Primary High-Grade Poorly Differentiated Angiosarcoma of an Intra-parotid Lymph Node

Eugenia Ducharne-Asuaje¹ · Dominique Dorion² · Louis Lamarre³ · Jean Michel Coindre⁴ · Sameh Geha¹

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Abstract Head and neck angiosarcoma is an infrequent malignant vascular tumor most commonly found in the skin and soft tissue of the head and neck. Most head and neck angiosarcomas are metastatic to cervical lymph nodes from other primitive location. We describe herein a case of primary high-grade poorly differentiated angiosarcoma arising in an intra-parotid lymph node, discuss the value of immunohistochemical stains for differential diagnosis, and review the literature concerning head and neck angiosarcoma. A 47-year-old man presented with a painless mass that had grown for a period of 6 months in the parotid area. The CT-scan revealed a left parotid lesion of 17 mm. Fine needle aspiration was considered suspicious for lymphoma or poorly differentiated carcinoma. A superficial parotidectomy was performed. On gross examination, the lesion was a well-defined, gray, homogeneous mass of 15 mm of diameter. Microscopic examination showed a normal parotid tissue and a poorly differentiated malignant neoplasm in an intra-parotid lymph node. The tumor had a pseudo-alveolar pattern, with large pleomorphic epithelioid cells, abundant eosinophilic cytoplasm, large vesicular nuclei, and one or more prominent nucleoli. Atypical

mitoses were seen. Neoplastic malignant cells stained positive for Vimentin, CD31, D2-40, factor VIII, ERG, and partially for CD34. A positron emission tomography scan was made to search for a primary neoplasia, but no other tumor was localized. The diagnosis of primary high-grade, poorly differentiated, intra-parotid lymph node angiosarcoma was established.

Keywords Primary angiosarcoma · Poorly differentiated angiosarcoma · Lymph node tumour · Markers of vascular tumors

Introduction

Angiosarcoma is a sarcoma of endothelial cell differentiation with vascular channel formation to various degrees. Head and neck angiosarcoma account for 1–2 % of all head and neck sarcomas, and the most common localizations are the skin (39 %) and the soft tissue of head and neck (27 %) [1, 2, 3]. Lymph node metastasis in head and neck is considered an infrequent event and has been reported between 10 % [1] and 13.5 % [4].

Primary vascular tumors of lymph node other than Kaposi sarcoma are extremely rare; only a small number of cases have been reported, most of them are benign subtype [5]. Given the rarity of angiosarcoma in lymph nodes, all cases should be considered as metastatic angiosarcoma until more investigations are conducted. [5] The diagnosis must be supported by immunohistochemical demonstration of endothelial-specific markers [2].

To date, to our knowledge, there is only one case report of primary low-grade angiosarcoma in a cervical lymph node [1].

✉ Eugenia Ducharne-Asuaje
eugenia.ducharne.asuaje@usherbrooke.ca

¹ Pathology Department, Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke University, 3001, 12e Avenue Nord, Sherbrooke, QC J1H 5N4, Canada

² Division of Otolaryngology-Head and Neck Surgery, Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke University, Sherbrooke, QC, Canada

³ Pathology Department, Charles Lemoyne Hospital, Sherbrooke University, Sherbrooke, QC, Canada

⁴ Institut Bergonié, Bordeaux, France

We herein describe a case with an exceptional presentation of a primary high-grade, poorly differentiated angiosarcoma of the lymph node.

Case Report

A 47-year-old man was referred to the head and neck service of our institution for a painless mass in the parotid area that had been growing for 6 months. A head and neck tomography revealed a 17 mm superficial mass in the left parotid. Fine needle aspiration (FNA) showed a very cellular material mainly composed of small mature lymphocytes, histiocytes and tingible body macrophages. There were also several sheets or individual large atypical cells. These cells had an increased nucleo-cytoplasmic ratio, nuclear atypia, and significant macro nucleoli. The FNA specimen was considered suspicious for lymphoma or poorly differentiated carcinoma. There was no history of cancer, trauma, or radiation in the area of the parotid and neck.

Physical examination revealed a superficial, rounded, soft, non-tender mass in the left parotid. No other cervical, supraclavicular, or retro auricular mass was present. A superficial parotidectomy was performed and total excision of the mass was done. The specimen was sent to our pathology laboratory.

In gross examination, the lesion was a homogeneous, gray, well-defined nodular mass of 15 mm or greater diameter.

On histopathology, we identified a lymph node within parotid parenchyma occupied by a poorly differentiated malignant proliferation that completely destroyed the lymph node architecture (Fig. 1).

Fig. 1 Left parotid gland. Right neoplastic proliferation with destruction of the lymph node architecture. Hematoxylin–eosin stain; ×2 original magnification

Tumor consisted mostly of discohesive cells without typical gland formation, but some areas showed a pseudo-alveolar pattern and pseudo-vascular channels (Fig. 2).

The malignant cells were epithelioid, large, with moderate well-defined eosinophilic cytoplasm and large, pleomorphic, hyper chromatic nuclei (Fig. 3). Some had one or two large nucleolus. Numerous atypical mitoses were seen; parotid tissue was otherwise normal.

