SAGE Open Medical Case Reports
Volume 11: 1–4

DOI: 10.1177/2050313X231193984
journals.sagepub.com/home/sco
Sage

A case of solitary digital glomus tumor associated with neurofibromatosis type 1

Koichiro Yanai[1], Tsuyoshi Tajika[2], Takuro Kuboi[1], Yuhei Hatori[1], Takahiro Umeyama[1], Shinsuke Arisawa[1], Ayaka Katayama[3], Takaaki Sano[3] and Hirotaka Chikuda[1]

Abstract

An association between glomus tumor and neurofibromatosis type 1 has been reported. It is characterized by multiple tumors and young age at onset. The early diagnosis of neurofibromatosis type 1 is important because it is associated with a high rate of malignancy. A 25-year-old man presented to our hospital with left index finger pain that had persisted for 6 years. Physical and imaging findings suggested a benign soft-tissue tumor. Surgery was performed, and the tumor was pathologically diagnosed as glomus tumor. In this case, the patient with a young-onset glomus tumor was suspected of having neurofibromatosis type 1. An additional medical examination led to the diagnosis of unrecognized neurofibromatosis type 1. We experienced a case in which the onset of a glomus tumor led to the diagnosis of neurofibromatosis type 1. Comorbid neurofibromatosis type 1 should be kept in mind when glomus tumors are diagnosed.

Keywords

Neurofibromatosis type 1, glomus tumor, complications, solitary, diagnosis

Date received: 15 May 2023; accepted: 25 July 2023

Introduction

Glomus tumors are benign tumors that account for 1%–5% of soft-tissue tumors of the hand and are most common in women in their 30s–50s.[1,2] Neurofibromatosis type 1 (NF1) is an autosomal dominant genetic disorder caused by mutations in the tumor suppressor gene *NF1*.[3–5] Its prevalence is 1 in 2,500–5,000 of the population.[3–5]

The association between glomus tumor and NF1 was first reported in 1938, and several case series have been published since then.[6–9] To date, it has been reported that the probability of a glomus tumor complicating NF1 is approximately 5% and that this complication is characterized by a tendency toward multiple tumors and a young age at onset.[5,10,11] The early diagnosis of NF1 is important because it has a high rate of malignancy.[5,12] Many reports have focused on the characteristics of glomus tumors associated with patients with NF1,[3,10,11,13] but there are no reports describing a case in which the onset of a glomus tumor led to the diagnosis of NF1. We experienced a case in which the onset of a glomus tumor led to the diagnosis of NF1.

Case report

A 25-year-old man presented to our hospital with left index finger pain that had persisted for approximately 6 years. Tenderness was observed on the index finger of the ulnar side of the lateral paronychium; however, there was no redness or swelling in the same area. The distal interphalangeal joint range of motion was preserved. The pain was aggravated by cold stimulation. A plain radiograph of the left index finger showed no morphological changes in the bone (Figure 1(a) and (b)). Contrast-enhanced MRI showed a nodular lesion with low T1 (Figure 2(a)), high T2/Short tau

[1]Department of Orthopaedic Surgery, Gunma University Graduate School of Medicine, Maebashi, Gunma, Japan
[2]Graduate School of Health Sciences, Gunma University, Maebashi, Gunma, Japan
[3]Diagnostic Pathology, Gunma University Graduate School of Medicine, Maebashi, Gunma, Japan

Corresponding Author:
Tsuyoshi Tajika, Graduate School of Health Sciences, Gunma University, 3-39-22, Showa-machi, Maebashi, Gunma 371-8511, Japan.
Email: tajika@gunma-u.ac.jp

inversion recovery (STIR) (Figure 2(b)), and contrast effect on the ulnar side under the left index fingernail (Figure 2(c)).

Based on the physical and imaging findings, a benign soft-tissue tumor (e.g., glomus tumor) of the left index finger was suspected. Surgery was performed under axillary block anesthesia. An incision was made along the ulnar margin of the left index fingernail, and the subungual area was dissected to reach the distal phalanx (Figure 3). When the nail plate and nail bed were lifted and expanded, a mass of approximately ϕ3–4 mm was found between the nail bed and the distal phalanx, which was excised. The tumor was pathologically examined. Hematoxylin and eosin (HE) staining showed glomus cells with small round nuclei and acidophilic cytoplasm proliferating in an alveolar configuration. Immunostaining was positive for CD34 and smooth muscle actin (Figure 4(c)), but desmin staining was negative. Based on these findings, a diagnosis of glomus tumor was made.

