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Glomus tumor of uncertain malignant potential in upper extremity: Case report and review of literature

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Abstract

Malignant glomus tumors are a extremely rare soft tissue sarcomas, supposed originated from a benign glomus tumor. We report a case of glomus tumor of uncertain malignant potential occurring on the skin of volar area of arm of a 56-year-old woman.

Were view the clinically features of the other similar cases that have previously been documented in the English literature and propose a guidelines treatment criteria

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Introduction

A glomus tumor is a benign neoplasm that derives from the glomus body, which is an anastomosis formed by an afferent arteriole and an anastomotic vessel called the Sucquet-Hoyer channel [1] and is surrounded by an efferent vein, nerve fibers and a capsule peripheral and has regulatory function of peripheral temperature.

The etiology is still unknown, through immunohistochemistry, its origin has been observed in vascular smooth muscle [3], it may be due to de novo mutations that affect the regulation of angiogenesis by activating a receptor specific for tyrosine kinase in the endothelial cell (TIE2) [3].

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Most glomus tumors are usually solitary, small, normally less than 1 cm and red-violet. They can cause paroxysmal and lancinating pain due to changes in temperature and pressure.

Malignant glomus tumors are very rare, they can be locally aggressive and recur, they do not usually metastasize. The first case was described by Lumley and Stanfield as an atypical and infiltrating glomus tumor [1] Khoury et al.

It is thought that it can originate from a benign glomus tumor but this supposed transformation is not clear [3] In 1990 Gould et al. proposed the first classification scheme, based on analysis of six tumors: (1) locally infiltrative glomus tumor (LIGT a cytologically benign tumour with an infiltrative growth pattern and higher local recurrence rate), (2) glomangiosarcoma a true morphologically malignant arising in a benign Glomus Tumor(GABGT) and (3) de novo Glomangiosarcoma (GADN). None of the glomangiosarcomas in their series metastasized; however, the number of cases was small.

Folpe et al. reviewed 52 GTs with atypical morphological features and proposed a classification scheme based on 5-year cumulative metastatic risk: (1) malignant GT, which is associated with a metastatic rate of 38% and is defined as a tumor with size larger than 2 cm and with a deep location,

or atypical mitotic figures, or moderate to high nuclear grade and with 5 or more mitoses/50 high power fields (HPFs); (2) GT of uncertain malignant potential, which has high mitotic activity and superficial location or large size only or deep location only; (3) symplastic glomus tumours, encompassing tumours with high nuclear grade in the absence of any other malignant features. probably reflecting a degenerative phenomenon; (4) glomangiomatosis, referring to tumours with histological features of angiomatosis coupled with an excess of glomus cells [6].

The last three categories did not show metastatic activity, which was restricted to the malignant GT subgroup only.

The latest edition of the World Health Organization (WHO) classification of tumors of soft tissue and bone indicates that the diagnosis of malignant GT should be made when a GT shows: marked nuclear atypia and any level of mitotic activity; or atypical mitoses [16].

These tumors seems to have an up to 40% metastatic rate. The term GT with 'uncertain malignant potential' is used for neoplasm not fulfilling criteria for malignancy but displaying at least one atypical morphological feature in addition to nuclear pleomorphism [7] Table 1.

Clinical Case

A 63-year-old woman referred in March 2016 by her Family Physician to the Dermatology Service for a reddish papular lesion with a 7-month history.

The patient has a reddish lesion on the right forearm since the beginning of summer 2015, which causes cramping and irradiated pain when touching the lesion. It has been growing gradually throughout this time and it has not bled.

In the initial physical examination, the lesion is described as reddish, vascularized, without erosions or ulceration, dome-shaped, on the right forearm. It measures 6 mm (Figure 1,2).

On the same day of the consultation, in Dermatology Unit, the lesion was removed.

The pathology result is a glomus tumor of uncertain malignant potential. The tumor has 6-9 mitosis per field. Knowing the result, patient is derived to our Musculoskeletal Tumor Unit (Figure 9).

