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# Castleman Disease in the Pediatric Neck: Case Report and Literature Review

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## ABSTRACT

**Objective:** To investigate the common features of cervical pediatric Castleman disease (CD).

**Study Design:** Case report and literature review of pediatric patients with cervical CD.

**Methods:** Online medical journal databases were searched for patients aged 18 years or younger. Eighteen published papers were found, comprising 29 cases. One case from our institution was also included for a total of 30 patients.

**Results:** An asymptomatic mass in level V was the most common presentation. No gender differences were noted. Multiple forms of imaging were pursued, and no particular modality showed signs specific for CD. All cases were treated with complete surgical excision and diagnosed as hyaline-vascular type on histology, except for one case, where histologic type was not reported. No reports of multicentric disease, plasma cell, or mixed histology were found. No recurrences were reported.

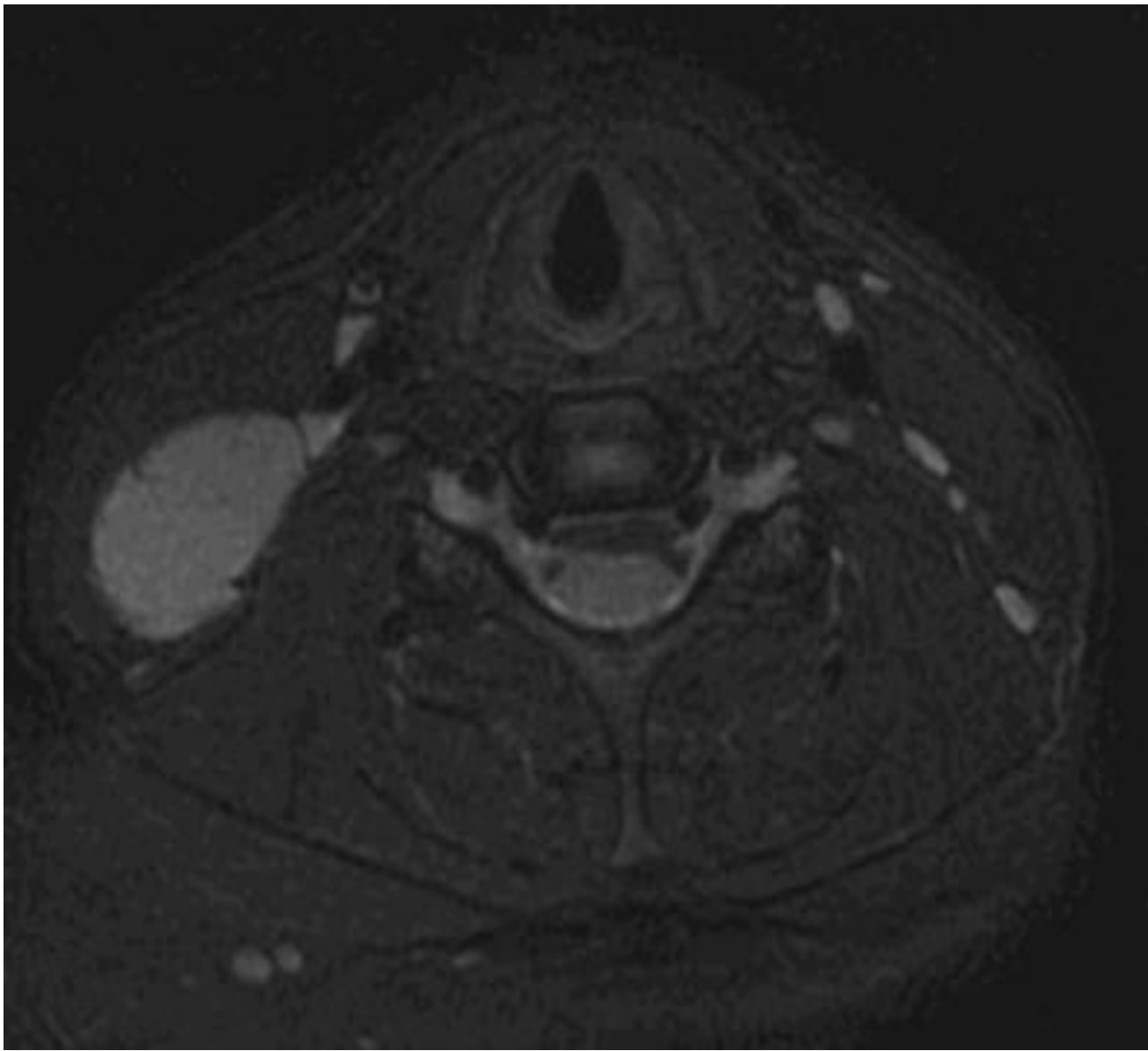
**Conclusions:** This poster provides the largest known literature review of pediatric patients with cervical CD. In our analysis, there is a higher propensity for level V than previously reported in small studies. While CD is rare, it should be considered on the differential for a pediatric neck mass, particularly when presenting with an asymptomatic posterior neck mass and equivocal work-up. Fortunately, our study suggests that, if diagnosed as CD, the most likely diagnosis is hyaline-vascular type for which the long-term prognosis is good. Surgical excision is both diagnostic and therapeutic.

