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30
31 **Highlights**

- 32 • Patients presenting symptoms of paroxysmal, throbbing pain exacerbated when exposed to a cold
33 environment must be tested using all three provocation tests specific to the glomus tumor and
34 transillumination test.
35 • T2-weighted MRI scan typically shows a well-demarcated hyperdense lesion and must be confirmed
36 with further histopathology examination following excision.
37 • Periodic follow-up for recurrences, adverse effects, and impaired daily functioning must be done to
38 provide comprehensive care for the patient.
39 • This article provides a real-life example of successful rare disease identification and treatment. It also
40 provides a guideline that may serve as future guidance on diagnosis and treatment.

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1 **ABSTRACT**

2

3 **Background:** Glomus tumors are rare benign hamartomas of the glomus body that occur mostly – though not
4 limited to - the distal phalanxes of the digits. This article provides a real-life example of successful rare disease
5 identification and treatment. It also provides a guideline that may help serve as future guidance on diagnosis
6 and treatment.

7 **Case:** A 41-year-old male came into our hospital presenting a chief complaint pain of episodes of throbbing
8 pain, which has occurred spontaneously on the left thumb for the past two years. The pain was said to worsen
9 in the past two weeks. The patient was positive for Hildreth's, Love's pin, and cold sensitivity tests. The previous
10 x-ray showed no abnormalities in the left thumb. MRI found a hyperdense subungual lesion in the dorsal
11 interphalangeal joint of the left thumb. We then performed an excision using the transungual approach.
12 Histopathological findings found a relatively well-circumscribed lesion of the glomus apparatus absent of
13 abnormal mitosis and necrosis. Two months after the excision, the patient reported no symptoms of recurrency,
14 nail deformity, or other adverse outcomes.

15 **Conclusion:** Patients typically present a chief complaint of chronic paroxysmal throbbing nail pain that persists
16 for years, increases following exposure to cold environments, and is disproportionately exacerbated due to the
17 slightest touch. Hildreth's, Love's Pin, and cold sensitivity Test were special examinations that elicit or suppress
18 pain. As with most benign tumors, complete excision usually yields good results. Adequate knowledge about
19 diagnostic methods will help patients achieve early intervention and resolvable.

20

21 **Key Words:** *Case Report, Glomus Tumour, Hand Surgery, Benign Tumour, Rare Diseases*

22

Accepted

1 INTRODUCTION.

2 Glomus tumors are rare benign hamartomas of the glomus body that occur mostly – though not limited to - the
3 distal phalanxes of the digits.^{1,2} Patients often present to the clinic with symptoms of paroxysmal pain in tissues
4 below the nail.³⁻⁵ These severity of the pain is proportionally correlated to the size of the tumor. The pain is
5 exacerbated when touched or exposed to cold environments.³⁻⁵ Studies reported that glomus tumors only form
6 about 1-5% of all hand tumors.² In most patients, initial pain was generally tolerable due to its paroxysmal and
7 non-severe nature, However, as the tumor grows, the pain may be felt more frequently, with each episodes
8 being progressively more painful. Furthermore, patients with chronic pain may develop a higher threshold when
9 tolerating pain. This creates a delay from the patient's side in seeking treatment.

10 Studies reported a mean length of time from initial symptom onset to diagnosis of around 7 years.⁶ Aside from
11 delays from the patient's side, it is reasonable to suspect our current understandings about the disease. The
12 lack of understanding and experience due to less to no contact to this disease during physician's training period
13 may well contribute to the number of misdiagnoses. Albeit its lack of emergency, glomus tumors may reduce
14 patient's quality of life, as they may be limited to perform specific movements such as gripping.

15 A knowledgeable and keen physician should be able to suspect a glomus tumor based on presented clinical
16 symptoms. This is due to the disease's generally unique and distinguishable symptoms. Additionally, several
17 specific tests may be performed to ensure the physician of the diagnosis. A transillumination test and MRI scan
18 may also be performed on the affected digit.^{7,8} However, a negative transillumination and MRI scan result do
19 not necessarily exclude the possibility of glomus tumors when specific symptoms are present.^{7,9-11} Prompt
20 treatment may restore lost quality of life by allowing the patient to function similar to before this tumor was
21 present. In this article, we provided a case of successful glomus tumor diagnosis and removal. This case is not
22 common, and therefore may serve as a learning material for medical students. This article is written while
23 adhering to CARE guidelines.¹² This article will also propose a diagnostic scheme to help physicians diagnose
24 glomus tumors.