A soft tissue MRI of the forearm is requested to rule out multifocal subclinical involvement and a TAC body. In MRI skin marking is performed in the area where the patient refers to the already excised lesion (lateral region of the forearm). Adjacent to the cutaneous and slightly anterior mark, a focal cutaneous thickening is identified that shows an increase in signal intensity in sequences with long TR and Gadolinium uptake of approximately 8 mm. It associates signal alteration and enhancement of the subcutaneous cellular tissue immediately underlying. In the recent surgical context, is not possible being able to rule out the presence of tumor residue locally. There no other lesions or presence of skin or subcutaneous pathological enhancement that suggests the presence of a multifocal affectation.

After evaluating the case in the tumor committee, it was decided to carry out an enlargement of surgical margins, and then refer the patient to assess adjuvant Radiotherapy treatment. Simulation CT was performed in supine position using isocentric technique and arm support in custom mold. 0.5cm bolus was used. Between the days 06/15/16 and 07/26/16 by means of a linear electron accelerator, it is carried out. Radiotherapeutic treatment with 6Mv photons to the following volumes: PTV1: bed. The total dose administered was 63Gy and a fractionation of 210cGy / session. Doses to risk organs meet the criteria established by the Quantitative Analyses of Normal Tissue Effects in the Clinic tables. (QUANTEC) [33] (Figures 3 to 8).

Table 1: Summary of clinical features (Folpe et al.) [15].

Malignant Glomus Tumor 1) Large size and deep location or 2) Atypical mitotic figures or 3) Marked atypia with mitoticactivity	Glomus Tumor of uncertain Malignant potential 1) Superficial location with high mitotic activity or 2) Large size only or 3) Deep location only
Symplastic Glomus Tumor 1) Lacks criteria for malignant glomus tumore and 2) Marked nuclear atypia only	Glomangiomatosis 1) Lacks criteria for malignantglomus tumore or glomus tumor of uncertain malignant potential and 2)Diffuse growth, resembling angiomatosis, with excess glomus cells

Table 2: Review of the cases of malignant glomus tumors of extremities including glomus tumor of uncertain malignant potential.

AUTHOR, YEAR	LOCATIÓN, SIZE	DIAGNOSIS	ADYUVANT TREATMENT	RECURRENCE	METASTASIS
Gould et al. 1990	Hand, 2.8 cm	glomangiosarcoma	No	No	No
Fernando et al. 1997	Thigh 0.8 cm	Glomangiosarcoma	No	No	No
Noer et al.1991	Knee 0.6 cm	Glomangiosarcoma	No	No	No
Aiba et al. 1988	Scapula 0.5 cm	Glomangiosarcoma	No	No	No
Folpe et al. 2001	Shoulder 5 cm.	Glomangiosarcoma	No	No	Yes (in the case of the shoulder)
	8 Arms				
	6 fingers				
	1 Wrist				
Khoury et al. 2005	Hand 3 cm	Glomangiosarcoma	Radiotherapy and Chemo-therap	No	Yes
Park et al. 2003	Hand 4.5 cm	Glomangiosarcoma	No	No	No
Watanabe et al 1995	Arm 1 cm	Glomangiosarcoma	No	No	No
Wetherigntonet al 1997	Finger 0.5 cm	Glomangiosarcoma	No	No	No
Rishi et al 2012	Shoulder 0.9 cm	Glomangiosarcoma	No	No	No
Perez de la Fuente et al 2005	Hand 0.5 cm	Glomangiosarcoma	No	No	No
Bolado et al 2017	Hand 5.2 cm	Glomangiosarcoma	Radiotherapy	No	No
Woodward et al 2016	Hand 5 cm	Glomangiosarcoma	No	No	No
Shinwer et al 2000	Scapula 1 cm	Glomangiosarcoma	No	No	No
Kreutz et al 1987	Thigh n/d	Glomangiosarcoma	No	No	Yes (to jaw)
Watanabe et al 1998	Hip n/d	Glomangiosarcoma	No	No	Yes
Baral et al	Left Thumb	Glomus tumor of uncertain malignant potential	No	No	No
2011	6x2cm				
Binesh et al 2012	Scapula 2 cm	Glomus tumor of uncertain malignant potential	Chemotherapy	Yes	Yes , (to the lung)
Luzar et al 2018	Legs 6	Glomangiosarcoma	No	Yes in one case	No
	Arms 4				
	Face 1				
Present case	Forearm 0.6 cm	Glomus tumor of uncertain malignant potential	Radiotherapy	No	No

