A sarcomatoid malignancy originating in the right cervical lymph nodes with atypical pathological characteristics: a case report of an incidental finding

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Background: Primary malignancies of the cervical lymph nodes with special pathological characteristics are relatively uncommon in clinical settings, and there have been few reports on these tumors. The precise basis for their pathogenesis is poorly understood, and their diagnosis can be challenging. In addition, no clinically validated treatments have been established to date for affected patients.

Case Description: Here, we describe a case of a 65-year-old male patient who exhibited the enlargement of several lateral and supraclavicular lymph nodes on the right side of his neck that presented as a large mass associated with a high fever and benign leukocytosis. He did not exhibit any relevant prior history. Radiological assessment revealed that this lesion was the primary tumor and that it has since spread to the liver. Histological assessment was unable to definitively classify the pathological characteristics of this tumor. Without any relevant morphological findings, immunohistochemical outcomes were not sufficiently specific to clarify the origin of these cells. When distinguishing it from similar sarcomas of the lymphohematopoietic system, it was found to not be typical of a histiocytic or dendritic cell tumor. Treatment to this patient was performed following multidisciplinary consultation and consisted of one course of a cyclophosphamide plus doxorubicin, vincristine, and dexamethasone regimen and two courses of the cyclophosphamide plus pirarubicin, vincristine, and dexamethasone regimen. However, the tumor exhibited minimal response to such treatment. While radiotherapy was proposed, the patient lacked confidence in the approach and declined treatment. He eventually developed severe tumor-associated complications. In the discussion section of this report, we detail and analyze the pathogenesis, diagnosis, and referential treatments of this rare malignancy.

Conclusions: This is the first report describing such a malignancy, and we hope that the publication of these findings can lead to the recognition of this tumor while supporting efforts to acquire greater experience in the diagnosis and treatment of affected patients.

Keywords: Malignant mass; cervical lymph nodes; atypical pathological type; case report

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Introduction

This report describes a malignant tumor with atypical pathology findings such that it was unable to be definitively identified despite multiple morphological and immunohistochemical staining efforts, underscoring the need for further differentiation from similar tumors to aid in its final recognition. While metastatic masses in one or more cervical lymph nodes are relatively common, and primary malignant neoplasms of multiple lymph nodes are generally identified to be lymphomas, primary cervical lymph node malignancies that are non-lymphomatous and that are not concealed metastases or ectopic tumors are very rare (1-16) (*Table 1*). Malignant masses that present with challenging pathology findings represent a clinical challenge, as further tumor classification can be very difficult. The etiology of such masses remains unknown, and final diagnoses are largely dependent on evidence derived from clinical analyses, with histologic examinations being particularly important for efforts to make comprehensive judgments. Treatment of affected patients is difficult and often requires the expertise and experience of many clinicians through multidisciplinary consultation, with the efficacy of suggested treatments being somewhat uncertain. In this report, we describe the case of one such malignant mass involving the lateral and supraclavicular lymph nodes in the right side of the neck of a 65-year-old man. We present this case in accordance with the CARE reporting checklist (available at https://acr.amegroups.com/article/view/10.21037/acr-23-147/rc).

Highlight box

Key findings

- The finding of a sarcomatoid malignancy of right cervical lymph nodes with unique pathological characteristics was an accidental event.

What is known and what is new?

- We have known that metastatic masses in one or more cervical lymph nodes are relatively common, and primary malignant neoplasms of multiple lymph nodes are generally identified to be lymphomas, compared to the very rare cases of primary cervical lymph node malignancies that are non-lymphomatous and that are not concealed metastases or ectopic tumors.
- The tumor in this report is atypical, which has not been recorded. When encountering a mass with unusual characteristics, clinicians often come to a conclusion following reliable pathological assessments and strict differential diagnosis. Our report is the case, and the course of the diagnosis is remarkable.

What is the implication, and what should change now?

- This case provides us reference for diagnosing same or similar masses. No matter how difficult to identify that lesion, those pathological assessments are always the most important.
- It also suggests us that to accumulate the information on successful treatment experiences and meaningful clinical data should be significant in the future for optimizing the treatment of these rare tumors.

Case presentation

A 65-year-old male farmer of Han Chinese ethnicity detected a painless mass approximately the size of an egg on the right side of his neck that was not associated with any precipitating factors in December of 2021. This mass grew rapidly over the following 2 months. When he presented to Jiangmen Central Hospital, he exhibited a high fever (maximum: 39.4 ℃) and leukocytosis detected through a routine blood test in an outpatient facility on January 25, 2022 with no obvious weight loss. He had lived a normal life and did not exhibit any significant personal or family history of similar disease.

