

## Castleman's disease presenting as persistent asymptomatic cervical lymphadenopathy in a child: A very rare disease with atypical presentation

Muhammed Basheer K T<sup>\*1</sup>, Shubhankar Mishra<sup>1</sup>, Pravakar Mishra<sup>2</sup> and Narendra Behera<sup>2</sup>

<sup>1</sup>Junior Resident, Department of Paediatrics, MKCG Medical College Brahmapur, Odisha, India.

<sup>2</sup>Associate Professor, Department of Paediatrics, MKCG Medical College Brahmapur, Odisha, India.

### \*Correspondence Info:

Dr. Muhammed Basheer K T

Junior Resident,

Department of Paediatrics,

MKCG Medical College Brahmapur, Odisha, India.

E-mail: [drbasheerkt@gmail.com](mailto:drbasheerkt@gmail.com)

### Abstract

Castleman's disease is a rare atypical lympho-proliferative disorder characterised by enlarged hyperplastic lymphnodes with striking vascular proliferations. A cervical location has very rarely been reported in paediatric literature. It can be unicentric or multicentric. There are mainly four histological variants, hyaline vascular type being the commonest one. Although unicentric Castleman's disease carries a favorable prognosis in children, surgical excision is recommended to confirm the diagnosis and to rule out other causes. We report a case of unicentric cervical Castleman's disease of neck in a 6-years old male child, who came to paediatric ward with history of right sided neck mass since 2yrs. After thorough clinical examination and investigations, complete excision of the mass was done. Histopathological examination confirmed the diagnosis of Castleman's disease-hyaline vascular type. On follow-up for two years no recurrence has been seen.

**Keywords:** Unicentric (UCD), Castleman's disease, Cervical lymphadenopathy

### 1. Introduction

Castleman's disease (giant or angiofollicular lymph node hyperplasia / angiofollicular ganglionic hyperplasia/ lymphoid hamartoma / lymphoma impostor) was first described by Benjamin Castleman in the year 1957 and was named after him.[2] Castleman disease (CD) is a rare lymph proliferative disorder. This means there is an abnormal overgrowth of cells of the lymphoid system that is similar in many ways to lymphomas. It can be localised to single lymphnode group (unicentric) or multicentric. Histological variants are hyaline vascular type, plasmacellular type, mixed type or plasmablastic type.[3] Due to rarity of diagnosis and reporting its true incidence in pediatric age group is unknown. Unicentric lesions are having excellent prognosis after surgery. Prognosis is worse in multicentric lesions especially if associated with HIV.

### 2. Case Report

We report a case of 6-years old male child who came to paediatric ward with history of right sided slowly progressing neck swelling since 2 years, sudden increase in size by last 6months. There was no history of fever or weight loss except mild fatigue. On examination firm, ovoid, non tender and mobile mass measuring  $3.5 \times 2 \times 3$  cm was situated in the right side of the neck (Figure-1). No significant lymphadenopathy in other groups of lymphnodes. ENT IJBAR (2015) 6 (11)

examination showed bulge in right tonsillar fossa and systemic examinations were normal (Figure-2). Investigations showed Hb-10.9g%, TLC-7540/ $\mu$ L, DLC-N<sub>66%</sub>L<sub>18.4%</sub>M<sub>3.3%</sub>E<sub>12%</sub>, TPC-3.16 lakhs/ $\mu$ L. Peripheral smear was normal. ESR - 37mm at the end of one hour and CRP was normal. ANA, C-ANCA, P-ANCA were negative. Fine needle aspiration cytology (FNAC) showed lymphoid cells in different stages of maturation. Mature lymphocytes and few mononuclear cells are with prominent nucleoli (suggestive of reactive hyperplasia). Computed tomography showed intensely homogeneously enhancing well defined lesion located on right cervical region without any infiltration to deeper structures. USG abdomen and X-Ray chest were done to rule out multicentric type of disease. Tests for HIV and HHV-8 were negative. It was decided to excise the mass and was meticulously dissected out in toto and sent for histopathological examination.