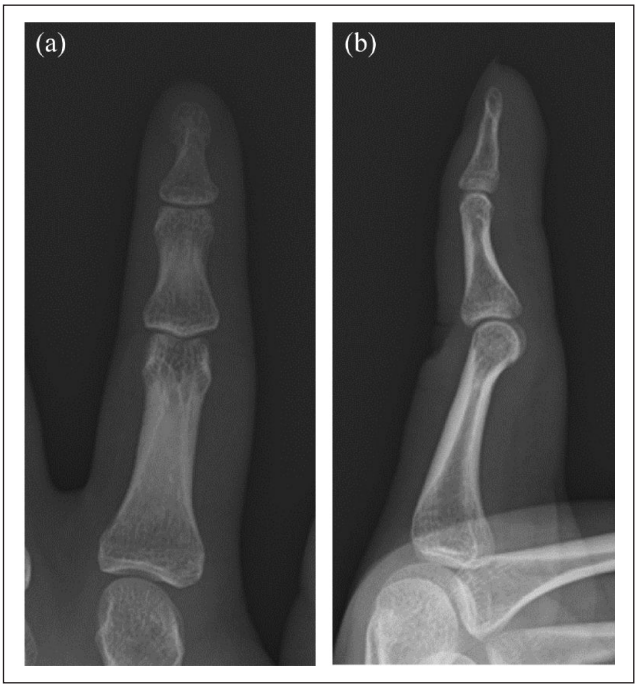

Figure 1. Plain radiograph of the left index finger showed no morphological changes in the bone. (a) Anteroposterior view and (b) lateral view.

Since this case involved a young-onset glomus tumor, we suspected an NF1 complication and performed a detailed physical examination and medical interview. The physical examination revealed numerous well-demarcated brown macules (café-au-lait spots), ranging in size from the tip of a little finger to the size of a chicken egg, from the thoracic abdomen to the back (Figure 5(a) and 5(b)). A soft tissue mass (neurofibroma) the size of an index finger was also noted on the left upper buttock (Figure 5(c)). In addition, an interview revealed a family history of NF1. Based on these findings, the patient met the clinical diagnostic criteria for NF1.

The comorbid NF1 lesions were evaluated. A detailed examination of the trunk and extremities revealed no suspicious lesions. Brain MRI showed no signs of a brain tumor or optic nerve glioma. In addition, electrocardiography and echocardiography were performed to evaluate the circulatory system, but revealed no abnormalities. In this case, there were no lesions that would have required early therapeutic intervention. However, multiple iris nodules (Lisch nodules) were observed, and thoracic scoliosis with a Cobb angle of approximately 15° was found (Figure 6).

After surgery, the finger pain improved, and there has been no evidence of recurrence for approximately 1 year since the operation. Complications of NF1 were also carefully monitored. No central or peripheral neurologic symptoms were observed, and there were no neoplastic lesions on the trunk or extremities. We will continue to monitor the patient for the development of a recurrent glomus tumor and other complications associated with NF1.

Discussion

We experienced a case in which the onset of a solitary glomus tumor led to the diagnosis of NF1. At the time of the

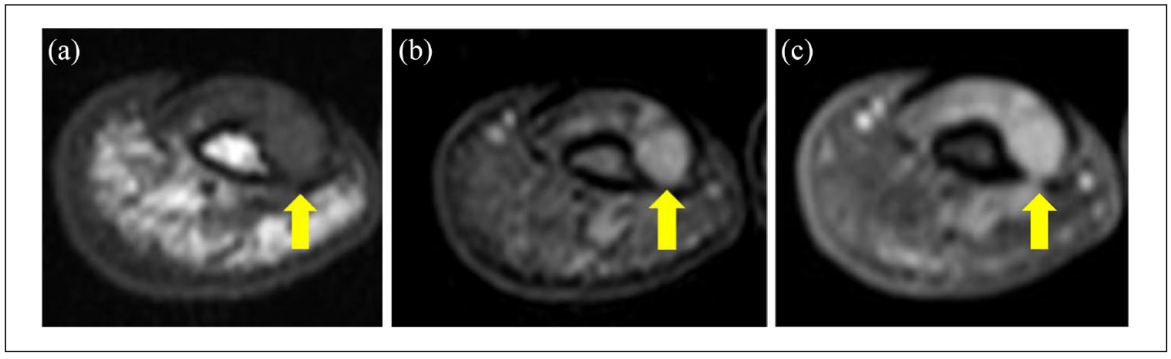

Figure 2. Contrast-enhanced MRI showed a nodular lesion with low intensity on T1, high intensity on T2/STIR, and contrast effect on the ulnar side under the left index finger nail. (a) T1 axial, (b) STIR, and (c) Contrast-enhanced axial.

diagnosis of glomus tumor, we examined the patient with the possibility of NF1 in mind and were able to diagnose NF1.