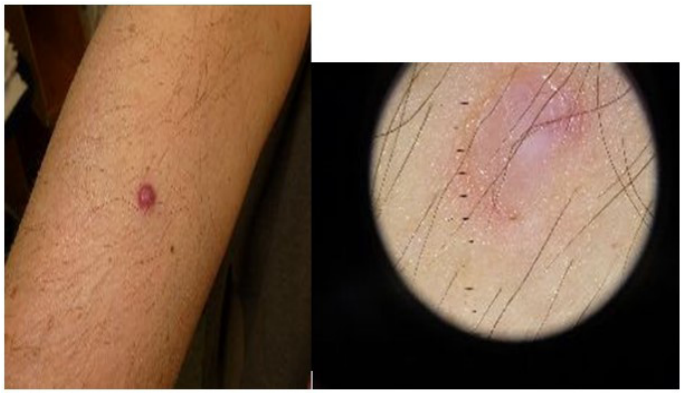

Figure 1 & 2: Initial papular lesion. Dermathoscopy.

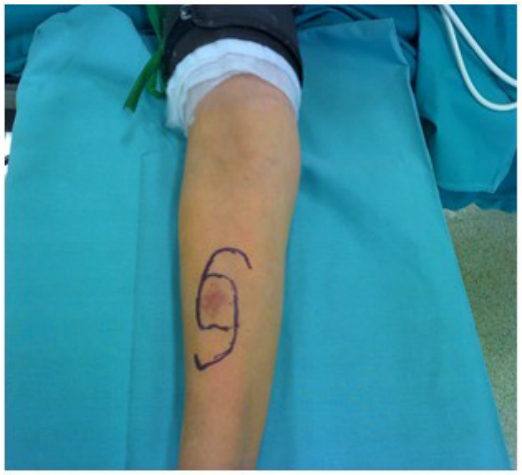

Figure 3: Surgery design: enlargement of surgical margins.

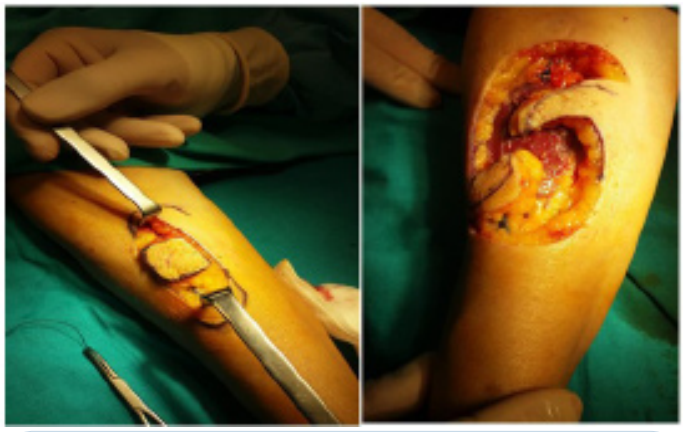

Figure 4 & 5: Block excision, including fascia, muscle and vessel.