Physical examination revealed multiple swollen lymph nodes in the right posterior triangle of the neck with a total size of approximately 80 mm × 90 mm. While these masses were painless to the touch, they exhibited general mobility and a leather-like texture. These enlarged nodes were partially fused with no evidence of local redness, swelling, ulceration, or pus.

Ultrasound analyses conducted on February 14, 2022 revealed a mass consisting of multiple enlarged lymph nodes, with diseased nodes being hypoechoic and pressing on one another, and with the largest node measuring 42 mm × 25 mm.

On February 21, 2022, bone marrow examination was conducted that included both a histological examination and smear, flow cytometry analysis, qualitative *BCR-ABL1* fusion genotyping testing, and karyotype analyses of bone marrow cells, all of which yielded negative results and suggesting that his high fever and leukocytosis were the result of regional inflammation stemming from rapid nodal enlargement.

On February 22, 2022, positron emission tomography-computed tomography (*Figure 1*) scanning revealed multiple swollen lymph nodes near the right oropharynx in the right level II to V and right clavicle region of the neck with abnormally elevated glucose metabolism [maximum standardized uptake value (SUVmax) =20.2], with the

Table 1 Primary malignancies of the cervical lymph nodes that are not lymphomas, ectopic tumors, or concealed metastases

Case report	Malignancy category
(1)	FDC tumor
(2)	Interdigitating dendritic cell sarcoma
(3)	SEH
(4)	Angiosarcoma
(5)	Schwannoma
(6)	FDCS
(7)	UCD
(8)	Leiomyosarcoma
(9)	Kaposi's sarcoma
(10)	IDCS
(11)	Angiosarcoma
(12)	Follicular dendritic reticulum cell sarcoma
(13)	Granuloma-like interdigitating dendritic cell sarcoma
(14)	Kaposi's sarcoma
(15)	Granulocytic sarcoma
(16)	Kaposi's sarcoma

FDC, follicular dendritic cell; SHE, spindle and epithelioid hemangio-endothelioma; FDCS, follicular dendritic cell sarcoma; UCD, unicentric Castleman disease; IDCS, interdigitating dendritic cell sarcoma.

largest node measuring approximately 54 mm × 72 mm. These nodes were partially fused and formed a mass that was visibly pressing on its surroundings and exhibiting moderate heterogeneous enhancement being evident on a contrast-enhanced scan. Given these findings, the potential of malignancy (e.g., lymph node metastasis of unknown origin or lymphoma) was considered. No abnormalities of the thyroid gland, oropharynx, or laryngopharynx were spotted. The left lateral wall of the nasopharynx exhibited a value of 4.4 in SUVmax thereby being considered to be chronic inflammation. Hepatic metastases and suspected bone infiltration or metastases were detected with no evidence of any other distant metastases.

On March 14, 2022, some of lymph nodes were resected from the right supraclavicular region, harvesting a small pile of gray-white, tough, nodular tissues with a total size of approximately 1.5 cm × 1.5 cm × 0.6 cm. Light microscopy revealed the obliteration of normal recognizable structures in these tissues, which instead presented as multiple nodules with myofibrous tissues surrounding each nodule. A range of atypical cells were evident within the lesion that were scattered or arranged as small nests against a background of large numbers of lymphocytes and eosinophils together with limited numbers of plasma cells and foamy histiocytes. These atypical cells exhibited abundant cytoplasm enclosing enlarged rounded or slightly irregular nuclei with some exhibiting vacuolation. These cells also presented with a thin nuclear membrane, a prominent nucleolus, and common mitotic figures. The periphery of these lesions exhibited some spindle-like tumor cells (*Figure 2*). Immunohistochemistry (IHC) results from these tumor cells were as follows: cytokeratin (CK), variably+; vimentin (VIM), +; leukocyte common antigen (LCA), –; p40, –; CK5/6, –; epithelial membrane antigen (EMA), variably+; high molecular cytokeratin (HCK), –; CK8/18, scattered individual, +; cluster of differentiation (CD)30, cytoplasm and membrane, +; podoplanin (D2-40), +; S-100, partial, +; CD21, –; CD35, –; CD1a, –; CD68, –; CD15, –; paired box 5 (PAX-5), –; multiple myeloma antigen 1 (MUM-1), –; B cell lymphoma 6 (BCL-6), partial, weakly+; B cell Oct binding factor 1 (Bob-1), –; octamer-binding transcription factor 2 (OCT-2), rare, weakly+; CD10, –; BCL-2, –; anaplastic lymphoma kinase (ALK), –; CD20, –; CD79a, –; CD3, –; CD5, –; CD7, –; myeloperoxidase (MPO), –; T cell restricted intracellular antigen (TIA), –; CD4, partial, +; granzyme B (GRB), –; Ki-67, +80%; and Epstein-Barr virus (EBV)-encoded small RNA (EBER) *in situ* hybridization, + (*Table 2*). These results were suggestive of a dendritic cell tumor, but its specific type, such as an inflammatory pseudotumor-like follicular dendritic cell sarcoma (FDCS), indeterminate dendritic cell sarcoma, or other rare dendritic cell tumor type, was difficult to establish, recommending to distinguish it from other tumors.