1 CASE PRESENTATION

2 A male in his 40s presented a chief complaint of pain under the nail of his left thumb in the past two years prior
3 to coming to our hospital, which worsened in the past two weeks. The pain was isolated and only felt on his left
4 thumb. The patient described the pain as episodes of throbbing pain that occur spontaneously. The patient felt
5 that pain episodes were more prevalent during certain times of the year, and the throbbing felt greater when
6 exposed to cold air from the refrigerator. The patient reported that he had previously sought care from multiple
7 doctors over the two years but to no avail. There are neither accompanying symptoms nor significant past,
8 family, or social history. There is also no history of trauma in the said location. Upon inspection, we found no
9 discoloration, swelling, or deformity. However, tenderness was present and can be localized into the dorsal side
10 of the distal interphalangeal joint. Albeit localized right within the joint, passive and active movement was not
11 restricted. The presentation of paroxysmal, throbbing pain, exacerbated following exposure to a cold
12 environment, warrants further provocation and transillumination tests, which, in our case, show positive results.

13 Insert Figure 1 here.

14 The patient came into our clinic with left thumb x-ray results from a scan he underwent after an appointment
15 with his previous doctor. The x-ray showed no abnormalities in the left thumb and, in general, his left hand. A
16 complete blood count found no significant results. Contrast-enhanced T2-weighted MRI scan found a well-
17 demarcated 1.7 cm x 0.6 cm x 0.6 cm hyperdense lesion in the dorsal interphalangeal joint of the left thumb
18 separate from the bone (Figure 1).

19 Initial findings and epidemiologic study made us suspect an early-formed ganglion cyst because it is one of the
20 most prevalent soft tissue masses in hand surgery.¹³ However, the feeling of pain was not typical of ganglion
21 cysts and warrants further investigation. This makes our working diagnosis the glomus tumor of the hand, and
22 further pathological examination was required to confirm this diagnosis.

23 Insert Figure 2 here.

24 We performed a surgical excision of the benign lesion using the transungual approach. This approach was
25 chosen due to the location of the tumor as shown by MRI. Under local digital block, a finger tourniquet was used
26 to exsanguinate the finger subjected to surgery. The surgical site was then prepared antiseptically. An incision
27 was made along the lateral aspect of the proximal nail fold, followed by nail plate extraction. An exposed nail
28 bed was then incised longitudinally right above the lesion site, allowing tumor exposure. Following the excision
29 of the encapsulated tumor, the nail bed was then sutured, and the lifted nail was replaced on top of the nail bed.
30 The nail was then sutured with the proximal nail fold, and wound dressing with gauze and antibiotic ointment
31 was changed daily until the wound was dry, after which it was kept open.

32 Following surgery, we successfully extracted two greyish-white tissues sized 0.4 cm x 0.2 cm x 0.2 cm and 0.3
33 cm x 0.2 cm x 0.2 cm, respectively. These tissues were then immersed in a 10% NBF (neutral buffered formalin).
34 The excised tissue's pathological findings (figure 2) correspond to the conventional morphology of the type II
35 glomus tumour.

36 Two months following the excision, we monitored for any possibility of recurrence or post-treatment adverse
37 effects. The patient reported no recurrence of symptoms such as pain, tenderness, or local inflammation. We
38 also observed no nail deformity or any other adverse outcomes. The patient can return to his work without any
39 meaningful limitations. He can now carry things that require extensive use of his thumb symmetrically with his
40 left and right hand. Provocation tests are performed again, showing negative results.

41

1 DISCUSSION.

2 In our study, the patient presented symptoms which correlates to two of the three tests specific for diagnosis of
3 glomus tumor: paroxysmal subungual throbbing pain exacerbated when exposed to cold environments. These
4 symptoms present in 90-100% of patients, as mentioned in several other studies which reports 10 or more
5 patients with digital glomus tumor.^{14,15} Patients may also present with other symptoms such as nail disfigurement
6 or discolor.^{14,15} However, these were not present in our patient. Following confirmation through physical and
7 supporting examination, we decided that excision via transungual approach is the best surgical method due to
8 the tumor being more centrally-located. Albeit being the method which offers the best visualization and
9 exposure, this technique is the most disruptive to the nail bed, increasing chances of complications such as
10 inaesthetic nail, nail ridging, and nail splitting.^{14,16,17} Other options include the lateral and volar approach, which
11 were more restricted in visualization but are less disruptive towards the nail bed.^{14,18,19}