The poorly differentiated aspect of this neoplasia and the anatomical localization of the mass, suggested a primitive or secondary malignancy; differential diagnosis includes high-grade carcinoma, lymphoma, sarcoma, and lymph node metastases. Several immunohistochemical stains were performed. The neoplastic cells did not stain for pankeratin (AE1-AE3) (Fig. 4a), keratin 7, EMA, TTF-1, BER-EP4, PSA, RCC, thyroglobuline, hepPar-1, synaptophysin, chromogranin, CD56; the diagnosis of metastatic carcinoma to lymph node was eliminated; desmin and myogenin were also negative excluding leiomyosarcoma. The Vimentin was strongly positive and the CD45 was weakly positive. To help discriminate between other types of sarcoma and lymphoma, further staining were performed. For lymphoma assessment, we performed CD20, CD3, PAX 5, and ALK. All these markers were negative. Among sarcomas, follicular dendritic cell sarcoma was eliminated because CD21 and CD23 were negative; interdigitating dendritic cell sarcoma and histiocytic sarcoma were both equally improbable because S-100 and CD68 were negative and CD45 was faintly stained. A senior hematopathologist (Dr. L.L.) confirmed the ruling-out of these types of sarcomas.

On the other hand, markers for sarcoma of vascular type: CD31, D2-40 (Fig. 4b, c), and factor VIII were strongly positive. The possibility of high-grade angiosarcoma was raised.

Fig. 2 Pseudo-alveolar pattern and vascular channels with discohesive tumor cells. Hematoxylin–eosin stain; ×20 original magnification

Fig. 3 Malignant pleomorphic epithelioid cells with hyperchromasia and large nuclei. Hematoxylin–eosin stain; $\times 100$ original magnification

Kaposi sarcoma was eliminated because of the epithelioid and high-grade aspect of the cells and the negative result of HHV8 on immunohistochemistry.

The case was sent to a senior pathologist (Dr. J-M.C.) for consultation to assess ERG transcription factor expression. The result was strongly positive (Fig. 5) and he confirmed the diagnosis of a high-grade poorly differentiated angiosarcoma.

A positron emission tomography (TEP) scan was conducted to identify a primary neoplasia, but no other tumor was localized. Due to the absence of any clinical source of metastasis, the histological characteristics and the strongly immunohistochemical stain for vascular tumor markers, we made the diagnosis of a primary high-grade poorly differentiated angiosarcoma in a lymph node. The patient had a good recovery without major complications and was discharged 4 days postoperatively.

At 12-month follow-up, a TEP scan was repeated and there was no residual neoplastic lesion in the left parotid or any other primitive or metastatic lesion. Thirty-two months post-surgery, the patient remains asymptomatic.

Discussion

Head and neck angiosarcoma is a rare vascular tumor. Around 50 % of cases are localized on the scalp and a few occur in the skull, nose, paranasal sinuses, external ear, submandibular gland, larynx, and thyroid [5]. Lymph node metastatic angiosarcoma can be present in 10 % [1] to 13.5 % [4] of the cases.

Kaposi sarcoma is the most frequent primary vascular tumor in a lymph node, followed by benign tumors like hemangioma [5]. These diagnoses were dismissed because

Fig. 4 Neoplastic cells were negative for pankeratin (a) and immunoreactive for CD31 (b) and D2-40 (c)

of a negative HHV8 and the undifferentiated character of the lesion.

To our knowledge there is only one case report in the literature, by Yilmaz et al. [1] of a primary low-grade angiosarcoma in a lymph node. In this case, the patient was a 38-year-old woman with a 2-year history of goitre and a mass in the neck that had been growing for 2 months. The CT showed a mass with central necrosis in the left posterior triangle of sternocleidomastoid muscle. On histopathology

Fig. 5 Neoplastic cells were immunoreactive for ERG

the mass in the neck was a primary low-grade angiosarcoma in a cervical lymph node. The tumor cells stained positively with endothelial marker CD34.

ERG is a transcription factor of the ETS family, previously known because of the presence of oncogenic ERG gene fusions in prostate cancer, acute myeloid leukemia, and Ewing sarcoma [6]. ERG is also expressed constitutively in normal and tumor endothelial cells; it regulates endothelial apoptosis and angiogenesis [6].

In 2011, Miettinen et al. concluded that the ERG transcription factor is a highly specific immunohistochemical marker for benign and malignant vascular tumors [6], obtaining a positive expression in 96 % of angiosarcoma [7].

A recent review published in 2014 by Miettinen highlights the importance of using immunohistochemical analyses to make a good differential diagnosis in soft tissue tumors [8, 9] and proposes the use of CD31 and ERG as principal markers in vascular endothelial tumors.

Our patient did not have a previous or actual history of primary angiosarcoma, nor risk factors for this tumor. All other investigations were negative. Thus we retain the

diagnosis of a primary high-grade poorly differentiated angiosarcoma of lymph node.

In summary, in the herein described case, the use of several immunohistochemical markers was mandatory to reach an accurate diagnosis for this complex and extremely unusual presentation of a primary high-grade, poorly differentiated angiosarcoma in an intra-parotid lymph node.

Conflict of interest The authors declare that they have no conflict of interest.

Human and Animal Rights This article does not contain any studies with human participants or animals performed by any of the authors.

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