



## Case report

## Castleman disease of the parapharyngeal space: Diagnosis and management

S. Jbali<sup>c,\*</sup>, S. Zarraa<sup>a</sup>, A. Hadhri<sup>a</sup>, G.E.F. Noubbigh<sup>b</sup>, S. Yahyaoui<sup>a</sup>, C. Nasr<sup>a</sup><sup>a</sup> Radiotherapy Department, Salah Azaiez Institute of Cancer, Tunis University of Medicine, University Tunis El Manar, Tunis, Tunisia<sup>b</sup> Radiotherapy Department, Principal Military Training Hospital, Tunis University of Medicine, University Tunis El Manar, Tunis, Tunisia<sup>c</sup> Head and Neck Department, Salah Azaiez Institute of Cancer, Tunis University of Medicine, University Tunis El Manar, Tunis, Tunisia

## ARTICLE INFO

## Keywords:

Castleman's disease  
Parapharyngeal  
Case report  
Surgery  
Radiation therapy

## ABSTRACT

**Introduction:** Castleman's disease (CD) is a rare and benign disease often identified in the mediastinum with few cases in the head and neck area. Parapharyngeal Castleman's disease was rarely reported in the literature.

The aim of our work was to discuss the management of this particular location of CD. It was about a case report that has been reported in line with the SCARE 2020 criteria (Agha et al., 2020 [1]).

**Case presentation:** We report the case of a 53-year-old female patient who presented a left parotid tumefaction. Radiological investigations showed a parapharyngeal mass that was surgically removed. Definitive pathologic report concluded to Castleman's disease. She presented, one year later, a retropharyngeal recurrence, which was treated by radiotherapy with good response.

**Clinical discussion and conclusion:** Castleman's disease located in parapharyngeal spaces is an entity that was rarely reported in the literature. Surgical excision is the golden standard treatment. Radiotherapy is also an effective treatment that can be offered for unresectable cases or recurrences of Castleman's disease.

## 1. Introduction

Castleman's disease (CD) is a benign lymphoid disorder described in 1954. It is a rare disease with two principal histological subtypes: hyalino-vascular and plasma cell variants and two clinico-radiological entities: unicentric and multicentric [2]. The head and neck is the second most commonly affected region of the body in CD after the mediastinum [3]. Parapharyngeal location of this disease is extremely rare. We report the case of 54-year-old woman who presented with parapharyngeal CD treated first with surgery then with radiation therapy. This clinical case has been reported in line with the SCARE 2020 criteria (Agha et al., 2020 [1]).

## 2. Case report

A 53-year-old woman presented to the department of otorhinolaryngology for a latero-cervical tumefaction in 2018. She had no specific medical history and was not taking any medication. Physical examination revealed a left parotid tumefaction. Computed tomography (CT) scan of the neck showed an expansive process of the left parapharyngeal space. After informed consent, she was operated by a senior ENT surgeon using a cervico-parotid approach. The postoperative period was

uneventful. Histopathology of the specimen revealed germinal centers with dense plasma cell infiltration and atretic follicles of the mantle zone lymphocytes as seen in Castleman disease.

The diagnosis of Castleman's disease was retained and an assessment was undertaken in search of other localizations of this disease. Clinical examination was normal: there were no general signs such as fever, weight loss or superficial lymphadenitis. Plasma protein electrophoresis did not find a monoclonal peak. The diagnosis of POEMS syndrome was, thus, improbable. Biological assessment did not find any elements in favor of a connective tissue disease. Anti-nuclear antibodies (ANA) and anti-DNA were negative. The whole body CT scan requested as part of this assessment found a 3 cm right renal mass consistent with an angiomyolipoma.

One year later, a cervical Magnetic Resonance Imaging (MRI) showed recurrence of the previously described mass with extension to the left retropharyngeal space measuring 53 \* 31 \* 17 mm (Fig. 1). Then the patient was referred for radiation therapy. After consultation with the staff of radiation oncologists, she received 40Gy of external beam radiation therapy (EBRT) with good tolerance. EBRT fractionation was classic at a rate of 2 Gy per day 5 days per week. A control MRI was done 3 months after the end of radiotherapy. It showed regression of the tumor with persistence of a residue measuring 38 \* 23 \* 13 mm (Fig. 1).

\* Corresponding author at: Head and Neck Department, Salah Azaiez Institute of Cancer, Boulevard du 9 Avril 1938 Bab Saâdoun, 1007 Tunis, Tunisia.