12 Structurally, a glomus apparatus consists of a single afferent arteriole and efferent venule, connected through
13 multiple arteriovenous anastomoses (Suquet-Hoyer canals), altogether encapsulated with α -actin containing
14 muscle fibers and glomus bodies.²⁰ The afferent arterioles were formed by endothelium, internal elastic lamina,
15 and pre-glomus muscle cells, while efferent venules comprised a thin endothelium layer.²⁰ The glomus apparatus
16 physiologically functions as a contractile neuro-myo-arterial unit that autonomically thermoregulates body
17 temperature through shunting and maximizing blood flow within the cutaneous microvasculature.²⁰ On exposure
18 to cold temperatures, a marked increase in norepinephrine results in constriction of blood vessels, shunting
19 blood flow towards the apparatus.²¹ Decrease of peripheral blood flow causes reduction of convection-mediated
20 heat loss. Hyperplasia of either one of the components within the glomus apparatus (i.e., blood vessel, glomus
21 body, muscle) will create a condition known as a glomus tumor.²² Generally, there are three types of glomus
22 tumors based on their histopathological differences. Albeit strictly differentiated into distinct types, there are
23 cases where patients may present multiple histopathological types concurrently.^{23,24} The three main
24 classifications were: (1) hyaline-mucoid type, (2) solid type, and (3) angiomatous type.^{23,24} Hyaline-mucoid type
25 glomus tumour is characterized by increased hyalinized connective tissue interspersed within islands of glomus
26 cells and vascular spaces.^{23,24} Solid-type glomus tumour is characterized by glomus cell masses and reduced
27 vascular and muscle space.^{23,24} This type was previously called the 'typical' glomus tumor histology. An increase
28 in intracapsular vasculature characterizes the angiomatous glomus tumor and is the rarest among the three
29 types.^{23,24}

30 Although glomus apparatuses can be found in various parts of the body, a typical glomus tumor occurs as a
31 solitary, benign lesion typically located on subungual tissues of the digits.¹ Patients typically present a chief
32 complaint of chronic paroxysmal throbbing nail pain, which persists for years, as it is often ignored or,
33 sometimes, misdiagnosed.³⁻⁵ This pain increases following exposure to cold environments and is
34 disproportionately exacerbated due to the slightest touch.³⁻⁵ In some cases, the tumor may present together
35 with a bluish-pink nodule or longitudinal nail splitting.^{4,5}

36 Insert figures 3 and 4 here.

37 Owing to the relatively unique symptoms, the differential diagnosis of glomus tumor must be added following
38 the presentation of paroxysmal throbbing pain, disproportionate pinpoint pain, and cold hypersensitivity, as
39 shown in Figure 3. Physicians generally perform three special examinations that aim to elicit or suppress pain
40 following exposure to certain conditions: Hildreth's Test, Love's Pin Test, and cold sensitivity Test. Love's pin
41 test is performed by applying pressure to the mass using a rounded-tip object such as a ballpoint pen, pinhead,

1 or the end of a paperclip.²⁵ Love's pin test is positive if the pain is elicited after applying pressure, commonly
2 demonstrated refractory withdrawal of hand.^{25,26} Love's pin test is also commonly used to roughly localize the
3 lesion by identifying areas exhibiting the most severe pain.²⁶ Hildreth's test is performed by exsanguinating the
4 affected digit using a tourniquet applied at the base of the digit.²⁷ The physician will then observe any signs of
5 reduction in pain and tenderness, indicating a positive Hildreth test.²⁷ A surge of sudden pain may occur
6 following the release of the tourniquet. Giele (2002) observed that this test was 92% sensitive and 91% specific
7 to glomus tumors.²⁷ Reduced or absence of pain by repeating Love's pin test following application of tourniquet
8 (sharpened Hildreth's test) also indicates a positive result.²⁶ Cold sensitivity test exposes the affected digit to
9 cold environments, usually by applying an ice pack or cubes directly above the suspected lesion site. Elicitation
10 of pain indicates a positive cold sensitivity test.²⁸ These tests can be seen in Figure 4.

11 Some studies also recommended the use of a transillumination test.⁷ The test is performed by placing a
12 flashlight on the palmar side of the affected digit and then looking for any inconsistencies in opacity within the
13 nail plate and bed.⁷ This method is an easy, non-invasive, cost-effective adjuvant diagnostic tool.⁷ In addition to
14 specific physical examinations, glomus tumors can be diagnosed using high-resolution magnetic resonance
15 imaging (MRI). In a contrast-enhanced MRI scan, a typical glomus tumor is a hyperintense lesion with a well-
16 demarcated border.⁸ However, it must be noted that a negative MRI result on a clinically suspected glomus
17 tumor patient does not exclude the possibility of a hidden tumor within the digits.⁹⁻¹¹