## INTRODUCTION

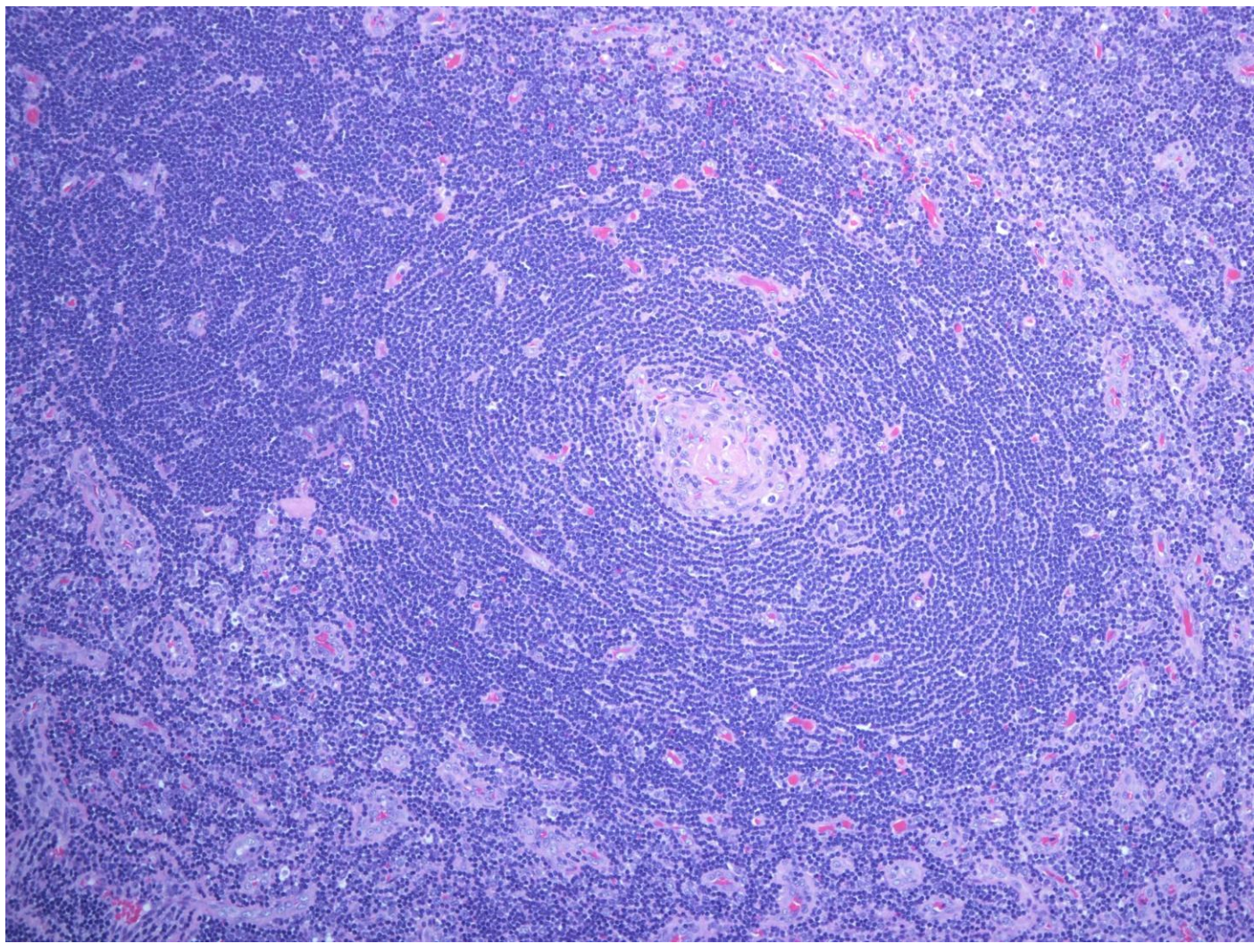
Castleman disease (CD) was first described by Benjamin Castleman in 1954.<sup>1,2</sup> Since that time, CD has become better known in literature as a lymphoproliferative disorder of unknown etiology.<sup>3-5</sup> Castleman disease can occur anywhere throughout the lymphatic system. The most common sites include the mediastinum (60%), neck (14%), abdomen (11%), and axilla (4%).<sup>6-11</sup> While the underlying etiology is unknown, several hypotheses have been suggested. One theory postulates that the disease represents a reaction to a chronic viral antigenic stimulation. Some studies cite a role for interleukin-6 (IL-6).<sup>8</sup>

