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Teaching Cases

Symplastic glomus tumor: Report of a challenging lesion with literature review

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ABSTRACT

Glomus tumors are uncommon mesenchymal tumors whose cells closely resemble those of a normal glomus body, and are found most commonly in the hand. Recently, a symplastic form exhibiting marked nuclear atypia, in the absence of any other malignant features, has been described. To date, only 14 cases of symplastic glomus tumor have been reported in the literature; hence, very little information is available about its diagnosis, treatment, and biological behavior.

The case reported here concerns a symplastic glomus tumor occurring in the right index finger of a 62-year-old woman. We reviewed the literature concerning previously reported cases, placing emphasis on the documented biological behavior, treatment, and demographic trend.

Physicians must be aware of this morphological variation of glomus tumor to avoid the mistake of malignancy, which results in over-treatment of the patient.

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Introduction

Glomus tumors are benign tumors whose cells closely resemble those of a normal glomus body [3]. They belong to the group of perivascular tumors, first described by Masson in 1924 [6]. Glomus tumors are uncommon and account for 1–5% of all soft-tissue tumors of the hand [7]. Although they may occur at any age [3], in 90% of the cases, glomus tumors present as sporadic solitary lesions in people aged between 20 and 40 years [6]. The location of a glomus tumor can vary widely. As cutaneous neoplasms, glomus tumors usually occur in the subungual regions of digits or in the deep dermis of the palm, wrist, and forearm [3,6]. However, their occurrence in extracutaneous sites such as bone, nerve, penis, mediastinum, stomach, colon, trachea, and lungs has also been reported in previously published literature [3,6].

Pathological examination reveals that a typical glomus tumor is characterized by a well-circumscribed lesion, consisting of tight convolutes of capillary-sized vessels, surrounded by collars of glomus cells, set in a hyalinized or myxoid stroma. Glomus cells appear typically monomorphous, round, regularly shaped, and with a sharply punched-out rounded nucleus, set off from the amphophilic or eosinophilic cytoplasm [11].

Rarely, when the glomus cells deviate from the foregoing description, “oncocytic”, “intravascular growth”, and “signet ring” changes are seen [11]. Moreover, a symplastic form exhibiting marked nuclear atypia with large hyperchromatic nuclei in the absence of any other malignancy features has been described recently [4].

To date, only 14 cases of symplastic glomus tumor have been documented in the literature [1,2,4,6], and therefore very little is known about the biological behavior and the demographic trend of this unusual lesion. We add to the literature a new case of symplastic glomus tumor occurring in the right index finger of a 62-year-old woman, and provide a literature review to better understand this pathology and to prevent a misdiagnosis of malignancy.

Case report

A 62-year-old woman presented with a 6-month-old bluish spot on the nail of her right index finger and a history of focal tenderness and pain when exposed to cold, pressure, or accidental trauma. Dermatological examination revealed a slightly bluish nail plate and tenderness in her finger (Fig. 1a). Radiographs showed a small scalloped osteolytic defect, with a sclerotic border, in the terminal phalanx of her finger (Fig. 1b).

This clinical appearance was diagnostic for glomus tumor, and therefore the patient underwent a surgical excision of the lesion through a trans-ungual approach (Fig. 1c and d).