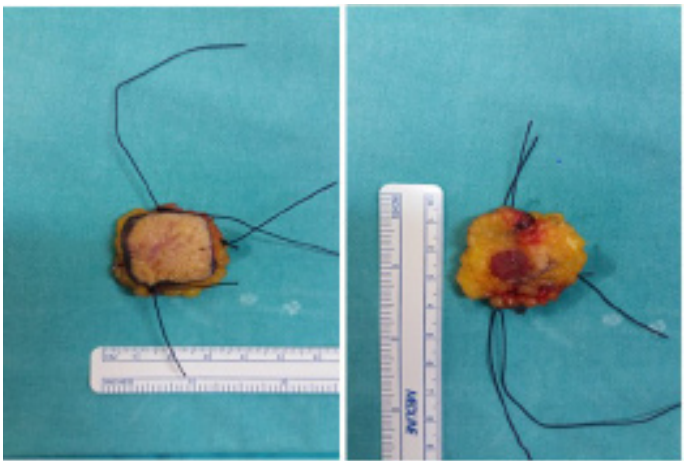

Table 6 & 7: Anatomopathological study piece.

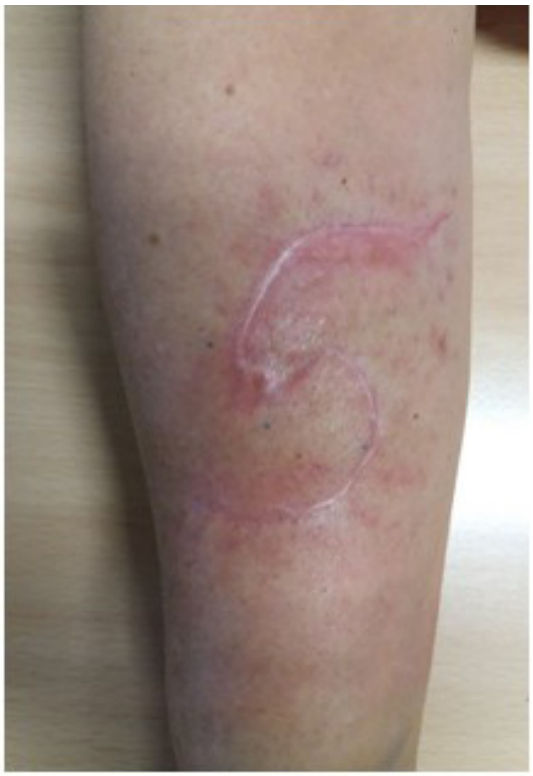

Figure 8: Scar after radiotherapy.

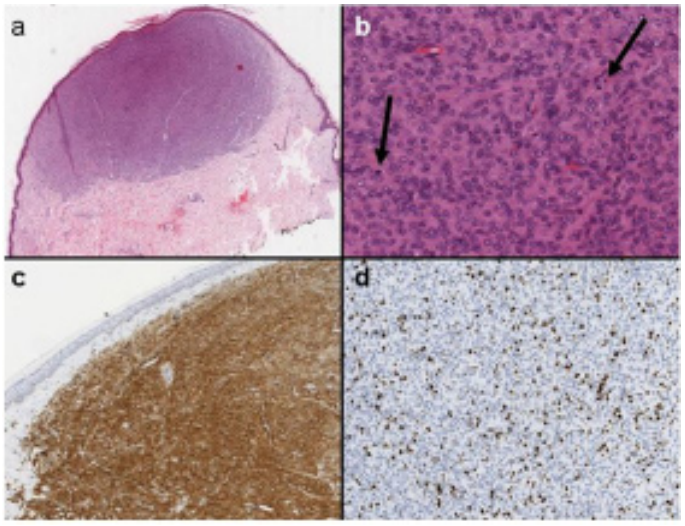

Figure 9: Patology findings: The lesion was located in the dermis, bulging the epidermis (photo 9-a) and had a maximum diameter of 0.5 cm. Histologically, it consisted of a homogeneous proliferation of cells of medium size, rounded or slightly fusiform, with central nuclei without evidence of atypia (photo 9-b). Necrotic areas were not observed. The mitotic index was moderately high, with a count of 6-9 mitosis per 10 high-power fields (photo 9-b, arrows). The immunohistochemical study showed positivity for vimentin and smooth muscle actin (remember that the glomocito cell is a modified muscle cell) (photo 9-c). It was negative for pancytokeratin (AE1-AE3) and CD34 (endothelial marker). The proliferation index, measured with immunostaining for ki67, was relatively high and, in zones, reached 30-35% (photo 9-d). All this was diagnosed as "glomus tumor of undetermined malignant potential (" borderline ")" because it included only one of the criteria for malignancy (excluding cytological atypia, if any) and was a mitotic index greater than 5 × 50 fields of great increase, lacking others (size greater than 2 cm, deep location, subfascial, presence of atypical mitosis or infiltrative pattern) that would have definitively labeled it as malignant (glomangiosarcoma).

