castleman’s disease,
hyaline vascular type. Six months after surgery, the patient remains asymptomatic and no other lymph node enlargement has been detected. A CT follow-up was performed and there were no abnormal findings.

**Discussion**

The etiology of CD is still unclear. Theories such as inflammatory origin, hyperplasia of hamartomatous lymphoid tissue or inappropriate immune response have been proposed [3,6]. CD has also been associated with human immunodeficiency virus and human herpes virus [6-8]. The differential diagnoses of a mediastinal mass include: thymoma, lymphoma, teratoma or unicentric CD. Normally, the former three would not show enhancement in a contrast CT scan [3]. In the case of unicentric CD, post-contrast enhancement is seen due to its hypervascularity [3]. A PET scan can be used to determine if there is any other lymph nodes involved [8]. To confirm the diagnosis, a core needle or open biopsy should be performed. This will show a polyclonal nodal expansion with the histologic features of one of the variants mentioned previously.

Diverse types of management have been proposed (Tables 1 & 2). Surgical resection is considered curative in the vast majority of cases [Bowne et al. [5]. A recent systematic review of 278 cases of unicentric CD showed that the outcomes for complete resection (R0) of the tumor were significantly better than for an incomplete resection [8,9]. Chronowski et al. [10], reported that radiotherapy has the ability to achieve complete radiographic and clinical resolution on unicentric CD in a selected group of patients, but the rates of disease free survival for surgical resection were still higher Bowne et al. [5] (Table 2). For this reason, radiotherapy should be considered for a poor surgical candidate or for unresectable unicentric CD. A study by Yoshizaki et al. [7] demonstrated that, in fact, the cells present in the germinal centers of the hyperplastic lymph nodes produce IL-6 and found a correlation of this production with the serum levels of IL-6 Abdessayed et al. [13]. Thus, another treatment modality that has been proposed is the blockage of the IL-6 dysregulated overproduction [7,11], especially in patients with plasma-cell variant [11] & Ren et al. [14].

**Table 1**: Review of literature about Unicentric Castleman’s Disease treated with complete surgical resection.

| Study            | Age | Sex | Year | Location    | Clinical Response |
|------------------|-----|-----|------|-------------|-------------------|
| **Bowne et al. [5]** |     |     |      |             |                   |
|                  | 47  | F   | 1999 | Chest wall  | NED at 10mo       |
|                  | 32  | F   | 1999 | Retropertitoneum | NED at 13mo     |
|                  | 46  | F   | 1999 | Axilla      | NED at 2 years    |
|                  | 22  | F   | 1999 | Retropertitoneum | NED at 2 years   |
|                  | 21  | F   | 1999 | Mediastinum | NED at 1 year     |
|                  | 53  | F   | 1999 | Retropertitoneum | NED at 37mo    |
|                  | 26  | M   | 1999 | Mediastinum | NED at 2 years    |
|                  | 33  | F   | 1999 | Mesentery   | NED at 1 year     |
|                  | 29  | F   | 1999 | Mesentery   | NED at 25mo       |
|                  | 45  | F   | 1999 | Mediastinum | NED at 10mo       |
| **Chronowski et al. [10]** |   |     |      |             |                   |
|                  | 45  | F   | 2001 | Cervical    | NED at 4mo        |
|                  | 21  | M   | 2001 | Hilum       | NED at 62mo       |
|                  | 26  | M   | 2001 | Cervical    | NED at 32mo       |
|                  | 51  | M   | 2001 | Cervical    | NED at 40mo       |
|                  | 15  | F   | 2001 | Axilla      | NED at 74 mo      |
|                  | 41  | M   | 2001 | Axilla      | NED at 26mo       |
| **Haro et al. [12]** | 77  | F   | 2016 | Mediastinum | Asymptomatic      |
| **Abdessayed et al. [13]** | 34  | F   | 2017 | Retropertitoneum | NED at 12mo     |
| **Ren et al. [14]** | 35  | F   | 2018 | Mediastinum | Recurrence after 14 years |

F: Female; M: Male; NED: No evidence of disease; Mo: Months.
Table 2: Review of literature about Unicentric Castleman’s Disease treated with Radiotherapy.

| Study                  | Age | Sex | Year | Location      | Clinical Response                              |
|------------------------|-----|-----|------|---------------|------------------------------------------------|
| Nordstrom et al. [15]  | 50  | F   | 1978 | Mesenteric    | NED at 8 mo                                    |
| Weisenburger et al. [16]| 51  | F   | 1979 | Mesenteric    | Decrease in size at 6mo, then regrowth at 10mo |
| Stokes et al. [4]      | 45  | M   | 1985 | Paraspinal    | Asymptomatic and no lymphadenopathy at 5 years |
| Sethi et al. [17]      | 25  | M   | 1990 | Submandibular | NED at 22mo                                    |
| Veldhuis et al. [18]   | 62  | F   | 1996 | Supraclavicular| NED after 2 years                              |
| Chronowski et al. [10] | 38  | F   | 2001 | Retroperitoneum| Complete response                              |
|                        | 24  | F   | 2001 | Mediastinum   | Asymptomatic; decrease in tumor size           |
|                        | 37  | M   | 2001 | Mediastinum   | Complete response                              |
|                        | 51  | F   | 2001 | Axilla        | Complete response                              |
| Neuhof et al. [19]     | 24  | F   | 2006 | Mediastinal   | Decrease size at 12mo                          |
|                        | 71  | M   | 2006 | Mediastinal   | Progressive disease after 3 mo                 |
|                        | 38  | F   | 2006 | Cervical      | Complete remission after 4 mo                  |
| Noh et al. [20]        | 20  | F   | 2013 | Supraclavicular| Decrease in size at 14mo                       |
|                        | 56  | F   | 2013 | Para-aortic   | NED after 12 months                            |

F: Female; M: Male; NED: No evidence of disease; Mo: Months.

Although unicentric CD is considered a benign condition, surgical resection is highly recommended because of mass effect on adjacent structures Nordstrom et al. [15]. A secondary consideration for surgery is that it may have malignant potential [6]. This neoplastic potential is higher with the plasma-cell variant [3]. In the case of multicentric CD, surgery does not have offer curative intent and the treatment focuses on symptom relief and clinical findings of each patient [9]. A study performed by The American Society of Hematology used a humanized anti IL-6 receptor antibody to treat patients with multicentric plasma cell or mixed type CD. After the administration of this antibody Weisenburger et al. [16], a clinical response was achieved [11-14]. Also, when histopathological examination was performed, pathological response was noted with a reduction of follicular hyperplasia and vascularity [15-18].

CD is an uncommon and poorly understood disease that warrants more investigation Stokes et al. [4], Sethi et al. [17], Chronowski et al. [10], Neuhof et al. [19], Noh et al. [20]. Further studies are required to identify an etiology and describe the epidemiology of CD [19,20]. Due to its low incidence, there have been no randomized clinical trials, and all the available data comes from systematic reviews, case series and case reports [8].

Acknowledgement

We thank the patient for allowing us to share her details.

Conflict of Interest

The authors declare that there is no conflict of interest.

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DOI: 10.19080/CTOIJ.2018.09.555775

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