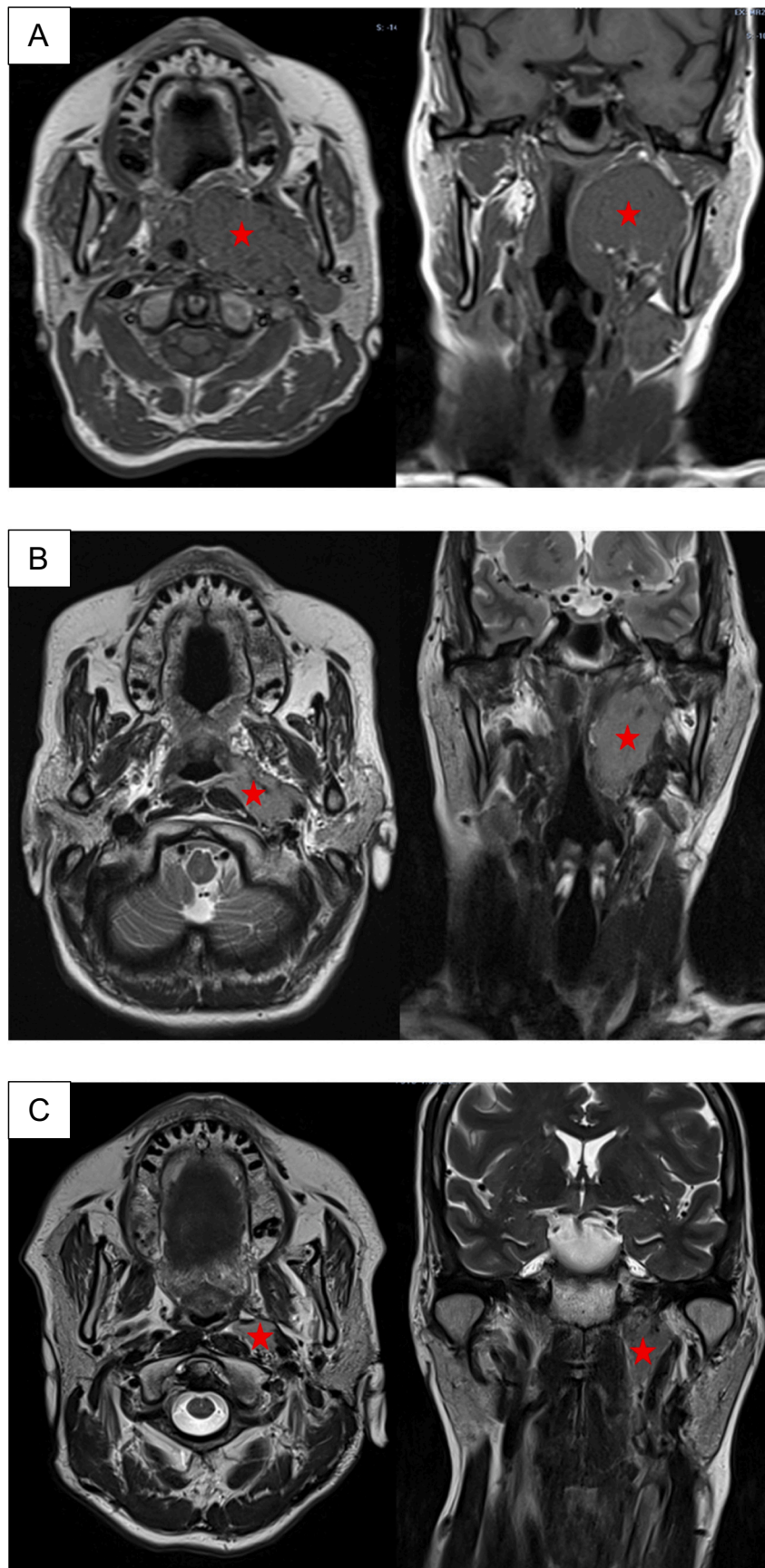
E-mail address: [jbalisouheil@gmail.com](mailto:jbalisouheil@gmail.com) (S. Jbali).

<https://doi.org/10.1016/j.ijscr.2022.107599>

Received 23 July 2022; Received in revised form 1 September 2022; Accepted 1 September 2022

Available online 5 September 2022

2210-2612/© 2022 The Authors. Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).