On March 15, 2022, IHC staining was re-evaluated in consultation with a higher cancer center, yielding the following results: CK, rare, +; VIM, +; p40, –; CK5/6, –; EMA, +; HCK, –; CK8/18, individual, +; CD30, +; D2-40, +; S-100, rare, +; CD35, –; CD68, +; BCL-6, +; CD7, rare, +; MPO (large cells, –, small cells, +); TIA, +; CD4, +; GRB, rare, +; and EBER *in situ* hybridization, + (*Table 2*).

On March 22, 2022, the remainder of the submitted specimens were evaluated by the cancer center, yielding the following results: CD30, +; CD15 (+/–); Ki-67, +75%;

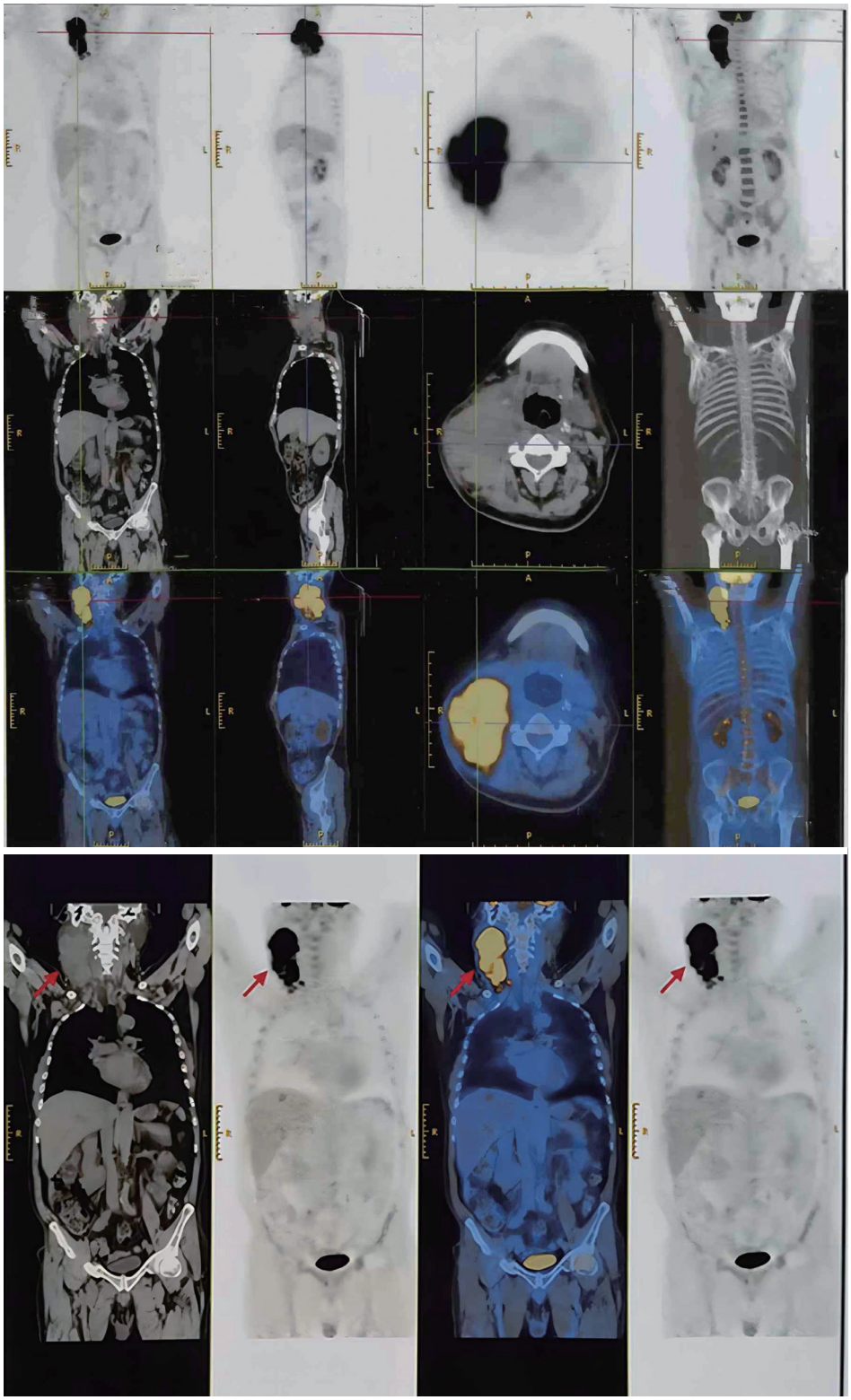