Castleman disease is rare in the pediatric population, although exact prevalence rates are not known.<sup>8,12</sup> In children, CD has a more benign prognosis. It also has a different propensity for certain anatomic sites compared to adults, most commonly affecting the chest (33%), abdomen (30%), neck (23%), and axilla (7%).<sup>12,13</sup> In contrast, the most commonly affected sites in adults are the chest (60%), neck (14%), abdomen (11%), and axilla (4%).<sup>7-11</sup>

To better understand the clinical characteristics of this rare entity in children, in this study, we present a case study followed by an extensive literature review of pediatric cervical CD.



**Figure 1.** Neck magnetic resonance imaging of right-neck mass. Axial T2-weighted cut shows a hyperintense mass.



**Figure 2.** Castleman disease showing lymphoid follicle with onion-skinning of the mantle zone lymphocytes; 200x.

## CASE REPORT

A 13-year-old female presented to our institution with a tender right-neck mass that appeared suddenly. It had been present for six weeks, during which time the mass had not changed in size but did cause mild pain with head movement to the right. She had no significant previous medical history. Exam revealed a 4 x 6-cm mass deep to the lower half of the sternocleidomastoid muscle on the right. It was non-tender to palpation with no overlying skin changes. Routine laboratory tests were within normal limits. Titters for toxoplasma, cytomegalovirus (CMV), and Bartonella were negative. Epstein–Barr virus (EBV) IgG titers were elevated. Chest radiograph was within normal limits. Magnetic resonance imaging (MRI) revealed a well-defined, right-sided level III mass measuring 1.8 x 3.0 x 4.2 cm. It was bright on T2- and intermediately to slightly brighter than muscle on T1-weighted imaging (**Figure 1**). Several small vascular channels were apparent on the lesion by MRI. Several small lymph nodes along the inferior margin of the lesion extending down to the thoracic inlet were also noted. An additional 12 x 6 x 9-mm lesion was noted in the paraspinal musculature. A decision was made not to pursue this lesion given its small size and location, which would be unusual for CD. Fine needle aspiration (FNA) revealed atypical lymphoid proliferation. After discussion with the patient and family regarding the options, she was taken to the operating room, where a complete surgical excision of the mass was performed. Histologically, the nodal mantle zone showed concentric rings with an onion-skin appearance. Piercing blood vessels were frequently seen in these follicles ("lollipop" feature) (**Figure 2**). The interfollicular areas showed prominent hyalinized venules. Based on these findings, the postoperative histopathological diagnosis was HV-CD. At three months' follow-up, she was doing well with no signs of recurrence.