18 Differential diagnoses include ganglion cysts, subungual melanoma, and subungual squamous cell carcinoma.
19 However, ganglion cysts should be characterized as a non-painful lump except if they compress a nearby
20 nerve.²⁹ In our case, the lesion was found to be more centrally-located and is not situated in a location highly
21 possible for nerve compression.³⁰ Patients with ganglion cysts may also report preceding traumatic event or
22 repetitive stretching of nearby capsular and ligamentous structure which stimulates production of tissue
23 hyaluronic acid.^{31,32} T2-weighted MRI of ganglion cysts may show hyperdense lesion(s) similar to glomus
24 tumour. However, lesions are usually situated above joints.³⁰ Subungual melanoma was also a possible
25 differential diagnosis. However, subungual melanoma tends to manifest nail discoloration, which was not
26 present in our patient.³³ As they are more malignant, lesions which had long durations since onset such as what
27 was seen in our case should include bone involvement, nail onycholysis, and erosion/ulceration of the nail
28 bed.^{34,35} This is not present in both results from our patient's X-ray and MRI scan. Similar to subungual
29 squamous cell carcinoma, lesions which had long durations since onset usually present larger mass with bony
30 involvement, nail onycholysis, nail dystrophy, and other more destructive symptoms which were not present in
31 our patient.³⁶ Keratotic/verrucous lesion may also be present on the nail bed following nail plate loss.³⁶

32 Insert Figure 5 here.

33 As with most benign tumors, complete excision usually yields good results. There are several approaches to
34 excision: the transungual, lateral, and volar approaches (shown in Figure 5).^{1,17-19,37} A transungual approach
35 generally involves an incision along the lateral aspect of the proximal nail fold to allow nail plate extraction.
36 Another longitudinal incision will then allow the excision of the tumor. The nail bed will then be sutured again,
37 and the lifted nail will be replaced on top of the nail bed. A lateral approach involves. The transungual approach
38 generally provides better exposure to the tumor, increasing certainty towards complete excision with the
39 expense of nail deformity due to massive manipulations.¹⁷ Transungual approach is generally used for the
40 typical centrally-situated subungual glomus tumour. A lateral approach involves a lateral high incision to the
41 side nearer the tumor. The incision was then extended distally to cover the pulp.¹ The incision was then followed

1 by a deep dissection, exploring subperiosteally to the distal phalanx, therefore raising a dorsal flap of the nail
2 matrix, nail bed, and nail plate in one single unit, therefore keeping the nail bed-to-plate integrity.¹ The magnitude
3 of elevation will depend on the proximity of the tumor.^{1,37} A modification to this technique is the lateral
4 subperiosteal approach, which omitted further incision towards the pulp.³⁷ This approach is advantageous due
5 to being less time-consuming and protects the nail against post-surgery deformity.³⁷ However, studies reported
6 that this approach might sometimes cause incomplete excision and early tumor recurrence. This approach is
7 generally used for a more laterally-situated subungual glomus tumor.¹⁷ The volar approach involves an incision
8 on the palmar side of the digits and is used only when the mass is situated more towards the palmar or volar
9 side.^{18,19}

10 Insert Figure 6 here.

11 Based on the literature review and our personal experience in this case, we propose a diagnostic and treatment
12 workflow, as shown in Figure 6. We suggest performing all provocation tests alongside transillumination test
13 even when only one symptom of the triad is present, especially on patients with a history of glomus tumor. The
14 provocation procedures are relatively easy and cheap, sparing the patient of further loss.

15 Although the typical glomus tumor often occurs as a benign solitary nodule in the digits, it is anatomically
16 possible for a glomus tumor to occur in other parts of the body, as other parts contain glomus bodies, too. These
17 glomus tumors outside of the digits usually present themselves with malignant-like characteristics such as being
18 multinodular and large, presenting atypical mitotic figures, infiltrative, and can metastasize.^{38,39} These types of
19 glomus tumors have a higher recurrence rate following excision.³⁹ Although this study reports a successful rare
20 tumor removal, data regarding long-term (>12 months) recurrency or adverse effects follow up was not
21 available. Literature reported that recurrence occurs in up to 18% of cases.⁴⁰ However, only tumors reoccurring
22 after 24 months post-excision can be regarded as true recurrence rather than pseudo-recurrence which occurs
23 due to inadequate excision.⁴¹

24 In conclusion, glomus tumors are rare benign hamartomas of the glomus body that occur mostly – though not
25 limited to - the distal phalanxes of the digits. Patients typically present a chief complaint of chronic paroxysmal
26 throbbing nail pain that persists for years, increases following exposure to cold environments, and is
27 disproportionately exacerbated due to the slightest touch. Hildreth's, Love's Pin, and cold sensitivity Test were
28 special examinations that elicit or suppress pain. We suggest performing all provocation tests and
29 transillumination test even when only one symptom of the triad is present, especially on patients with a history
30 of glomus tumor. The provocation procedures are relatively easy and cheap, sparing the patient of further loss.
31 As with most benign tumors, complete excision usually yields good results. Adequate knowledge about
32 diagnostic methods will help patients achieve early intervention and resolvent.

33 Upon follow up, the patient stated an almost 100% functional daily activity recovery. The patient reported that
34 he is satisfied with the results, both cosmetically and functionally. Provocation tests specific for glomus tumour
35 was redone and found negative.