On gross examination specimen consists of single grey white soft tissue bit measuring  $3 \times 2 \times 2.5$ cm, external surface was glistening. Microsection studies show lymphoid follicles with atrophic germinal centre surrounded by variable sized or broad mantle zones. Interfollicular vascularity is prominent. The germinal centres are depleted of lymphocytes and predominantly consist of dendritic reticulum cells and endothelial cells. Some of the germinal centres are hyalinised. The onion skin pattern and **LOLLIPOP** appearance of the

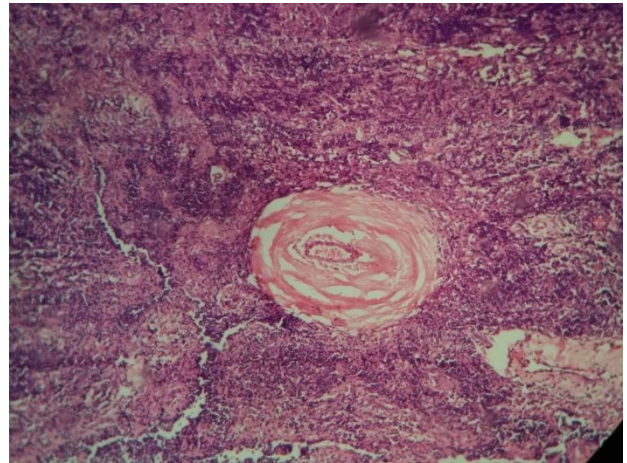
follicle is evident (Figure 3&4). It was confirmed as hyaline-vascular type of Castleman's disease. Interleukin-6 (IL-6) level estimated and was elevated. On follow up patient is asymptomatic with normal blood pictures for last two years.



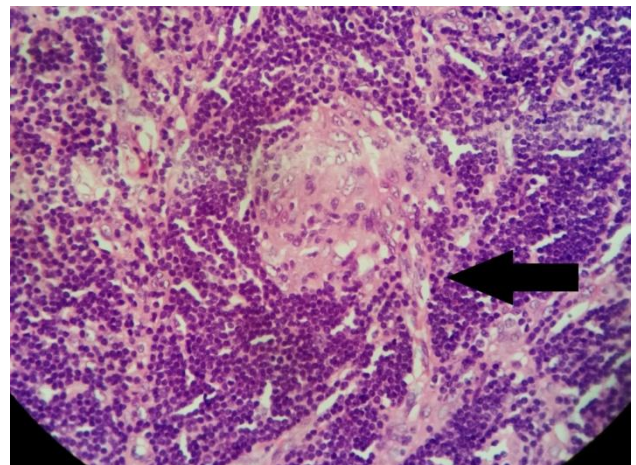
**Figure 1: Child showing persistent right sided cervical lymphadenopathy**



**Figure 2: Right tonsillar enlargement**



**Figure 3: HPE-H&E staining low power view showing lymphoid follicles with atrophic germinal centre surrounded by variable sized or broad mantle zones**



**Figure 4: Characteristic lollipop appearance**

### 3. Discussion

Castleman's disease (CD) is a rare disease of lymph nodes and related tissues. It was first described by Dr. Benjamin Castleman in the 1957.[2] The main way to classify CD is based on how much of the body it affects: Unicentric VS multicentric. Histologically, it is classified into 4 variants; a: hyaline-vascular type, b: plasma cellular type and c: mixed type or d: plasmablastic type [3]. Hyaline-vascular type is the most common variant.<sup>3</sup> This type is usually localized to mediastinum or pulmonary hilum.[4,5] This is in contrast to our patient who presented with cervical lymphadenopathy. Location of lesion has nothing to do with the prognostic significance.[6] Although the exact underlying cause of unicentric Castleman disease (UCD) is unknown, it is thought to occur sporadically in people with no family history of the condition. While Castleman's disease can occur at any age, most cases occur in adolescents or young adults. The youngest patient reported to have this disease was 6 months old. No significant sex predilection has been found, regardless of the histologic type. Clinically, localized disease tends to be seen more commonly in younger patients, while the more severe multicentric variant affects older individuals.

Several immunological mechanisms have been proposed including over production of interleukin-6 and human herpes virus type -8 infections.[3,7,8] Interestingly, HIV status may influence the constellation of signs and symptoms in MCD patients: based on epidemiologic data from the pre- and post-HIV eras, HIV-negative individuals may take years to manifest any signs or symptoms of the disease, while HIV-positive patients may rapidly develop symptoms over a period of months. The diagnosis is done by histology thereby requiring either biopsy or resection of the mass.

The treatment options for UCD are mainly surgical resection of the abnormal node. In patients where the lesion cannot be fully resected, the partially resected mass may simply be observed for progression. But for progressing masses 30 to 45 Gy external beam radiation can be considered.[8,9] For multicentric disease, chemotherapy and radiation had been the cornerstones of treatment, but have been largely supplanted by newer, more directed therapies.[10] These include a drug which targets the IL-6-producing plasma cells for destruction (rituximab) and drugs which either block the action of IL-6 (tocilizumab or Actemra) or scavenge IL-6 from the bloodstream (siltuximab or CNTO328).[13,14] Additional symptomatic and supportive therapy may include corticosteroids or autologous bone marrow transplantation (used most frequently for severe disease or disease associated with POEMS syndrome).[11,12] Tocilizumab (Actemra) can be prescribed "off label" for the treatment of Castleman's disease.