Figure 1 Positron emission tomography-computed tomography imaging performed on February 22, 2022 revealed the involvement of the lateral and supraclavicular lymph nodes on the right side of the neck, with evidence of increased fluorodeoxyglucose uptake. The arrows on the second picture are pointing to the malignancy with high fluorodeoxyglucose uptake.

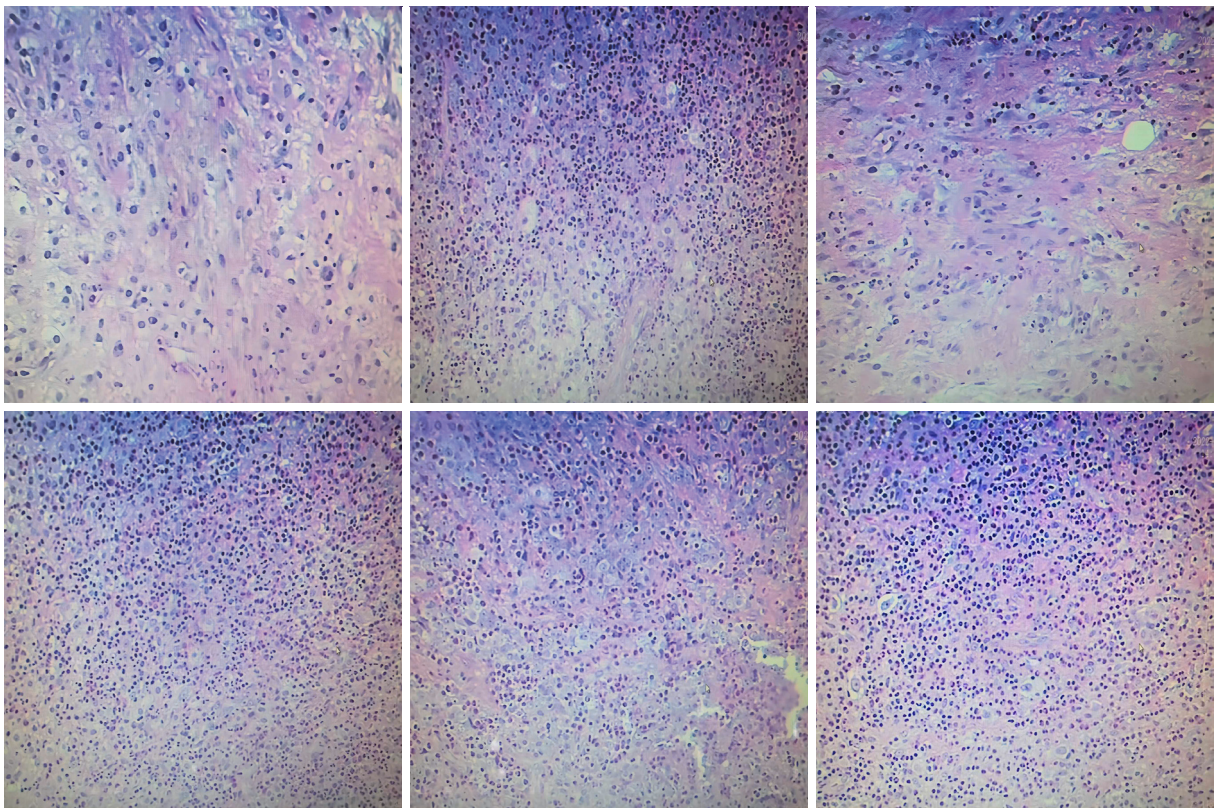

Figure 2 Hematoxylin and eosin staining results for the lesion based on the staining of resected lymph nodes from the supraclavicular region on the right side of the neck (100×).