## MATERIALS AND METHODS

Online medical journal databases were used for data collection. “Castleman’s disease” in combination with “neck”, “cervical,” and “pediatric”, were keywords used for searching the PubMed database. Only patients aged 18 and younger were included for analysis. After excluding reports on CD in other locations (ie, non-neck sites), 18 published papers were found, comprising 29 total reported cases of pediatric cervical CD (**Table 1**). The earliest case report published was in 1991 and the latest in 2012.<sup>5,19</sup> In addition, one patient was diagnosed and treated at our institution. This patient was also included and brought our final patient count to 30 cases. This study was IRB exempt. All diagnoses of CD were based on histopathology.

**Table 1.** Castleman data

Reference	Year	Age	Gender	Location/Level	Signs/symptoms	Duration (mo)	Size (cm)	CT Neck	MRI Neck	US Neck	CXR	CT C/A/P	Other Imaging	FNA?	Abnormal Labs	DDx	Treatment	Path	F/U (mo)	Recurrence?	
Lee <sup>1</sup>	2010	9	M	L level V	parietal neck mass		6	1.5 x 2.0	well-defined neck mass	x	x	x	CT C/A- neg	x	x	x	excision	CD, HV-type	36	none	
Pardoll <sup>2</sup>	1991	11	M	L level V ("post-neck")	enlarging mass x 6mo	132	3.0	x	x	x	nl	x	x	x	x	x	excision	CD, HV-type	x	x	
Glezer <sup>3</sup>	1995	11	F	R level V ("post-neck")	slow growing mass	3	3.2 x 2.5 x 1.8	x	isointense w/ muscle, central hypodense, no enhance	appearance of large LN	x	MRI C/A- neg	x	x	none	x	excision	CD, HV-type	x	x	
Kadiri <sup>4</sup>	1985	17	M	R neck	nascent growth, no pain, dysphagia, dysphasia, hoarseness, fatigue, wt loss	5	3.6 x 3.6	homogeneously enhancing, displaced vascular bundle medially	x	x	x	x	Angio-mass w/ vascular blush	x	x	x	excision	CD, HV-type	x	x	
Chen <sup>5</sup> / Saklany <sup>17</sup>	1999	5	M	R level V ("post-neck") L cervical	neck swelling slow growing mass	12 24	4.0 x 2.0 x 2.5 4.0 x 2.5 x 2.5	irregular borders	x	x	x	x	x	x	x	x	excision	CD, HV-type	7	none	
Patel <sup>6</sup>	1998	12.5	M	L level II ("ant tr, level thyroid cart")	asymptomatic	x	5.0 x 2.5 x 1.0	x	intermediate T1 signal, elevated T2 signal	x	x	x	x	x	x	x	excision	CD, HV-type	x	x	
Bord <sup>7</sup>	2003	13	F	Level I (midline submental)	unsightly neck mass	24	2.0	x	intermediate T1 signal, elevated T2 signal	central flow	x	x	x	x	x	x	excision	CD, HV-type	x	x	
Tueltch <sup>8</sup>	1997	14	M	R lateral neck	asymptomatic	24	4.2 x 3.0 x 1.9	x	enhancing mass, Homogeneous, dense	x	x	x	CT C/A- neg	x	none	x	excision	CD, HV-type	8	none	
Tueltch <sup>9</sup>	1997	7	M	L cervical	increasing mass size	2	5.0 x 4.5 x 2.0	x	homogeneous, isointense T1 signal, hypointense T2 signal, moderate enhancement	x	nl	x	BM aspiration neg	x	none	x	excision	CD, HV-type	5	none	
Zhong <sup>10</sup>	2010	14	F	R neck	none	12	2.0 x 2.0	x	x	x	x	x	x	x	x	none	x	excision	CD, HV-type	34	none
Zhong <sup>11</sup>	2010	13	F	R neck	none	3	2.0 x 3.0	x	uniform signal T1, nonuniform signal T2	oval shadow w/ clear boundary, uniform low-level echo, no vasc	x	x	x	x	none	x	excision	CD, HV-type	60	none	