The long-term outlook (prognosis) for people with unicentric Castleman disease (UCD) is generally excellent. In many cases, the condition can be cured by surgically removing the affected lymph node. In fact, one study found that disease-free survival in people with UCD following surgery was approximately 93%. In general the prognosis is worse in people with MCD who do not receive appropriate treatment especially if HIV associated.

#### 4. Conclusion

Castleman's disease is rare in children. It is a precancerous condition of lymphoma. It should be thought as a differential diagnosis of persistent lymphadenopathy in a child after ruling out common causes like tuberculosis and malignancy. Early diagnosis and timely surgical management can check its progression to lymphoma.

#### Acknowledgements

Special thanks to Department of Paediatrics and Department of Pathology for precious works.

#### References

- [1] Zawafi F, Varshney R, Haegert DG, Daniel SJ. Castleman's disease: a rare finding in paediatric neck. *Int J Paediatr Otorhinolaryngol.* 2014; 78(2):370-2.
- [2] Castleman B, Iverson L, Menendez VP. Localized mediastinal lymph node hyperplasia. *Cancer.*1956; 9:822–30.
- [3] AR Keller, L Hochholzer, B Castleman. Hyaline Vascular & Plasma Cell types of giant L.Node hyperplasia of the mediastinum & other localisations. *Cancer.* 1972; 29:670–83.
- [4] Kraus DH, Huo J, Burt M: Surgical access to tumors of the cervicothoracic junction. *Head Neck* 1995; 17(2):131-6.
- [5] McAdams HP, Rosado-de-Christenson M, Fishback NF, Templeton PA: Castleman disease of the thorax: radiologic features with clinical and histopathologic correlation. *Radiology* 1998; 209:221-8.
- [6] Herrada J, Cabanillas F, Rice L, Manning J, Pugh W: The clinical behavior of localized and multicentric Castleman disease. *Ann Intern Med* 1998, 128(8):657-62.
- [7] Yoshizaki K, Matsuda T, Nishimoto N, Kuritani T, Taeho L, Aozasa K, Nakahata T, Kawai H, Tagoh H, Komori T, Kishimoto S, Hirano T, Kishimoto T: Pathogenic significance of interleukin-6 (IL-6/BSF-2) in Castleman's disease. *Blood* 1989; 74(4):1360.
- [8] GM Chronowski, CS Ha, RB Wilder, F Cabanillas, J Manning, JD Cox. Treatment of Unicentric and Multicentric Castleman's disease and role of radiotherapy. *Cancer.* 2001; 92:670–76.
- [9] J Herrada, F Cabanillas, L Rice. The clinical behavior of localized and multicentric Castleman disease. *Ann Intern Med.* 1998; 128:656–62.
- [10] Marti S, Pahissa A, Guardia J, Moragas A, Bacardi R: Multicentric giant follicular lymph node hyperplasia. Favorable response to radiotherapy. *Cancer* 1983; 51(5):808.
- [11] Summerfield GP, Taylor W, Bellingham AJ, Goldsmith HJ: Hyaline-vascular variant of angiofollicular lymph node hyperplasia with systemic manifestations and response to corticosteroids. *J Clin Pathol* 1983; 36(9):1005.
- [12] Ganti AK, Pipinos I, Culcea E, Armitage JO, Tarantolo S: Successful hematopoietic stem-cell transplantation in multicentric Castleman disease complicated by POEMS syndrome. *Am J Hematol* 2005, 79(3):206-10.
- [13] Teipel R, Ordemann R, Proske U, Dietrich F, Mende M, Ehninger G, Kroschinsky, Platzecker. Siltuximab for multicentric Castleman's disease –Letter. *Clinical Cancer Research.* 2015; 21(20).
- [14] Van Rhee F, Fayad L, Voorhees P, Furman R, Lonial S, Borghaei H, Sokol L, Crawford J, Cornfeld M, Qi M, Qin X, Herring J, Casper C, Kurzrock R: Siltuximab, a Novel Anti-Interleukin-6 Monoclonal Antibody for Castleman's Disease. *J Clin Oncol* 2010; 28(23): 3701-3708.