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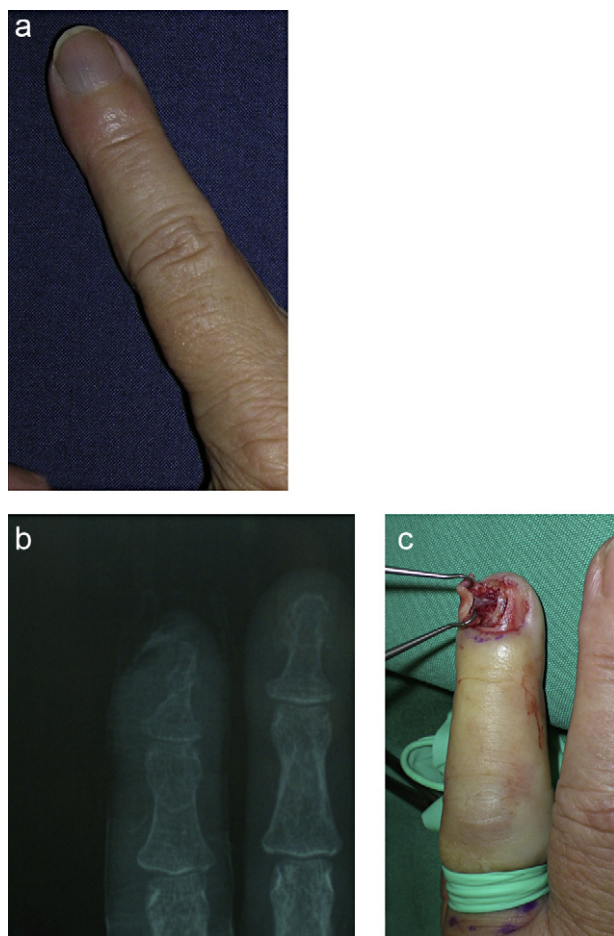


Fig. 1. (a) Physical examination shows a bluish nail plate over the nail of the right index finger; (b) radiogram of the terminal phalanx of the right index finger showing a small scalloped osteolytic defect with a sclerotic border; (c) and (d) intraoperative image of the excision through a trans-ungual approach.

The excised sample consisted of a 1 cm large skin ellipse. On sectioning the ellipse, a 0.7-cm, well circumscribed sub-epidermal nodule was seen.

Histological evaluation showed a dermal tumor with unremarkable overlying epidermis. The tumor was circumscribed but encapsulated and consisted of multiple foci of proliferation of polygonal cells surrounding capillary-sized vessels, and a setting in a myxoid stroma in which some nerve fibers and bone were scattered (Fig. 2a). Most cells showed prominent cytological atypia with nuclear enlargement, pleomorphism, anisonucleosis, hyperchromasia, pseudoinclusions, bizarre nuclei, coarse chromatin, and irregular nuclear membrane (Fig. 2b). Cellularity was moderate, and no necrosis or mitotic figures were identified throughout the neoplasm. On immunohistochemical assay, the neoplastic cells expressed vimentin, actin, and CD34 (Fig. 3a and b); however, no expression was found for S-100 protein. Proliferation index, evaluated with Mib 1/Ki 67 labeling Index, was virtually negative (expressed by less than 1% of the tumor cells) (Fig. 3c).

The symplastic glomus tumor was diagnosed on the basis of the “pericitoma-like appearance” and the immunophenotype. Because of the presence of small foci of neoplasia on a fragment indicated as “bottom of the lesion” and little information about this entity, the patient again underwent a wide re-excision without any residual tumor on subsequent histopathological examination. The patient was found to be disease-free at 6 months of follow-up.