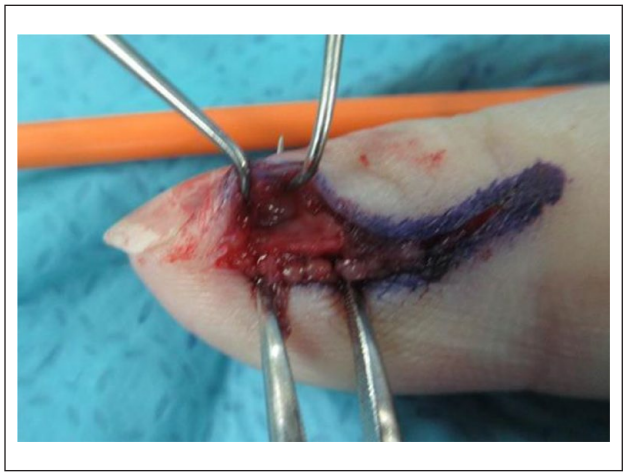

Figure 3. The nail plate and nail bed were lifted and expanded, and a mass of approximately ϕ3–4 mm was found between the nail bed and the distal phalanx.

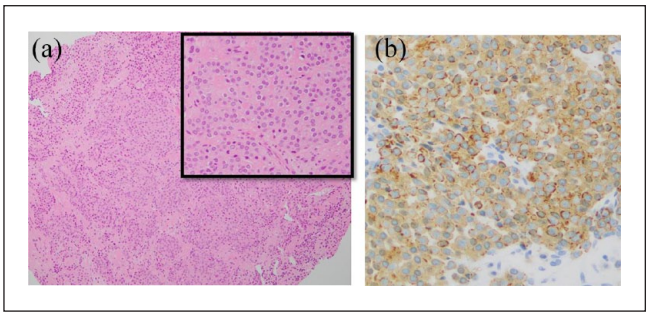

Figure 4. (a) Glomus cells with small round nuclei and acidophilic cytoplasm proliferating in alveolar configuration. Hematoxylin and eosin staining, original magnification 100×, 200× (inset). (b) Immunostaining was positive for smooth muscle actin. Immunostaining, original magnification 200×.

Glomus tumors are benign tumors of the vascular system that arise from the glomus organ, which regulates blood flow in the skin concentrated in the fingers and toes.[1,2] Glomus tumors are usually solitary, and cases of multiple glomus tumors in the general population are very rare.[14] NF1 is characterized by café-au-lait spots and neurofibromas, with various symptoms throughout the body.[3,4] The early diagnosis and evaluation of complicated lesions are important because the rate of malignancy is approximately four times higher than that of healthy individuals.[5,12] Among them, malignant peripheral nerve sheath tumors, which are said to occur in 10% of cases, and the 5-year survival rate is reported to be 15%–50%.[15] Other lesions, including brain and spinal cord tumors and ocular lesions (e.g., glioma opticis), and less frequently, cardiovascular lesions (e.g., pulmonary artery stenosis and aneurysms), should also be kept in mind.[4]

Several studies have reported an association between NF1 and glomus tumors.[8,9] In 2009, Brems et al. reported a genetic link between NF1 and glomus tumors based on a genetic analysis.[3] They showed that germline and somatic *NF1* mutations and RAS-MAPK hyperactivation were observed in NF1-associated glomus tumors, but no similar changes were observed in sporadic glomus tumors. In this report, they showed a genetic link between NF1 and glomus tumors and reported that a loss of function due to mutation in *NF1* is crucial in the pathogenesis of glomus tumors in NF1. To date, it has been reported that the probability of glomus tumor as a complication of NF1 is approximately 5% and the complication is characterized by a tendency toward multiple tumors and young age at onset.[5,10,11] Although this case was monogenic, the onset of the disease when the patient was in his teens suggested that the glomus tumor was associated with NF1.