Table 2 Immunohistochemical findings for the tumor cells

Marker classification	Initial immunohistochemical staining	Reobservation of the first staining results	Re-staining for a second consultation
LCA	LCA (–)	NE	NS
B cell-related markers	CD20 (–)	NE	CD20 (rare, +)
	CD79a (–)	NE	NS
	Bob-1 (–)	NE	Bob-1 (rare, +)
	PAX-5 (–)	NE	PAX-5 (rare, +)
	OCT-2 (rare, w+)	NE	OCT-2 (rare, +)
	NS	NS	CD23 (+)
T cell/NK cell-associated markers	CD3 (–)	NE	NS
	CD5 (–)	NE	NS
	CD7 (–)	CD7 (rare, +)	NS
	TIA (–)	TIA (+)	NS
	CD4 (partial, +)	CD4 (+)	NS
	NS	NS	CD56 (–)

Table 2 (*continued*)

Table 2 (*continued*)

Marker classification	Initial immunohistochemical staining	Reobservation of the first staining results	Re-staining for a second consultation
Markers related to lymphocyte activation/differentiation	CD30 (cytoplasm and membrane, +)	CD30 (+)	CD30 (+)
	BCL-6 (partial, w+)	BCL-6 (+)	NS
	MUM-1 (–)	NE	NS
	CD10 (–)	NE	NS
Tumor genes and proliferation-related markers	ALK (–)	NE	ALK (–)
	Ki-67 (80%, +)	NE	Ki-67 (75%, +)
	BCL-2 (–)	NE	NS
Histiocyte, dendritic cell and myeloid associated markers	S-100 (partial, +)	S-100 (rare, +)	NS
	CD21 (–)	NE	CD21 (–)
	CD35 (–)	CD35 (–)	CD35 (+/–)
	CD1a (–)	NE	CD1a (–)
	CD68 (–)	CD68 (+)	CD68 (+)
	CD15 (–)	NE	CD15 (+/–)
	MPO (–)	MPO (large cells, –, small cells, +)	MPO (+)
	NS	NS	CD163 (+)
	NS	NS	CD123 (w+)
Others	CK (var+)	CK (rare, +)	NS
	EMA (var+)	EMA (+)	EMA (+)
	VIM (+)	VIM (+)	NS
	D2-40 (+)	D2-40 (+)	NS
	CK8/18 (scattered individual, +)	CK8/18 (individual, +)	NS
	CK5/6 (–)	CK5/6 (–)	NS
	HCK (–)	HCK (–)	NS
	p40 (–)	p40 (–)	NS
	GRB (–)	GRB (rare, +)	NS
	NS	NS	p53 (+)
	NS	NS	CD34 (–)
	NS	NS	ERG (–)
EBER	EBER (+)	EBER (+)	EBERs (+++)

Reactivity: +, 75–100% of tumor cells; +/–, 50–75% of tumor cells; rare, 10–25% of tumor cells; –, <10% of tumor cells; w+, weakly+; var+, variably+; unspecified, strong reactivity. Partial: 100% > tumor cell percentage >25%. LCA, leukocyte common antigen; NE, not evaluated; NS, not stained; CD, cluster of differentiation; Bob-1, B cell Oct binding factor 1; PAX-5, paired box 5; OCT-2, octamer-binding transcription factor 2; NK, natural killer; TIA, T cell restricted intracellular antigen; BCL, B cell lymphoma; MUM-1, multiple myeloma antigen 1; ALK, anaplastic lymphoma kinase; MPO, myeloperoxidase; CK, cytokeratin; EMA, epithelial membrane antigen; VIM, vimentin; D2-40, podoplanin; HCK, high molecular cytokeratin; GRB, granzyme B; ERG, ETS related gene; EBER, Epstein-Barr virus-encoded small RNA.

