An atypical localization of glomus tumor in the leg

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ABSTRACT
Extradigital localizations of glomus tumors (GTs) remain rare and can often lead to missed or delayed diagnosis due to nonspecific symptoms. In this article, we report a case of a GT with a rare localization in the proximal third of the lower leg.

Introduction
Glomus tumors (GTs) are rare, mostly benign neoplasms but often lead to disabling conditions for the patient. The precise origin remains unclear. However, it is suspected that GTs develop from glomus bodies sitting at the dermo-hypodermic junction [1]. They are important for regulating local blood flow and temperature of the integument [2]. The first case of a GT was described by Wood in 1812 as a ‘painful subcutaneous tubercle’ [3]. Although Wood’s report is compatible to the clinical signs of GTs, no pathological confirmation was performed. In 1924, Masson first published a histopathological description of GTs [4].

Extradigital GTs have been reported several times in the past but are limited to single case reports only. They usually occur in regions with high density of glomus bodies [2]. GTs mostly appear in solitary forms, multiple occurrences remain unusual and differ from the common cases in both clinical and histological presentation [5]. They often occur in a sporadic form [5] but if there is a family history, GTs seem to be preferably inherited in an autosomal dominant form [6]. The most common localization is the subungual area of the digits, but also the deep dermis of the palm, wrist and forearm are described to be common regions [2,7–9]. Other anatomical localizations remain rare. It has been reported that GTs account for 1.6% of all soft tissue tumors of the upper and lower extremity [9,10]. A retrospective review encompassing 20 years of experience revealed that GTs of the lower extremity share only 14% of all diagnosed GTs [11]. While there is a female predominance for subungual GTs to be observed, extradigital localizations show a predilection to the male sex [12].

Digital GTs clinically present with the triad of excruciating pain, tenderness and hypersensitivity to cold [3]. Classically, pain is not proportional to the size of the tumor. Because of these symptoms and the rare localization, GTs of the lower extremity can mimic other pathologies and are therefore difficult to diagnose.

In this article, we present a rare case of a GT located in the pretibial area of the knee. The aim of this article is to raise more awareness to the glomus tumor as a potential diagnosis for pain in the soft tissue.

Case report
A 32-year old male patient presented a 3-year long history of persistent pain in his left knee. He reported an injury of his left knee during a semi-professional football activity 4 years ago. Ever since the incident, he complained of severe pain and hyperesthesia. He described the pain as burning and occurring spontaneously with exacerbations by slight touch and movement. The patient could identify the exact point of the
most intense pain medial and just caudal the patella (Figure 1). These symptoms were debilitating and affected his daily routine and his sleep.

Various treatments, inter alia physiotherapy, local and systemic analgesics as well as injection of cortisone did not alleviate the symptoms. A knee arthroscopy with partial medial meniscectomy and debridement of cartilage did not lead to clinical improvement. The patient was then referred to the chronic pain department, who referred the patient to plastic surgery for suspected injury to the infrapatellar branch of the saphenous nerve.

Physical examination revealed no signs of inflammation or injury of the knee. No muscle atrophy or weakness was observed. The sensibility was intact, no hyperesthesia for temperature was documented. Tinel’s sign was positive at the level of the pes anserinus with radiating pain into the posterior and inferior area of the patella.

A sensitive electroneurography of the left saphenous nerve revealed no abnormalities. Further examination with ultrasonography detected a pressure-sensitive round subcutaneous mass measuring 1.5 cm in diameter without perilesional hypervascularization. An ultrasonography-guided blockade with lidocaine 1% led to symptomatic relief for several hours.

A subsequent surgical exploration of the symptomatic medial area of the left knee revealed a well-encapsulated, round and red-livid mass measuring 1 cm in diameter (Figure 2). No pathological signs, e.g. neuroma, in the immediate vicinity were found. The histopathological examination showed isomorphic cell nuclei and lack of atypical mitosis (Figure 3(A,B)). Immunohistochemical analysis demonstrated positivity for smooth muscle actin (SMA) and focally distributed CD34 and negativity for S100 and Ki67, pan cyto keratin b (panCKb) and desmin (Figure 3(C,D)). Taking into account of the anamnestic, clinical and histopathological findings, the diagnosis of a glomus tumor was confirmed. After surgical excision, the patient reported improvement of his clinical condition and pain relief after 2 weeks. No recurrence was reported to date after 2 years.

Discussion

GTs are rare and benign neoplasms arising in the dermo-hypodermic junction and suspected to develop from glomus bodies functioning as thermoregulators through arteriovenous anastomoses [1]. They are typically located in the subungual areas of the digits, mostly described in the hands [2]. GTs are often misdiagnosed initially and can lead to severe and disabling symptoms unproportionate to the nature of the tumor.