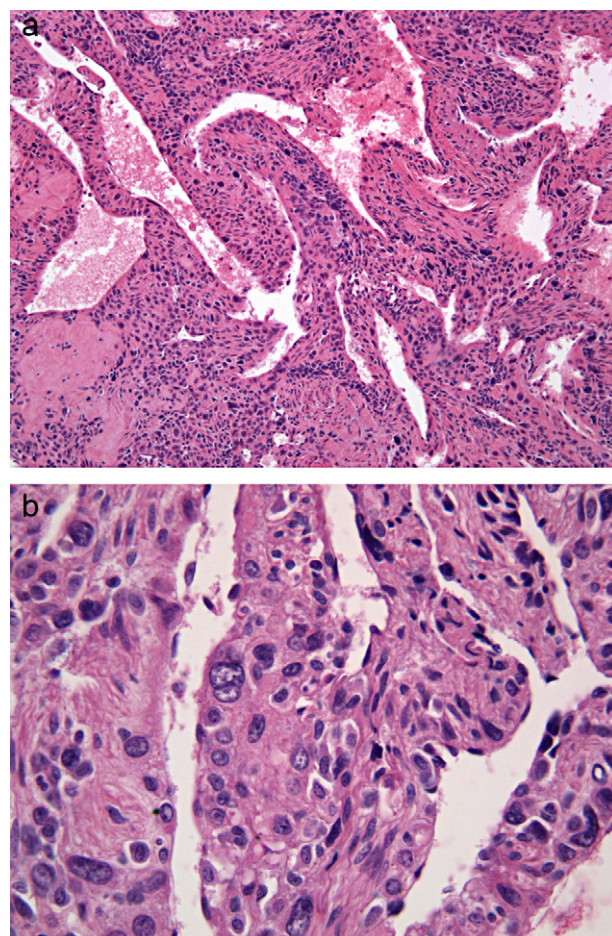


Fig. 2. (a) Symplastic glomus tumor. The photomicrograph shows the multiple foci of proliferation of glomus cells surrounding capillary-sized vessels and setting in a myxoid stroma within which were scattered some nerve fibers and bone (H/E, 100×); (b) note, at high magnification, glomus cells showing prominent cytological atypia with nuclear enlargement and pleomorphism, anisonucleosis, hyperchromasia, pseudoinclusions, bizarre nuclei, coarse chromatin, and irregular nuclear membrane (H/E, 400×).

Discussion

Glomus tumors are benign hamartomas that closely resemble the normal glomus apparatus [7,11].

Glomus tumors are rare and represent less than 2% of soft tissue tumors [3]. They are most commonly known as “painful subcutaneous nodule” and are characterized by a triad of spontaneous pain, tenderness, and cold sensitivity [10]. Additional clinical signs are hypesthesia, muscle atrophy, or osteoporosis [8,11].

In some cases, glomus tumor is undiagnosed because of obscure symptoms, such as chronic pain and hypersensitivity. Therefore, high-resolution magnetic resonance imaging (MRI) is a useful diagnostic method, in addition to radiography and ultrasonography [5,10,11].

The widely preferred treatment is the complete meticulous surgical excision with different available approaches, such as dorsal trans-ungual approach, lateral subperiosteal approach, and Keiper–Litter approach. Choosing an approach depends on the location of the tumor and the risk of iatrogenic nail injury for the nail bed and the matrix. However, tumor recurrence varies from 5 to 50%, depending on surgical procedures and the surgeon's skill [10].

Generally, glomus tumors have a characteristic morphology. They are typically composed of small, uniform glomus cells surrounding capillary-sized vessels and showing benign behavior. The