CD163, +; CD23, +; CD123, weakly+; CD68, +; MPO, +; CD35 (+/–); p53, +; EMA, +; (CD20, OCT-2, PAX-5, and Bob-1) rare, +; (CD21, ALK, CD1a, CD34, CD56, and ERG) –; EBER *in situ* hybridization, +++ (*Table 2*). Negative immunoglobulin heavy chain (*IGH*), immunoglobulin kappa (*IGK*), immunoglobulin lambda locus (*IGL*), T cell receptor beta chain (*TCRB*), T cell receptor gamma chain (*TCRG*), and T cell receptor delta chain (*TCRD*) gene rearrangement results were obtained on March 25, 2022. Given these results, the lesion was considered to be a tumor prone to malignancy, necessitating differentiation from epithelial or histiocytic cell tumors, or dendritic cell tumors.

Over the course of this diagnostic process, the patient reported that his tumor began to cause aching pain without evidence of ulceration. He did not elect to undergo aggressive treatment until the pain had become intolerable.

A treatment plan was then developed through multidisciplinary consultation, consisting of one cycle of a cyclophosphamide plus doxorubicin, vincristine, and dexamethasone regimen (cyclophosphamide 1,170 mg on day 1, doxorubicin 60 mg on day 1, vincristine 2 mg on day 1, and dexamethasone 15 mg on days 1–5) that was given on May 23, 2022, followed by two cycles of a cyclophosphamide plus pirarubicin, vincristine, and dexamethasone regimen (cyclophosphamide 1,170 mg on day 1, pirarubicin 60 mg on day 1, vincristine 2 mg on day 1, and dexamethasone 15 mg on days 1–5, repeating every 3 weeks), which were administered on July 14, 2022 and August 11, 2022.

Even with treatment, no significant decrease in size of these swollen lymph nodes was observed, with physical examination revealing an approximate size of 100 mm × 110 mm, with the three largest being 80 mm × 110 mm, 30 mm × 30 mm, and 15 mm × 15 mm in size.

While radiotherapy was advised, the patient lacked confidence and declined to undergo such treatment.

In the absence of any practical curative interventions, the patient developed complications that became increasingly severe, with eating difficulty resulting from esophageal compression and consequent hypoglycemia and electrolyte disturbances, which had put him into the stage of tumor cachexia since November of 2022.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient and his son for publication of this case report and any accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

Given the rarity of the malignancy described in this report, no definite mechanisms have been proposed that may account for its pathogenesis. Given the *in situ* hybridization results (EBER, +/+++), however, we speculate that it may be related to EBV infection. Studies have shown that latent viral material in the form of intracellular free circular DNA can be integrated into host chromosomes, with the EBV genome generally expressing latency genes including EBV nuclear antigen (*EBNA 1*, *2*, *3A*, *3B*, and *3C* and EBNA leader protein), latent membrane protein (*LMP*)*-1* and *LMP-2* (involves two isoforms, *LMP-2A* and *LMP-2B*), EBER (*EBER1* and *EBER2*), and EBV-microRNAs. These genes, alone or in combination with one another, can activate *BCL-2*, myelocytomatosis viral oncogene homolog (*MYC*) or other oncogenes and can activate the nuclear factor-kappa B (NF-κB), c-Jun N-terminal kinase (JNK), Janus kinase (JAK)/signal transducer and activator of transcription (STAT), and phosphoinositide 3-kinase (PI3K)/protein kinase B (Akt) signaling pathways while interfering with the tumor suppressors downstream of tyrosine kinase 1 (*DOK1*), double-stranded RNA-dependent protein kinase (*PKR*), p53, PR domain zinc finger protein 1 (*PRDM1*), deleted in cancer 1 (*DICE1*), phosphatase and tensin homolog (*PTEN*), $p27^{kip1}$, $p21^{WAF1/CIP1}$, $p16^{INK4A}$, and *p73*, thus progressing the cell cycle and driving oncogenic transformation through a range of mechanisms (17). There is growing evidence suggesting that lytic genes encoded by EBV in cells infected with this virus can contribute to tumorigenesis through the evasion of immune detection, the induction of genomic instability, and the enhancement of cellular survival (18). Whether these mechanisms are related to the formation of the mass in the present case remains to be determined.