Discussion

Glomangiosarcoma is very rare. The first case was reported by Lumley and Stansfeld in 1972, who used the term of malignant glomus tumor to described a lesion located deep to the Achilles tendon in a 24-year-old female with severe and persistent right distal lower extremity pain that finally required an above-knee amputation [1]. The first case series of glomangiosarcoma was reported by Gould et al in 1990. Glomus Tumors (GTs) are uncommon, comprising 1.6% of 500 consecutive soft tissue tumours reported from the Mayo Clinic. The great part of GTs are small, benign tumors that occur in the dermis or subcutaneous tissue of the extremities. 1However, GTs may show unusual clinical features, such as large size, deep soft tissue or visceral location, infiltrative growth pattern or multicentricity became malignancy [10]. Over the years, the malignancy of GTs has been more of a concept than a reality. Although several histologically malignant GTs have been reported, biological confirmation of malignancyin these cases was lacking,1 probably because many were superficial and therefore cured by therapy. A second compounding factor was the fact that the rare malignant GTs that produced metastases lacked a benign glomus component, and hence the accuracy of the diagnosis was questioned. The first report of a clinically malignant (ie, metastatic) GT is that of Brathwaite ann Poppiti [6].

Aiba et al suggested using the term glomangiosarcoma when a sarcomatous component arises in the background of a pre-existing glomangioma [3]. Rodríguez-Justo et al reported a clinicopathological review of 19 cases of glomangiosarcoma and de novo glomangiosarcoma, including their case of glomangiosarcoma arising in benign glomus tumor [4]. Kreutz et al reported the first metastatic glomangiosarcoma in 1987 in a 33-year-old male with a large lesion found superficially on the thigh with metastasis to maxilla [5]. Since then, a few more cases with metastasis have been reported and outcome in most of them was lethal [5-7].

The criteria for malignancy in GTs proposed by Folpe et al., has a main limitation, the fact that they do not reflect the true biological potential of GTs when occurring at sites different from deep soft tissues, such as visceral organs and skin. Furthermore, it has been argued that, due to the significantly smaller size of GTs presenting in the skin in comparison to their deep soft tissue and visceral counterparts, such malignancy criteria are also difficult if not impossible to apply.

The treatment for glomangiosarcoma is complete surgical excision. No radiation or chemotherapy is recommended at this time for primary, recurrent or metastatic disease, although their use had been reported by several authors [8,9].

A glomus tumor of uncertain malignant potential is defined as a glomus tumor with some, but not all, criteria for malignancy and without a known metastasis. the designation of a "uncertain malignant potential" was based on the high proliferative activity, the tumor size and location, and the lack of WHO malignancy criteria such as marked nuclear atypia, necrosis, or atypical mitoses [12].

Prognosis of glomus tumor of uncertain malignant potential is good but the number of cases is small and the follow up relatively short. Metastasizing GTs are rare and according to some reports, Gts of uncertain malignant potential did not metastasize [3]. However, it was not true about a case presented by Binesh et al in 2012 [27] of glomus tumor of uncertain malignant potential raised in scapula and characterized by a relatively large size 2cm and high mitotic activity. and lack of atypical mitotic figures, which recurred three months after surgery with bilateral pulmonary metastasis, they considered it as clinically malignant (metastasizing) atypical GT. Folpe reported that high nuclear grade, infiltrative growth and vascular space involvement were not associated with metastasis, however in Binesh case, vascular invasion was present, even in the initial specimen, which shows that vascular invasion is an ominous finding.