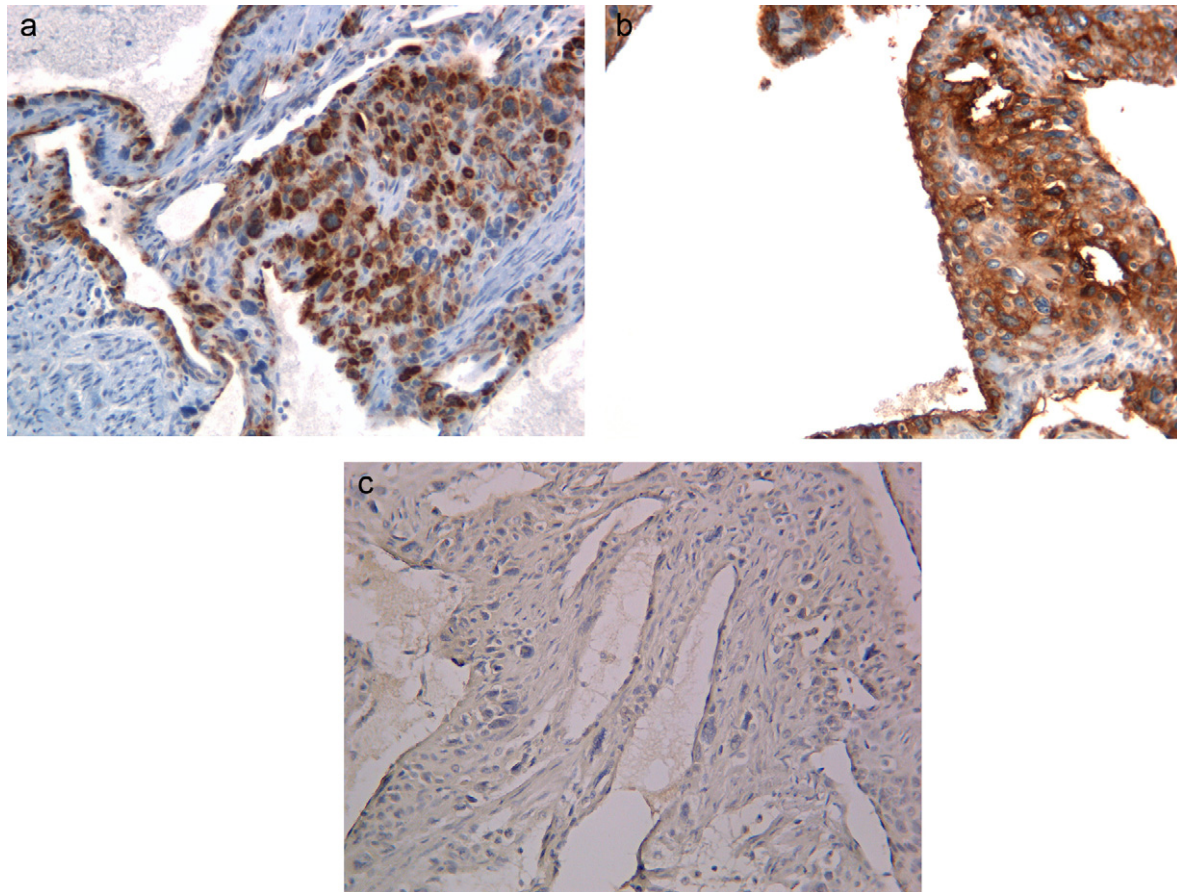


Fig. 3. Immunohistochemistry showing a strong reaction for actin (a) and CD 34 (b), while ki-67 is virtually negative (c) (a–c at 200×).

glomus tumors can also be subcategorized as “solid glomus tumor”, “glomangioma”, and “glomangiomioma” [3], depending on the relative prominence of glomus cells, vascular structures, and smooth muscle components.

Although the most common forms are benign, an atypical or malignant counterpart of this lesion still exists. Folpe et al. [4] investigated 52 cases of unusual glomus tumors, previously diagnosed as “atypical” or “malignant”, and estimated their five-year cumulative metastatic risk. They proposed a classification scheme and criteria to distinguish “malignant glomus tumors”, “glomus tumor of uncertain malignant potential”, “glomangiomatosis”, and “symplastic glomus tumor”. Malignant glomus tumors occur in deep locations and are characterized by a size of more than 2 cm, or atypical mitotic figures, or moderate to high nuclear grade and ≥ 5 mitotic figures/50 HPF (high power field). Glomus tumors of uncertain malignant potential have high mitotic activity and superficial location. Glomangiomatosis encompasses tumors with histological features of diffuse angiomatosis and excess glomus cells. Symplastic glomus tumors show high nuclear grade in the absence of any other malignant feature.

Using this classification scheme, metastasis was observed in 38% of tumors fulfilling the criteria for malignancy [4].

According to Folpe’s criteria, WHO defines symplastic glomus tumor as a tumor exhibiting marked nuclear atypia, in the absence of any other significant feature of malignancy [3].

Nuclear atypia, which is a characteristic feature of this lesion, is related to degenerative change or senescence rather than malignant transformation. It is similar to that seen in other benign stromal tumors, i.e., symplastic leiomyoma, symplastic hemangioma,

and “ancient” change in schwannomas, melanocytic nevus, and blue nevus [1,6]. Some authors have suggested that nuclear atypia may be due to the accumulation of heterochromatin, associated with DNA inactivation [1].