Meticulous histomorphological examination combined with appropriate IHC staining has long been central to efforts to accurately diagnose solid malignancies (19-21). Leong *et al.* (21) reported the case of a nodule within a papillary thyroid carcinoma (PTC) exhibiting morphological arrangement as a loose fascicle of spindle

Table 3 The immunohistochemical staining profile of HS

Markers	Reaction	Positivity
CD68	+	100% (26)
LYS	+ to –/+	94% (26)
S-100	+ to –/+	50% (25)
CD163	+	100% (26)
CD1a	–	
CD21	–	
CD35	–	
CD23	–	
CNA.42	–	
CD14	+	NC
CD11c	+	NC
CD15	–/+	11.1% (26)
CD4	+	50% (26)
CD34	–	
CD13	–	
CD33	–	
MPO	–	
CD207	–	
LCA	W+ to rare	77.8% (26)
CD3	–	
CD20	–	
CD79a	–	
CD30	–	
Ki-67%	5–40% (26)	
p53	+ to rare	53.3% (26)
EMA	–	
CK	–	
HMB45	–	
EBER	–	

Reactivity: +, 75–100% of tumor cells; +/–, 50–75% of tumor cells; –/+, 25–50% of tumor cells; rare, 10–25% of tumor cells; –, <10% of tumor cells; w+, weakly+; unspecified, strong reactivity. Positivity, positive case/total cases in current reference. HS, histiocytic sarcoma; CD, cluster of differentiation; Lys, lysozyme; CNA.42, follicular dendritic cell associated antigen; NC, not counted; MPO, myeloperoxidase; LCA, leukocyte common antigen; EMA, epithelial membrane antigen; CK, cytokeratin; HMB45, glycoprotein 100, pre-melanosome protein 17; EBER, Epstein-Barr virus-encoded small RNA.

cells that was only identified as spindle cell metaplasia in PTC following IHC staining for thyroid transcription factor 1 (TTF-1) and thyroglobulin in those spindle cells, together with the observation of focal p53 and B-Raf serine/threonine kinase (BRAF) V600E mutant protein immunoexpression and the loss of calcitonin, S-100, desmin, E-cadherin, and CK19. This case of PTC with spindle cell metaplasia remains a rare and largely uncharacterized PTC variant. Morphological appearance is currently used as an indicator when selecting antibodies for use in IHC staining (19-22). Diagnostic specificity can also be improved through the application of molecular techniques including *in situ* hybridization, fluorescence in situ hybridization (FISH), gene rearrangement testing, tissue microarrays, and next-generation sequencing (19,21-24). In this case, the morphological characteristics observed on initial observation failed to offer sufficient insight into whether this mass was a tumor or a proliferative lesion. Further IHC staining revealed positive staining consistent with a likely malignant tumor, but these results lacked the specificity necessary to determine the tumor pathological type owing to ambiguity with respect to the cell types from which these atypical cells were derived. Given this unusual finding, differential diagnosis efforts aimed to exclude one or more other types of possible malignancies, as this strategy can be an effective means of arriving at a definitive diagnosis (25) or narrowing the list of possible malignancies. The IHC staining profiles of several comparable malignant tumors are presented in *Tables 3-5* (25-27).

The present case did not share clear morphological similarities with these three sarcomas. Immunophenotyping revealed that most atypical cells in this case expressed CD68, CD163, CD23, CD30, CD123, CD4, D2-40, EMA, VIM, p53, and MPO, whereas they did not express CD1a, CD21, CD34, CD56 (*Table 2*). A subset of the tumor cells were positive for CD35, CD15, and S-100, while a small number of these malignant cells were positive for CD7, CD20, Bob-1, PAX-5, OCT-2. This tumor also presented with a high Ki-67 index and a marked EBER reaction. Based on these results, this malignancy did not present with the typical characteristics of a histiocytic sarcoma (HS) or a dendritic cell tumor such that it remains unclassifiable.

For low-incidence malignancies, there is generally very little therapeutic experience and no established standard treatment protocols. The available treatment can entail surgery, chemotherapy, radiotherapy, and/or targeted therapy based on the stage of the disease and whether

Table 4 The immunohistochemical staining profile of interdigitating dendritic cell tumor/sarcoma

Markers	Reaction	Positivity
CD68	Var+	40% (26)
LYS	–	
S-100	+	100% (26)
CD163	Var+	NC
CD1a	–	
CD21	–	
CD35	–	
CNA.42	–	
CD34	–	
MPO	–	
CD207	–	
LCA	Var+	40% (26)
CD3	–	
CD20	–	
CD79a	–	
CD30	–	
EMA	–	
Ki-67%	10–15% (26)	
p53	+	25% (26)
EBER	–	