**Fig. 1.** Magnetic resonance imaging (MRI): axial and coronal sections weighted T1 (A) and T2 (B and C): Evolution of the parapharyngeal tumor before surgery (A), after surgery and before radiation therapy (B) and three months after radiation therapy (C).

Clinically the patient presented no local recurrence signs. The present therapeutic history was marked by the patient's complete compliance with the explorations and the treatment.

### 3. Discussion

Castleman disease (CD) is a rare benign disorder characterized by a hyperplasia of lymphoid tissues that was defined by Castleman in 1956 [2,4].

The etiology of Castleman's Disease remains unknown even if many studies have linked it to other disorders such as HIV and HHV-8 infection, amyloidosis and renal insufficiency [5,6].

Two main histological variants and an intermediate variant of CD were defined [2,7]. The most common is the hyalino-vascular type accounting for >90 % of all cases. The second variant is the plasma cell type (PC) [2,7].

McCarty and al have classified Castleman's disease into two clinical entities: unicentric and multicentric forms [8]. Unicentric CD (UCD) associate a single lymph node or a single sector involvement, whereas multicentric CD (MCD) presents with multiple adenopathies and frequently multi-organ involvement and is associated with systemic symptoms [9].

Castleman's disease occurs in the mediastinum in approximately 70 % of all cases. It could also be seen in other sites like axilla, retroperitoneum, mesentery and pelvis [10]. Few cases arise in the head and neck region [10–14].

In our reported case, the castleman's disease was located in left retro and para-pharyngeal spaces. Para-pharyngeal spaces are, in fact, a complex anatomical area [15,16] and tumors originating in this area represent 0.5 % of all head and neck tumors [17].

Clinically these tumors are often asymptomatic [18].

Imaging, including CT scan and/or MRI is fundamental in the diagnosis of para-pharyngeal space tumors. Confirmation and typing remain histological [11,17].

Considering CD, magnetic resonance imaging usually reveals homogeneous masses isointense to muscle on T1 sequences and intermediate or hyper-intense on T2 sequences [10,19].

In order to verify the unicentric nature of CD, a minimal assessment is recommended (Table 1). This assessment associates complete physical examination, total body radiological investigation and biological assessment including virological status, inflammatory response and autoimmunity assessment. Positive Immunostaining for HHV-8 was reported to be associated with MCD but it was observed in rare cases of UCD.

Some diseases may present with a solitary enlarged lymph node with CD-like histopathology. These diseases include lymphomas, thymomas, lympho-proliferations with regressive germinal centers, such as angio-immunoblastic T-cell lymphoma, autoimmune diseases and primary or acquired immune-deficiencies such as advanced phases of HIV-related lymphadenopathy. Various investigations requested help to exclude these diagnoses.

According to PubMed search engine, only ten publications of Castleman disease located in parapharyngeal spaces were reported between 1999 and 2022. These publications were mainly case reports. We used these observations and other literature data when reviewing the treatment of Castleman disease.

Indeed, surgical excision with minimal morbidity of unicentric CD including that located in para-pharyngeal space is obviously the treatment of choice when possible [18,20]. Surgical approach should take into consideration exact tumor localization, its size and relation to the carotid artery and jugular vein [18,20,21].

Radiotherapy is also an effective treatment. It can be proposed for unresectable or recurrent cases of unicentric CD [12,18].

Tomita et al. [22] reported a case of cervical Castleman disease treated with Intensity Modulated Radiation Therapy (IMRT). The cervical lymphadenopathy regressed after a dose of 44 Gy radiation

therapy. This latter was delivered in 22 fractions. Four years later, there was no disease progression.

In a study of Chronowski and al., four patients had exclusive radiotherapy with two fractionation schemes: 40 Gy (2 Gy/Fraction) and 39.6 Gy (1.8 Gy/Fraction). Three of these patients had complete radiologic response [23].

A Turkish retrospective study, conducted between 1980 and 2012, examined the efficiency of radiation therapy in the treatment of unresectable and recurrent CD. Six unicentric locations underwent complete surgical excision followed by radiotherapy for recurrence in the follow-up period. These patients received 30 Gy of EBRT. Only one patient in the study presented an unresectable disease and therefore received 45 Gy external radiation therapy. The authors concluded that radiotherapy is an efficient therapeutic modality for recurrent or unresectable unicentric CD. Three-year overall survival (OS) was 83 %, and three-year disease free survival (DFS) was 91 % [24].