The recognition of typical glomus tumor areas is the most important clue for the diagnosis of a symplastic glomus tumor. Typical glomus tumor areas can be usually found at the periphery of the lesion. However, some typical features revealed by histological examination, such as the prominent branching capillary vasculature, the perivascular arrangement of the tumor cells, the generally uniform cell shape and size, the presence of distinct cell borders, and the uniform cellular investment by basement, suggest a glomus tumor [4]. In certain difficult cases, the immunohistochemical assay for smooth muscle actin and type IV collagen can be useful for the diagnosis [4].

We agree with Kamarashev et al. [6] regarding the significant overlap between the term “symplastic glomus tumor” and “epithelioid glomus tumor”. Therefore, the previous reports of “epithelioid glomus tumor” by Pulitzer [9] and Yanagi [12] must also be referred to as “symplastic glomus tumor”.

Table 1 displays a summary of the 14 previous reports on symplastic glomus tumor in the literature [1,2,4,6]. The average age was recorded as 42.8, ranging from 16 to 83 years. Females are most commonly affected, and fingers are the most common sites of occurrence with seven subungual locations. The demographic trend appeared to be similar to that of classic glomus tumor, as well symptoms, although they are available only in two reports [2,6]. The radiographic findings, disposable in our case, are similar to those of a classic glomus tumor.

Table 1
Review of the literature for simplastic glomus tumor.

Ref.	Age	Sex	Site	Size (cm)	Preexisting glomus	Margin status	Follow-up length	Re-excision	Recurrence
6	78	F	Finger (subungual)	NA	Y	NA	NA	N	N
	52	F	Finger	0.5	N	Neg	4y	N	N
	23	F	Buttock	1.3	Y	Neg	10y	Y, x2	Y, 3y
	55	M	Arm	0.4	Y	NA	13y	Y, x2	Y, 10y
	67	F	Finger	0.5	Y	NA	13y	N	N
4	78	M	Arm	4	N	NA	3y	N	N
	34	F	Thigh	1.8	Y	NA	Lost		
	16	M	Finger (subungual)	NA	N	P	Lost		
	23	F	Toe	NA	Y	NA	Lost		
	25	F	Finger (subungual)	0.3	Y	P	20y	N	N
1	83	F	Finger	0.7	Y	Neg	NA	N	N
	44	F	Finger (subungual)	0.4	N	Neg	NA	N	N
2	45	F	Finger (subungual)	0.3	NA	NA	1y	NA	N
	38	M	Finger (subungual)	0.3	NA	NA	14mo	NA	N
Present case	62	F	Finger (subungual)	0.7	N	P	6mo	Y	N

Ref.: reference; Y: yes; N: no; NA: not available; Neg: negative; P: positive; mo: months; y: years.

Among the 15 cases, we could see only two recurrent tumors with an average recurrence rate of 13.3%; rates of recurrence have been reported to range between 4–15% (5) and 5–50% (10). However, 15 cases constitute a very small series to evaluate this feature.

The treatment of choice for symptomatic symplastic glomus tumor is surgical excision. Some authors have suggested that recurrence may not be due to incomplete excision but also to pre-existing synchronous satellite lesions missed during surgery [5].

In our case, on the basis of the previous biopsy and in the absence of sufficient data on the biological behavior of glomus tumors, a wide re-excision, with preservation of the distal phalanx and nail bed, was performed to remove a residual lesion.

Finally, striking nuclear atypia in the absence of any other malignant features is a well recognized event in glomus tumor [1]. However, it can be a challenge for inexperienced pathologists [2], and it can be difficult for the surgeon to manage this unusual “diagnosis”.

Therefore, more reports on this rare entity must be published to achieve a better diagnosis and to improve care of the patients.

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