Reactivity: +, 75–100% of tumor cells; –, <10% of tumor cells; var+, variably+; unspecified, strong reactivity. Positivity, positive case/total cases in current reference. CD, cluster of differentiation; LYS, lysozyme; NC, not counted; CNA.42, follicular dendritic cell associated antigen; MPO, myeloperoxidase; LCA, leukocyte common antigen; EMA, epithelial membrane antigen; EBER, Epstein-Barr virus-encoded small RNA.

it exhibits localized or distant spread. In FDCS cases, surgery is often combined with or without chemotherapy and/or radiotherapy (28,29), with patients presenting with unresectable disease receiving lymphoma-like chemotherapy regimens (25), although the efficacy of this approach remains uncertain (30,31). The overexpression of programmed death protein 1 and its ligands by FDCS has offered new insight into the approaches to treat these tumors (25,32,33). HS cases are commonly treated with combinations of surgery, radiotherapy, and chemotherapy, but optimal radiotherapy and chemotherapy regimens have yet to be established (25,34). Targeted treatment with the

Table 5 The immunohistochemical staining profile of follicular dendritic cell tumor/sarcoma

Markers	Reaction	Positivity
CD68	Var+	38% (25)
LYS	–	
S-100	Var+	13% (25)
CD1a	–	
CD21	+	89% (25)
CD35	+	78% (25)
CD23	+	73% (25)
CNA.42	+	71.4% (26)
CLUST	+	100% (25)
CXCL13	+	89% (25)
D2-40	+	100% (25)
MPO	–	
CD4	+	57% (25)
CD20	–/+	21.4% (26)
CD31	+	20% (25)
CD30	+ to rare	35% (25)
CD79a	–	
HMB45	–	
EMA	+	17% (25)
Ki-67%	Ave. 25% (25)	
p53	Var+	21% (26)
CD163	+	20% (25)
LCA	+	25% (25)
CD3	–	
CD34	–	
Desmin	+	NC
Clau4	+	NC
VIM	+	NC
Fascin	+	NC
EBER	–	

Reactivity: +, 75–100% of tumor cells; –/+, 25–50% of tumor cells; –, <10% of tumor cells; var+, variably+; unspecified, strong reactivity. Positivity, positive case/total cases in current reference. CD, cluster of differentiation; LYS, lysozyme; CNA.42, follicular dendritic cell associated antigen; CLUST, clusterin; CXCL13, C-X-C motif chemokine 13; D2-40, podoplanin; MPO, myeloperoxidase; HMB45, glycoprotein 100, pre-melanosome protein 17; EMA, epithelial membrane antigen; Ave., average; LCA, leukocyte common antigen; NC, not counted; clau4, claudin 4; VIM, vimentin; EBER, Epstein-Barr virus-encoded small RNA.

mitogen-activated protein kinase kinase (MEK) inhibitor trametinib and the BRAF inhibitor vemurafenib has yielded acceptable remission rates in some HS cases over recent years (25,35). We were unable to identify any precedent for the treatment of our case. Therapeutic planning took the close proximity of this mass to the hypopharyngeal structures such that surgical resection was not considered viable. Given the detection of distant liver metastases, systemic chemotherapy mimicking the lymphoma-oriented regimens was regarded as the most promising strategy, but little efficacy was observed even following three courses. While radiotherapy was recommended in this case, its efficacy remains uncertain. When treating these rare malignancies, achieving satisfactory treatment outcomes can be very difficult and the accumulation of more meaningful information regarding appropriate treatments is challenging owing to the small number of affected individuals. We hope that future efforts will help mitigate the suffering of patients suffering from similar conditions.

Conclusions

This is the first report of a primary malignancy of the cervical lymph nodes exhibiting this atypical array of pathology findings. The process of diagnosing such tumors is time-and-energy-extensive, entailing extensive IHC staining, a range of molecular biology assays, and efforts to distinguish among several possible malignancies, even after which it can remain difficult to clearly define its pathologic type. No standard treatment options for these rare tumors are currently available. The accumulation of further clinical data and reports on treatment experiences may help improve the management of these tumors.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://acr.amegroups.com/article/view/10.21037/acr-23-147/rc

Peer Review File: Available at https://acr.amegroups.com/article/view/10.21037/acr-23-147/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://acr.amegroups.com/article/view/10.21037/acr-23-147/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient and his son for publication of this case report and any accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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