36

1 **SUMMARY - ACCELERATING TRANSLATION**

2 Glomus tumors are rare benign hamartomas of the glomus body that occur mostly – though not limited to - the
3 distal phalanxes of the digits. Patients typically present a chief complaint of chronic paroxysmal throbbing nail
4 pain that persists for years, increases following exposure to cold environments, and is disproportionately
5 exacerbated due to the slightest touch. Hildreth's, Love's Pin, and cold sensitivity Test were special
6 examinations that elicit or suppress pain. We suggest performing all provocation tests and transillumination test
7 even when only one symptom of the triad is present, especially on patients with a history of glomus tumor. The
8 provocation procedures are relatively easy and cheap, sparing the patient of further loss. As with most benign
9 tumors, complete excision usually yields good results. Adequate knowledge about diagnostic methods will help
10 patients achieve early intervention and resolutent.

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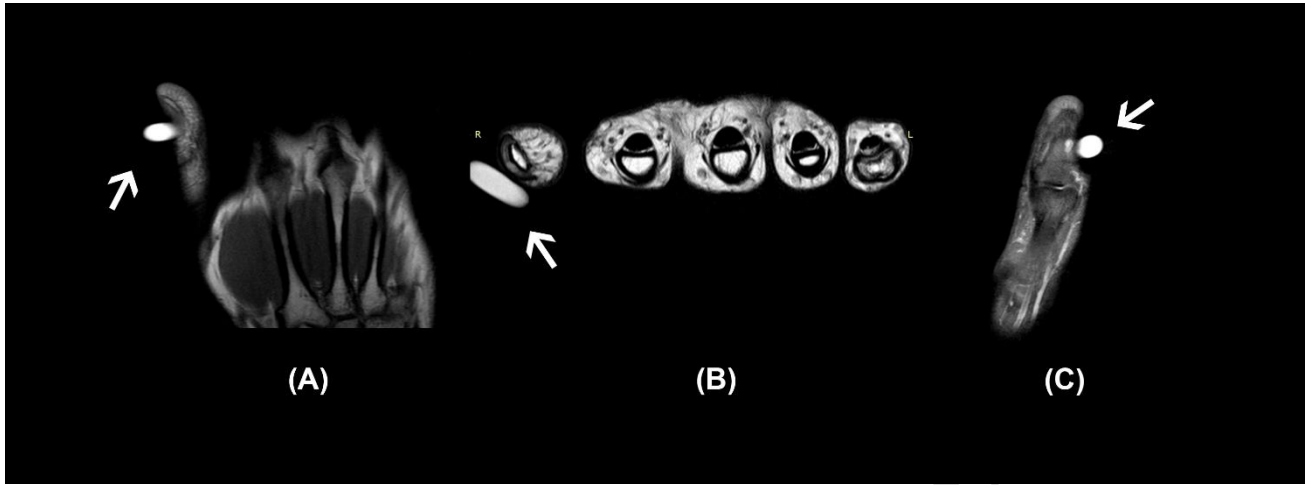
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1 **FIGURES AND TABLES.**