### 4. Conclusion

To date, few cases of CD localized in the parapharyngeal space have been reported. Most patients were treated with surgery with minimal complications. Our patient was first treated by surgery then by radiotherapy for local recurrence. The last X-ray check showed a regression of the disease and clinically there were no signs of recurrence.

In short, the clinical case that we report, although rare given the parapharyngeal localization of the disease, confirms the literature data concerning the priority of surgery and the effectiveness of radiotherapy for unresectable cases or recurrences of unicentric CD.

### Provenance and peer review

Not commissioned, externally peer-reviewed.

### Funding

The authors declare that there are not any sources of funding for the present research.

### Ethical approval

Our work is a case report. It did not reveal any information that could help identifying the patient. Otherwise, Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

### Consent

There are no identifying details of the patient in our case report.

### Author contribution

Writing the paper: Jbali Souheil, Hadhri Asma, Zarraa Semia, Nouhigh GEF.

Data collection: Yahyaoui Safia.

Manuscript revision: Nasr Chiraz.

### Registration of research studies

Not applicable.

### Guarantor

Dr. Jbali Souheil.

**Table 1**  
Recommended check-up when investigating Castleman disease.

Assessment type	Details
Biopsy and Histopathology	HV/PC or mixed CD. Staining for EBER, LANA-1, and lymphoma or plasmacytoma markers if suspected.
Complete physical examination	IgH gene rearrangement, TCR clonality. Night sweats, fever >38 °C, weight loss, fatigue Features such as fluid accumulation (peripheral edema, pleural effusion, ascites).
Imaging	FDG CT-PET or CT of the neck, chest, abdomen and pelvis.
Virological status	HIV serology, HHV-8 qPCR (peripheral blood).
Inflammatory response and auto-immunity assessment	CBC, renal function, liver function, CRP, ESR, fibrinogen, immunoglobulins and free light chains, albumin. ANA, rheumatoid factor, other markers when suspecting connective tissue diseases.

(HV: hyalino-vascular; PC: plasma cell; CD: Castleman disease; EBER: EBV-encoded RNA; LANA: latency-associated nuclear antigen; Ig H: Immunoglobulin heavy chain; TCR: T cell receptor; FDG PET: Fluorodeoxyglucose (FDG)-positron emission tomography; CT: computerized tomography (CT) scan; HIV: Human immunodeficiency virus; HHV: Human Herpes Virus; PCR: Polymerase Chain Reaction; CBC: complete blood count; ESR: Erythrocyte Sedimentation Rate; ANA: antinuclear antibodies).

### Declaration of competing interest

The authors declare that there are not conflicts of interest.