Souza <sup>12</sup>	2008	12	F	L Level III	none	6	3.4 x 0.9 (max, 4 LN in total)	no description	x	performed no characteristics	x	CT C/A- neg	x	x	unspecific reactive lymphoid hyperplasia	pos- IgG2, RAI-65, CMV hypochromic monocytes	lymphoma, reactive lymphadenitis	excision	CD, HV-type	36	none
Souza <sup>13</sup>	2008	16	F	R Level III	slow growing mass	96	10.0	x	x	performed no characteristics	x	x	x	x	unspecific lymphoid hyperplasia from previous otitis	high ESR, rheumatoid factor pos	lymphoma, reactive lymphadenitis	excision	CD, HV-type	34	none
Souza <sup>14</sup>	2008	11	F	R neck	increasing mass size	5	3.6	x	performed no characteristics	x	x	x	x	x	performed no characteristics	performed no characteristics	excision	CD, HV-type	25	none	
Chen <sup>15</sup>	2012	13	F	L level II	x	24	4.0 x 4.0	performed no characteristics	x	x	x	x	x	x	x	x	excision	CD, HV-type	62	x	
Chen <sup>16</sup>	2012	13	M	R level II	x	12	4.0 x 3.0	performed no characteristics	x	x	x	x	x	x	x	x	excision	CD, HV-type	109	x	
Chen <sup>17</sup>	2012	13	F	L level II	x	12	3.5 x 2.5	performed no characteristics	x	x	x	x	x	x	x	x	excision	CD, HV-type	83	x	
Chen <sup>18</sup>	2012	13	M	L level II	x	12	2.5 x 2.5	performed no characteristics	x	x	x	x	x	x	x	x	excision	CD, HV-type	16	x	
Chen <sup>19</sup>	2008	12	F	L level I	asymptomatic	6	5.0 x 4.0 x 2.5	x	x	x	x	x	x	x	x	x	excision	CD, HV-type	x	none	
Zhong <sup>20</sup>	2004	6	F	R neck	asymptomatic mass	2	2.5 x 2.0 x 2.5	x	homogeneous mass	x	nl	x	MRA	x	none	x	excision	CD, HV-type	6	none	
Song <sup>21</sup>	2006	7	M	Level IV	x	x	2.0 x 1.0	isointense to soft tissue, well circumscribed	x	x	x	x	x	x	2 Hcortisone (don't say what pos got NA)	x	excision	CD, HV-type	10	none	
Song <sup>22</sup>	2006	11	M	Level IV	x	x	2.0 x 1.0	isointense to soft tissue, well circumscribed	x	x	x	x	x	x	2 Hcortisone (don't say what pos got NA)	none	x	excision	CD, HV-type	11	none
Song <sup>23</sup>	2006	17	F	Level IV	x	x	3.0 x 3.0	isointense to soft tissue, well circumscribed	x	x	x	x	x	x	2 Hcortisone (don't say what pos got NA)	x	excision	CD, HV-type	13	none	
Lee <sup>24</sup>	2010	16	F	Level III	asymptomatic	2	4.2 x 2.5 x 2.0	x	x	x	x	x	x	x	x	x	excision	CD, HV-type	x	none	
Lee <sup>25</sup>	2010	9	M	Level V	asymptomatic	6	2.5 x 2.0	x	x	x	x	x	x	x	x	x	excision	CD, HV-type	x	none	
Rao <sup>26</sup>	2008	5	M	L Level V	parietal neck mass	11	1.5 x 1.5	x	x	performed no characteristics	nl	x	abd us	x	none	reactive lymphadenopathy	excision	CD, type not mentioned	6	none	
Chen <sup>27</sup>	2007	9	F	L neck	x	24	x	x	x	x	x	x	x	x	x	x	excision	CD, HV-type	39	none	
Yang <sup>28</sup>	2003	12	M	L level III	non-tender, mobile mass	3	4.0	oval enhancing nodule, low-attenuation satellite band in the center of mass	x	x	x	x	x	x	x	x	excision	CD, HV-type	x	x	
Reinhardt <sup>29</sup> (not yet published)	2012	13	F	R Level III	parietal neck mass	4	1.8 x 3.0 x 4.2	x	bright T2, w/ a slightly brighter to muscle on T1, slight uniform enhancement	hypovasc	nl	x	x	x	atypical lymphoid proliferation	high IgG, EBV	lymphoma, Borna, follicular, anaplastic	excision	CD, HV-type	6	none