None of the clinicopathological parameters evaluated to date have shown to predict the disease outcome (e.g., local recurrence, development of metastatic spread) in cutaneous or superficial malignant GTs. Furthermore, the currently established malignancy criteria for cutaneous GTs can be difficult to apply mainly due to their smaller size. Likewise, counting mitotic activity per 50 HPFs can often not be accomplished in GTs occurring at superficial locations.

Luzar et al [11] suggest that cutaneous malignant GTs follow a more indolent clinical course than their deep soft tissue counterparts, probably reflecting their earlier detection at superficial sites and their smaller size on detection.

Although it has been described that this type of tumors of uncertain malignant potential, does not metastasize, there is a published case with early recurrence and pulmonary metastasis, so that in this case despite the small size of the lesion, because it was an unplanned surgery with marginal margins we decided to perform a margin expansion surgery with free margins and posterior adjuvant radiotherapy treatment. After three years of follow-up, the patient has not presented local recurrence or metastatic disease.

Conclusion

We believe that in Glomus tumor of uncertain malignant potential it is necessary to perform a surgery with wide margins and to propose adjuvant radiotherapy in case of narrow margins as well as a close and long term follow-up in the same way as if it were a glomangiosarcoma. In case of unplanned surgery is necessary perform a margin expansion surgery followed by adjuvant radiotherapy [34].

References

1. Lumley JS, Stansfeld AG. Infiltrating glomus tumour of lower limb. Br Med J. 1972; 1: 484-485.
2. Gould EW, Manivel JC, Albores-Saavedra J, Monforte H. Locally infiltrative glomus tumors and glomangiosarcomas. A clinical, ultrastructural, and immunohistochemical study. Cancer. 1990; 65: 310-318.
3. Aiba M, Hirayama A, Kuramochi S. Glomangiosarcoma in glomus tumor. An immunohistochemical and ultrastructural study. Cancer. 1988; 61: 1467-1471.
4. Rodríguez-Justo M, Aramburu-González JA, Santoja C. Glomangiosarcoma of abdominal wall. Virchows Arch. 2001; 438: 418-420.
5. Kreutz RW, Christensen RE Jr, Fish LR. Glomangiosarcoma with metastasis to the maxilla. Int J Oral Maxillofac Surg. 1987; 16: 116-118.
6. Brathwaite CD, Poppiti RJ Jr. Malignant glomus tumor. A case report of widespread metastases in a patient with multiple glomus body hamartomas. Am J Surg Pathol. 1996; 20: 233-238.
7. Watanabe K, Sugino T, Saito A, Kusakabe T, Suzuki T. Glomangiosarcoma of the hip: report of a highly aggressive tumour with widespread distant metastases. Br J Dermatol. 1998; 139: 1097-1101.
8. Rishi A, Dulanto F, Chen S. Glomangiosarcoma in the shoulder of a 51-year-old man. Dermatol Pract Conc. 2012; 2: 9.
9. Baral R, Limbu H. Glomus tumor of uncertain malignant potential. Journal of Pathology of Nepal. 2011; 1: 66-68.
10. Lars B. Dahlin, Peter Scherman, Jack Besjakov, Eva Lindberg, David A. Solomon,Andre E. Horvai, Arie Perry. Intraneural glomus tumor of “uncertain malignant potential” and with BRAF mutation in the median nerve – an unusual case. Clinical Neuropathology. 2017; 36: 164-170.
11. Luzar B., Martin B., Fisher C., Calonje E. Cutaneous malignant glomus tumours applicability of currently established malignancy criteria for tumours occurring in the skin Pathology. 2018; 50: 711-717.
12. Tsuneyoshi M, Enjoji M. Glomus tumor: a clinicopathologic and electron microscopic study. Cancer 1982; 50: 1601-1607.

13. Chou T, Pan SC, Shieh SJ, et al. Glomus tumor. Twenty-year experience and literature review. Ann Plast Surg. 2016; 76: 35-40.