### References

- [1] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, A. Kerwan, The SCARE 2020 guideline: updating consensus Surgical CAse REport (SCARE) guidelines, *Int. J. Surg.* 84 (2020) 226–230.
- [2] R. Madan, J.H. Chen, B. Trotman-Dickenson, F. Jacobson, A. Hunsaker, The spectrum of Castleman's disease: mimics, radiologic pathologic correlation and role of imaging in patient management, *Eur. J. Radiol.* 81 (1) (2012) 123–131.
- [3] D.L. Choi, K. Brannock, A.L. Tang, Castleman disease presenting as a parapharyngeal mass: a case report and review of the literature, *Clin. Med. Insights Case Rep.* 12 (2019), 1179547619853799.
- [4] I.A. de Vries, M.M. van Acht, T. Demeyere, M.L. Lybeert, J.P. de Zoete, G. A. Nieuwenhuijzen, Neoadjuvant radiotherapy of primary irresectable unicentric Castleman's disease: a case report and review of the literature, *Radiat. Oncol.* 5 (2010) 7.
- [5] W.B. Bowne, J.J. Lewis, D.A. Filippa, R. Niesvizky, A.D. Brooks, M.E. Burt, et al., The management of unicentric and multicentric Castleman's disease: a report of 16 cases and a review of the literature, *Cancer* 85 (3) (1999) 706–717.
- [6] C. Casper, The aetiology and management of Castleman disease at 50 years: translating pathophysiology to patient care, *Br. J. Haematol.* 129 (1) (2005) 3–17.
- [7] A.R. Keller, L. Hochholzer, B. Castleman, Hyaline-vascular and plasma-cell types of giant lymph node hyperplasia of the mediastinum and other locations, *Cancer* 29 (3) (1972) 670–683.
- [8] M.J. McCarty, S.J. Vukelja, P.M. Banks, R.B. Weiss, Angiofollicular lymph node hyperplasia (Castleman's disease), *Cancer Treat. Rev.* 21 (4) (1995) 291–310.
- [9] C.Y. Lin, Y.L. Chang, Castleman's disease in the head and neck region: meta-analysis of reported cases in Taiwan and literature review, *J. Formos. Med. Assoc.* 109 (12) (2010) 913–920.
- [10] J.C. Chaloupka, M. Castillo, P. Hudgins, Castleman disease in the neck: atypical appearance on CT, *AJR Am. J. Roentgenol.* 154 (5) (1990) 1051–1052.
- [11] J.B. Clain, S. Scherl, W.E. Karle, A. Khorsandi, V. Ghali, B. Wang, et al., Castleman disease in the parapharyngeal space: a case report and review of the literature, *Head Neck Pathol.* 7 (4) (2013) 389–392.
- [12] O. Karakoc, E. Kilic, T. Ilica, F. Tosun, Y. Hidir, Castleman disease as a giant parapharyngeal mass presenting with dysphagia, *J. Craniofac. Surg.* 22 (6) (2011) e54–e57.
- [13] F. Ottaviani, J. Galli, S. Di Girolamo, G. Almadori, Castleman's disease restricted to the parapharyngeal space, *J. Otolaryngol.* 28 (2) (1999) 95–98.
- [14] O.B. Ozgursoy, M. Demirtas, I. Kuzu, T. Akturk, Castleman disease in the parapharyngeal space: unusual presentation and differential diagnostic imaging features of the disease, *J. Otolaryngol. Head Neck Surg.* 38 (5) (2009) E118–E120.
- [15] G. Grilli, V. Suarez, M.G. Muñoz, M. Costales, J.L. Llorente, Parapharyngeal space primary tumours, *Acta Otorrinolaringol. (Engl. Ed.)* 68 (3) (2017) 138–144.
- [16] V. Suárez-Fente, J.L. Llorente-Pendás, J. Gómez-Martínez, L.A. García-González, F. López-Alvarez, C. Suárez-Nieto, Primary tumours of the parapharyngeal space. Our experience in 51 patients, *Acta Otorrinolaringol. Esp.* 60 (1) (2009) 19–24.
- [17] M.V. Dimitrijevic, S.D. Jesic, A.A. Mikic, N.A. Arsovic, N.R. Tomanovic, Parapharyngeal space tumors: 61 case reviews, *Int. J. Oral Maxillofac. Surg.* 39 (10) (2010) 983–989.
- [18] F. Bozza, M.G. Vigili, P. Ruscito, A. Marzetti, F. Marzetti, Surgical management of parapharyngeal space tumours: results of 10-year follow-up, *Acta Otorhinolaryngol. Ital.* 29 (1) (2009) 10–15.
- [19] X.H. Jiang, H.M. Song, Q.Y. Liu, Y. Cao, G.H. Li, W.D. Zhang, Castleman disease of the neck: CT and MR imaging findings, *Eur. J. Radiol.* 83 (11) (2014) 2041–2050.
- [20] X. Shi, L. Tao, X. Li, H. Wu, W. Huang, X. Chen, et al., Surgical management of primary parapharyngeal space tumors: a 10-year review, *Acta Otolaryngol.* 137 (6) (2017) 656–661.
- [21] S. Jbali, A. Khaldi, S. Touati, S. Gritli, Surgical approaches to parapharyngeal space tumors: an example and review of the literature, *Case Rep. Surg.* 2021 (2021) 3536145.
- [22] N. Tomita, T. Kodaira, T. Tomoda, K. Nakajima, T. Murao, K. Kitamura, A case of cervical multicentric Castleman disease treated with intensity-modulated radiation therapy using helical tomotherapy, *Jpn. J. Radiol.* 30 (4) (2012) 349–353.
- [23] G.M. Chronowski, C.S. Ha, R.B. Wilder, F. Cabanillas, J. Manning, J.D. Cox, Treatment of unicentric and multicentric Castleman disease and the role of radiotherapy, *Cancer* 92 (3) (2001) 670–676.
- [24] B. Uysal, S. Demiral, H. Gamsiz, F. Dincoglan, O. Sager, M. Beyzadeoglu, Castleman's disease and radiotherapy: a single center experience, *J. Cancer Res. Ther.* 11 (1) (2015) 170–173.