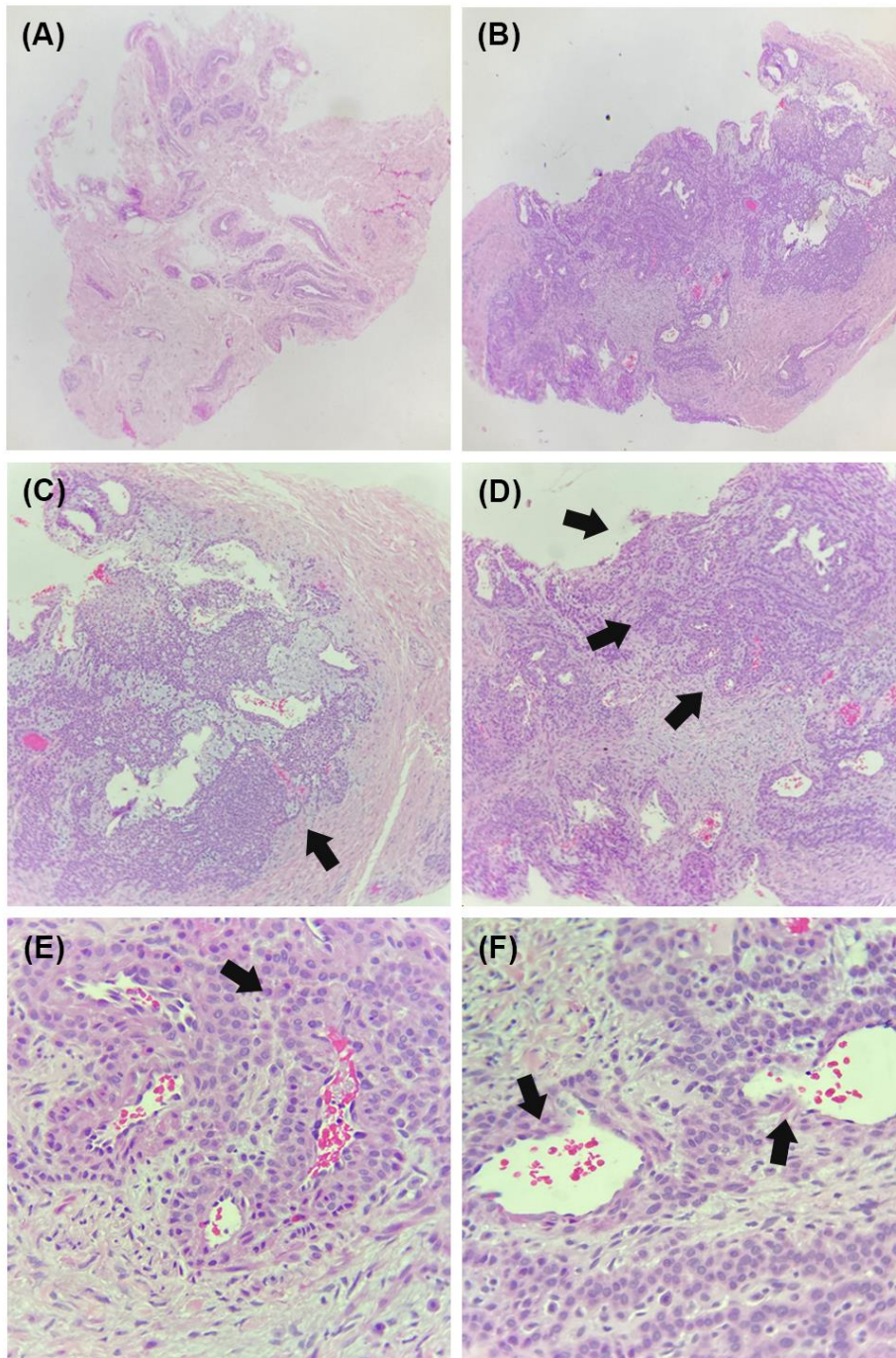
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3 **Figure 1.** Contrast-Enhanced T2-Weighted MRI Scan; (A) Coronal, (B) Axial, and (C) Sagittal Sections of Left
4 Hand (figure by authors)



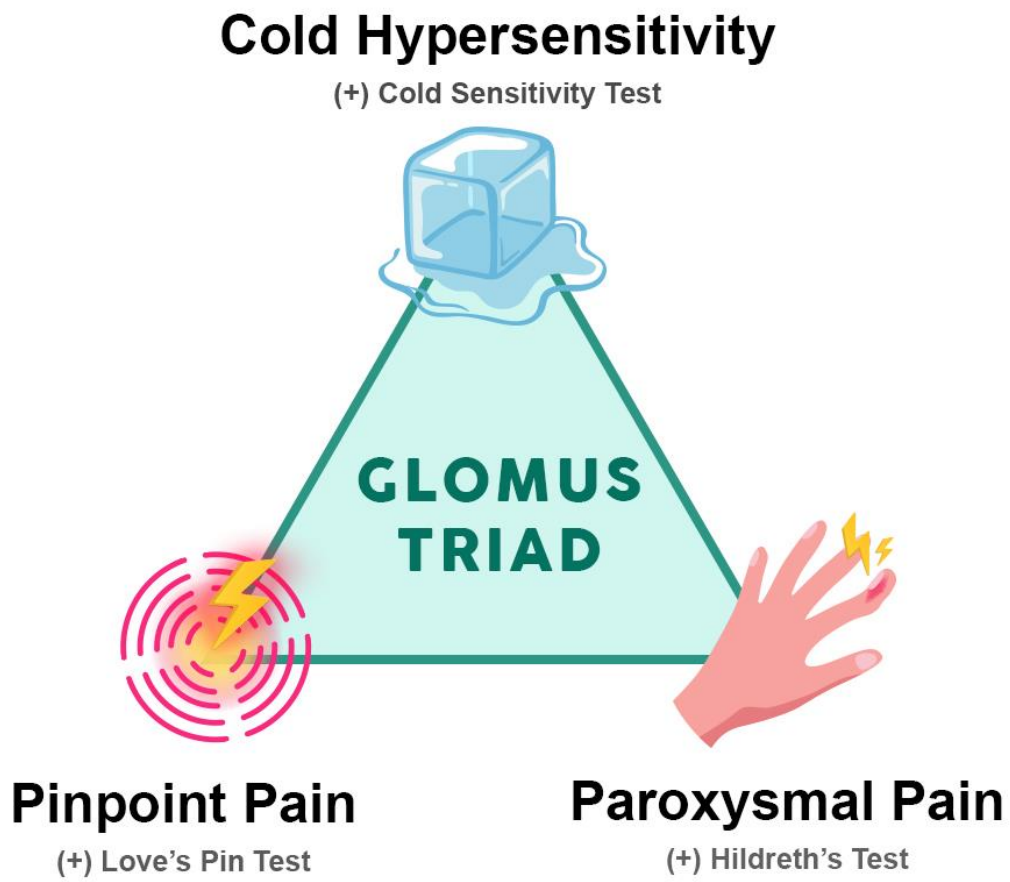
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1 **Figure 2.** Histopathological Findings (A and B); Sample view under 40x magnification; (C and D) A sample view
 2 under 100x magnification shows a relatively well-circumscribed lesion with a solid nest and cuffing;
 3 under 400x magnification, showing uniform rounded cells with pale eosinophilic and amphophilic
 4 cytoplasm, relatively sharp-defined cell border, centrally-located nucleus (arrow), surrounded with myxoid
 5 stroma; (F) Sample view under 400x magnification, showing that some cells (arrow) surround small and ectatic
 6 blood vessels, creating a staghorn appearance. There were no signs of abnormal mitosis and necrosis (figure
 7 by authors)