14. Gombos Z, Zhang PJ. Glomus tumor. Arch Pathol Lab Med. 2008; 132:1448-1452.

15. Folpe AL, Fanburg-Smith JC, Miettinen M, et al. Atypical and malignant glomus tumors. Analysis of 52 cases, with a proposal for the reclassification of glomus tumors. Am J Surg Pathol. 2001; 25: 1-12.

16. Folpe AL, Brems H, Legius E. Glomus tumors. In: Fletcher DM, Bridge JA, Hogendoorn PCW, Mertens F, editors. WHO Classification of Tumors of Soft Tissue and Bone. 4th ed. Lyon: IARC, 2013; 116-117.

17. Watanabe K, Hoshi N, Tsu-Ura Y, et al. A case of glomagiosarcoma. Fukushima J Med Sci. 1995; 41: 71-77.

18. López-Ríos F, Rodríguez-Peralto JL, Castaño E, et al. Glomangiosarcoma of the lower limb: a case report with a literature review. J Cutan Pathol. 1997; 24: 571-574.

19. Hegyi L, Cormack GC, Grant JW. Histochemical investigations into the molecula mechanisms of malignant transformation in a benign glomus tumour. J Clin Pathol. 1998; 51: 872-874.

20. Kayal JD, Hampton RW, Sheehan DJ, et al. Malignant glomus tumor: a case report and review of the literature. Dermatol Surg. 2001; 27: 837-840.

21. Park J-H, Oh S-H, Yang M-H, et al. Glomangiosarcoma of the hand: a case report and review of the literature. J Dermatol. 2003; 30: 827-833.

22. De Chiara A, Apice G, Mori S, et al. Malignant glomus tumour: a case report and review of the literature. Sarcoma. 2003; 7: 87-91.

23. Khoury T, Balos L, McGrath B, et al. Maligant glomus tumor. A case report and review of the literature, focusing on its clinicopathologic features and immunohistochemical profile. Am J Dermatopathol. 2005; 27: 428-431.

24. Perez de la Fuente T, Vega C, Gutierrez Palacios A, et al. Glomangiosarcoma of the hypothenar eminence: a case report. Chir Main. 2005; 24: 199-202.

25. Cibull TL, Gleason BC, O'Malley DP, et al. Malignant cutaneous glomus tumor presenting as a rapidly growing leg mass in a pregnant woman. J Cutan Pathol. 2008; 35: 765-769.

26. Lancerotto L, Salmaso R, Sartore L, et al. Malignant glomus tumor of the leg developed in the context of a superficial typical glomus tumor. Int J Surg Pathol. 2012; 4: 420-424.

27. Binesh F, Akhavan A, Zahir ST, et al. Clinically malignant atypical glomus tumour. BMJ Case Rep 2013: bcr2012007618.

28. Terada T. Malignant glomus tumor of the foot with obvious neuroendocrine differentiation: a case report with immunohistochemical studies. Pol J Pathol. 2014; 65: 241-247.

29. Dumavandy AA, Anatelli F, Skelsey MK. Malignant glomus tumor arising in a long standing precursor lesion. Am J Dermatopathol. 2016; 38: 384-387.

30. Miettinen M, Paal E, Lasota J, et al. Gastrointestinal glomus tumors: a clinicopathologic, immunohistochemical, and molecular genetic study of 32 cases. Am J Surg Pathol. 2002; 26: 301-311.

31. Zhu YZ, Li WP, Wang ZY, et al. Glomus tumor of uncertain malignant potential arising in the bronchus. J Cardiothorac Surg. 2013; 8: 146.

32. Karamzadeh Dashti N, Bahrami A, Lee SJ, et al. BRAF V600E mutations occur in a subset of glomus tumors, and are associated with malignant histologic characteristics. Am J Surg Pathol. 2017; 41: 1532.

33. Marks LB. Use of normal tissue complication probability models in the clinic." Int J Radiat Oncol Biol Phys. 2010; 76: S10-S19.

34. Yang JC, Chang AE, Baker AR, et al. Randomized prospective study of the benefit of adjuvant radiation therapy in the treatment of soft tissue sarcomas of the extremity. J Clin Oncol. 1998; 16: 197-203.