x, unknown or not reported; \*, unknown size; CD HV, Castleman disease hyaline-vascular type; abd, abdomen; u/s, ultrasound; CXR, chest x-ray; CT, computed tomography; MRI, magnetic resonance imaging; f/u, follow-up; C/A/P, CT chest/abdomen/pelvis; FNA, fine needle aspiration; DDx, differential diagnosis; mo, months

## DISCUSSION

- In adults, the most common locations for CD include the chest (60%), neck (14%), abdomen (11%), and axilla (4%); in children, the chest (33%) remains the most common site of disease, followed by the abdomen (30%), neck (23%) and axilla (7%).<sup>6-13</sup> Data are currently inconclusive as to the most common neck level for pediatric CD. In our literature analysis, level V was the most common location, representing 25% of lesions.
- All of the evaluated children had unicentric masses. While no multicentric disease was found, it is important to note that only 17% (5 of 30) of children in this literature review received full body work-ups to rule out this possibility. Therefore, it is difficult to make this conclusion definitively.
- Radiographic imaging is non-specific.<sup>4</sup>
- CT was the most common modality used for neck mass work-up in this analysis (47%); however, the results argue that CT is no more specific for diagnosing CD than any other modality. As such, it is reasonable to conclude that while CD should remain on the differential diagnosis for any pediatric neck mass, the imaging modality of choice should be whichever modality will evaluate for the etiology highest on the differential diagnosis for an individual patient. Additionally, since most of these patients will proceed to surgery, pursuing CT or MRI may serve a dual purpose of both attempted diagnosis and preoperative planning. Imaging to search for multicentric disease should be based on the patient's symptoms and on clinical suspicion.
- Definitive treatment of unicentric CD involves surgical excision, with excellent prognosis. Lin et al reported no recurrence after 109 months of follow-up in one patient, which represents the longest follow-up of pediatric neck CD to our knowledge.<sup>17</sup> Another study showed a 100% five-year control rate after surgical excision of an isolated cervical mass.<sup>12</sup> Our analysis supports this data with no recurrences seen during a mean follow-up of 30 months.

## CONCLUSIONS

Cervical pediatric CD is rare. It most commonly presents as an asymptomatic or slowly enlarging level V mass. Imaging characteristics are often non-specific and do not aid in the diagnosis. Imaging is important in excluding other diagnoses and to allow for preoperative planning. No specific lab abnormality is consistently seen in these patients, nor is FNA diagnostic. Excision is ultimately diagnostic and therapeutic, and when presenting in the pediatric neck, the diagnosis is likely HV-CD, which holds a favorable prognosis.

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