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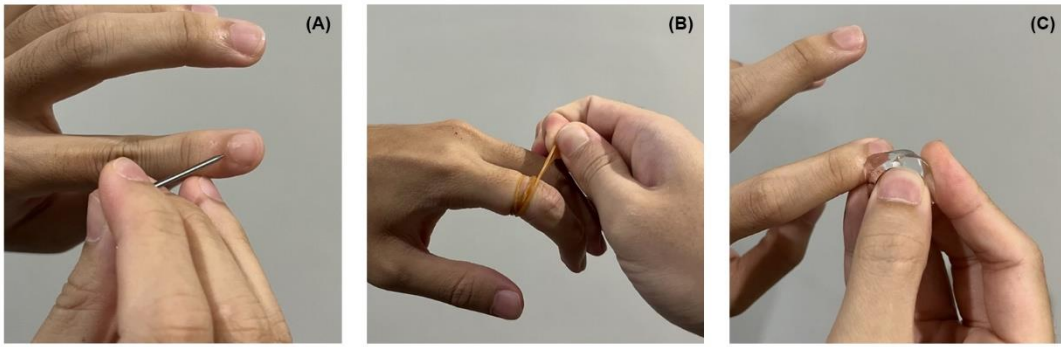
- 1 **Figure 3.** Glomus Triad: Cold Hypersensitivity (Elicited with cold sensitivity Test), Paroxysmal Pain (Elicited
2 with Hildreth's Test), and Pinpoint Pain (Elicited with Love's Pin Test) (figure by authors)



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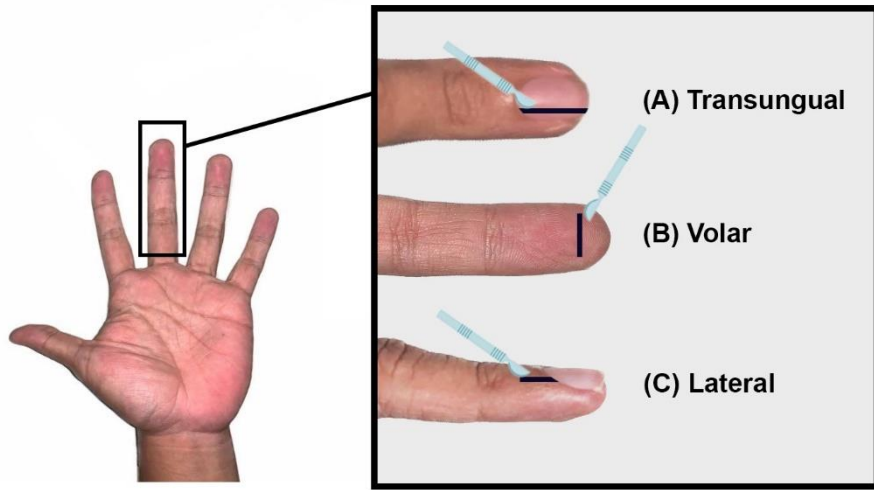
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1 **Figure 4.** Provocation Tests: (A) Love's pin test, (B) Hildreth's test, (C) Cold sensitivity test (figure by authors)