Macroscopically GTs typically appear as blue-red nodules and show a subcentimeter tendency in size [4]. GTs are typically composed of three components in varying proportions: glomus cells, blood vessels and smooth muscle cells [13]. Depending on the percentages of these elements, three types of glomus tumors can be distinguished: the solid glomus tumors, glomangiomas and glomangiomyomas [14]. According to Lee et al., glomangiomas are more common in extradigital GTs than in subungual areas of the digits [15]. The immunohistochemical profile include a high rate of SMA and typically focal CD34 positivity [16] reflecting the perivascular phenotype [13,16] and rare immunohistochemical reaction to S100-protein and negativity to desmin [13,17,18].

Malignant GTs are rare with a little evidence in the literature regarding treatment and outcomes [9].
Malignant GTs and GTs of uncertain malignant potential can be locally aggressive and have the potential to metastasize [19].

GTs in the knee remain rare [1]. To our knowledge, there is a paucity in the literature describing a GT in the proximal pretibial region. This pathology can be a diagnostic challenge for the surgeon. This can expose the patient to unnecessary procedures before understanding the nature of the lesion. Unfortunately, GTs are not often initially considered and largely neglected as a differential diagnosis in the lower extremity despite severe symptoms. Anagnostou et al. reported that the average number of years for establishing the diagnosis after the onset of symptoms is 6.5 years [20]. Individual cases reported a delay of 20 and 40 years, respectively [20,21].

Clinical examination is usually inconclusive. Our patient suffered from tenderness and severe pain whereas cold hypersensitivity as the third element of the pathognomonic triad was absent. The missing cold hypersensitivity, however, is supported by previous case reports where the typical triad of symptoms described in subungual glomus tumors is not commonly reflected in its entirety when it comes to extradigital glomus tumors [22]. Also, clinical palpation, which is already difficult in the fingertips due to the small size of GTs, is rendered impossible in the lower extremity with its significantly thicker soft tissue envelope.

Although not specific, dermoscopy could complement the differential diagnosis of GT in extradigital locations. Dermoscopic presentation can revealed homogeneous, structureless lesions including a central purple area, a peripheral whitish homogeneous area and in some cases multiple peripheral telangiectasias on the surface [23–25].

As clinical signs are mostly inconclusive, specialists often rely on imaging. To date, however, there are no specific imaging tools recommended in the literature to confirm GTs. Several imaging examinations have been reported to guide the diagnosis. Angiography, magnetic resonance imaging (MRI) with T2-weighted images, computed tomography (CT) or ultrasonography have been used to detect the nodule [1,26,27].

MRI remains a useful imaging modality with 82–90% sensitivity in detecting the lesion [28]. In the

Figure 3. Histological and immunohistochemical findings. (A) The tumor consists of a well-defined and encapsulated tumor (H&E staining; magnification ×1.5). (B) The majority of the tumor presented a solid pattern. In other areas, tumorous cells clustered around thin, branching, and dilated vessels on a myxoid stroma (H&E staining; magnification ×10). (C) High-power examination revealed that the glomus tumor cells exhibited monotonous cells with hyperchromatic nuclei and pale cytoplasm (H&E staining; magnification, ×40). (D, E) Immunohistochemistry showed tumor cells respectively to be strong and diffuse positive for SMA, focal positive (arrow) for CD34 (magnification x10) and negative for Ki67.
study proposed by Ham et al., MRI imaging had a 100% positive predictive value for finding small mass lesions as a preoperative test [29].

As a natural consequence, patients with lower limb GTs may suffer unnecessary intractable symptoms accompanied by enhanced healthcare expenses due to inadequate diagnostic and therapeutic measures. A protection against pain by physical inactivity may lead to vasomotor disturbances and even atrophy of the affected limb [30]. Moreover, the pain may prompt costly redundant psychiatric consultations, multiple interventions and even amputation [26]. Although no drastic interventions were carried out in our case, our patient still underwent a time-consuming trial of conservative therapy with numerous consultations that may have been avoided by earlier and directed diagnostics.

In our experience, the diagnostics of choice was a cost-efficient ultrasonography. But MRI seems to have a higher sensitivity for GTs. Surgical excision with histopathologic examination is a reliable method of treatment. A thorough and complete resection of the GT is crucial with variable recurrence rate reported in the literature [9,11,27]. We recommend suspecting extradigital GTs as a differential diagnosis of unclear untreatable pain of long-lasting onset.

Conclusions

Glomus tumors of the pretibial area of the knee represent a rare localization of extradigital GTs. This uncommon occurrence together with the nonspecific and often incomplete triad of symptoms composed of pain, tenderness and hypersensitivity to cold may lead to missed or significantly delayed diagnosis of extradigital GTs. Raising the physician’s awareness and clinical suspicion for a GT is of paramount importance. The authors strongly believe that sonography provides a reliable, fast and cost-efficient first-line diagnostic tool in many unclear extremity conditions like GTs and should be followed by surgical exploration and biopsy with histopathological examination to confirm the suspected diagnosis. Complete excision is the therapy of choice which often results in positive outcomes with immediate relief of symptoms.

Ethical approval

An approval from the Ethics Committee of our institution was not requested.

Statement of human and animal rights

No experiments on animals were performed for this study. No experimental procedures were performed in any human subject for this study.

Statement of informed consent

Informed consent was obtained from the patient of the study.

Disclosure statement

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

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