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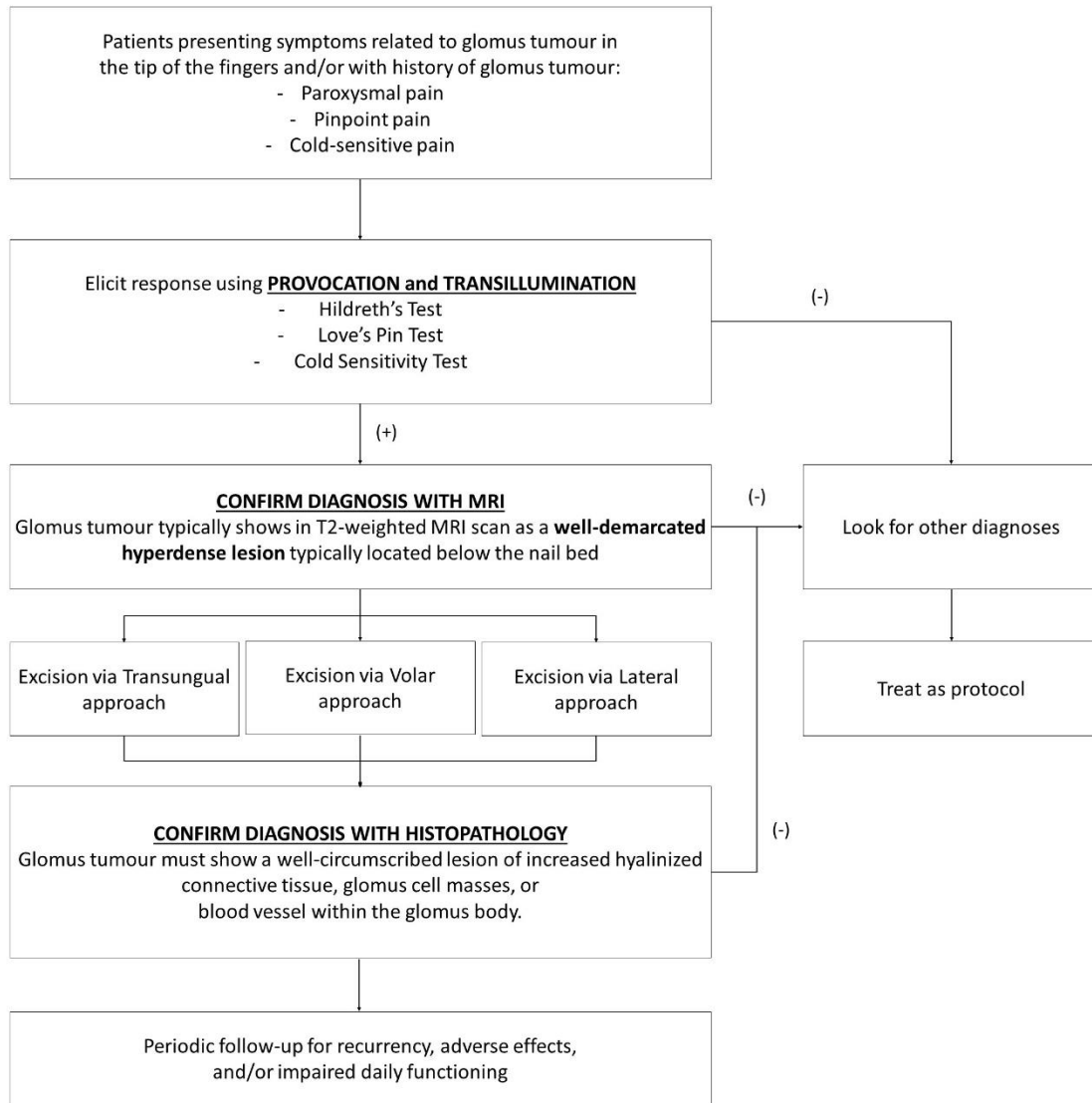
- 1 **Figure 5.** Various Approaches in Surgical Excision of Digital Glomus Tumour (A) Transungual Approach, (B)
- 2 Volar Approach, (C) Lateral Subperiosteal Approach (figure by authors)



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1 **Figure 6.** Diagnostic and Therapeutical Algorithm for Glomus Tumours



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1 **Table 1.** Key Symptoms and Diagnostic Findings

Key Symptoms
<ul style="list-style-type: none"> • Chief complaint of subungual pain at left thumb. • Pain was progressive (onset of two years, worsened in past two weeks). • Pain was exacerbated when exposed to cold air from the refrigerator or under cooler weather. • Pain can be localized in the dorsal side of the distal interphalangeal joint. • History of trauma was denied. • Significant past medical history, family history, and social history was denied.
Key Diagnostic Findings
<ul style="list-style-type: none"> • Patient was positive of Hildreth's, Love's pin, cold sensitivity, and transillumination test. • X-ray scan found no abnormalities. However, contrast-enhanced T2-weighted MRI scan found a 1.7 cm x 0.6 cm x 0.6 cm hyperdense lesion. • Location based on clinical localization and MRI warrants excision via transungual approach.

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