This case was left without medical attention due to the lack of subjective symptoms, although he was aware of the skin rash. There are many asymptomatic complications in the early stages of NF1. Therefore, it is expected that there are a certain number of other cases, such as ours, that develop NF1 which are left undiagnosed and untreated. An early

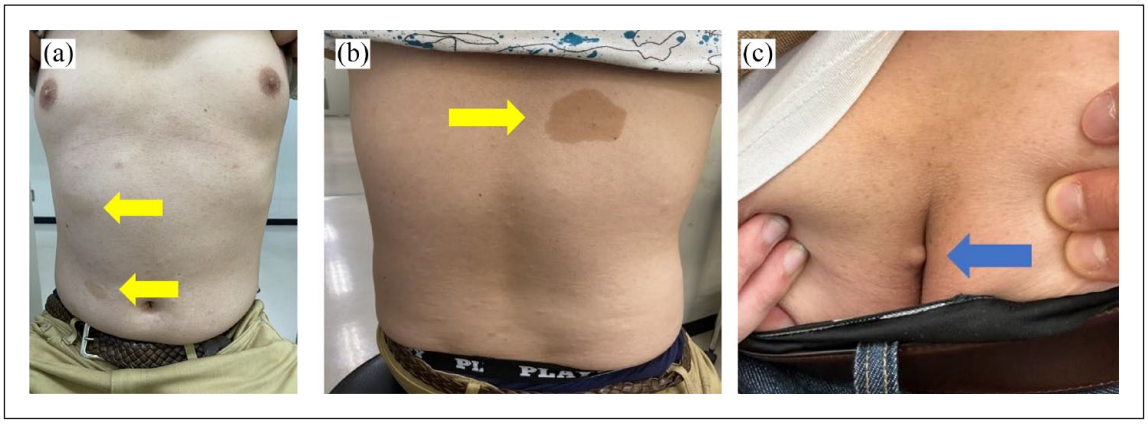

Figure 5. Multiple brown macules and soft masses, thought to be café-au-lait spots and neurofibroma were observed. (a) Thoracic abdomen, (b) Back, (c) Upper buttock.

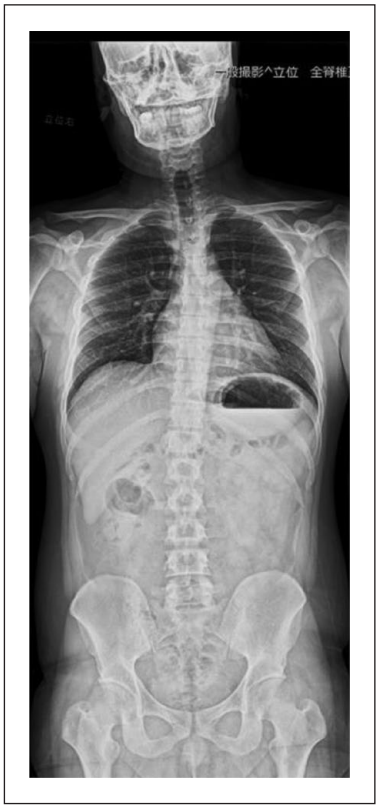

Figure 6. Anteroposterior plain radiograph shows scoliosis with a Cobb angle of approximately 15°.

diagnosis of NF1 is important because there are many complications that can have a major impact on daily life. Therefore, it is necessary to understand the relationship between NF1 and glomus tumors and to search for complications when NF1 is diagnosed.

Conclusion

We experienced a case in which the onset of a glomus tumor led to the diagnosis of NF1. It is important to keep the possibility of comorbid NF1 in mind when a glomus tumor is diagnosed.

Acknowledgements

None.

Declaration of conflicting interests

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.

Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed consent

Written informed consent was obtained from the patient(s) for their anonymized information and accompanying images to be published in this article.

ORCID iD

Tsuyoshi Tajika https://orcid.org/0000-0003-1021-5315

References

1. Rettig AC and Strickland JW. Glomus tumor of the digits. *J Hand Surg Am*. 1977;2:261–265.
2. McDermott EM and Weiss AP. Glomus tumors. *J Hand Surg Am*. 2006;31(8):1397–1400.
3. Brems H, Park C, Maertens O, et al. Glomus tumors in neurofibromatosis type 1: genetic, functional and clinical evidence of a novel association. *Cancer Res*. 2009; 69: 7393–7401.
4. Ferner RE, Huson SM, Thomas N, et al. Guidelines for the diagnosis and management of individuals with neurofibromatosis. *J Med Genet*. 2007;44(2):81–88.
5. Wilson BN, John AM, Handler MZ, et al. Neurofibromatosis type 1: new developments in genetics and treatment. *J Am Acad Dermatol*. 2021;84(6):1667–1676.
6. Klaber R. Morbus Recklinghausen with glomoid tumors. *Proc Roy Soc Med*. 1938;31:347.
7. Stewart DR, Sloan JL, Yao L, et al. Diagnosis, management, and complications of glomus tumours of the digits in neurofibromatosis type 1. *J Med Genet*. 2010;47:525–532.
8. Sawada S, Honda M, Kamide R, et al. Three cases of subungual glomus tumors with von Recklinghausen neurofibromatosis. *J Am Acad Dermatol*. 1995;32:277–278.
9. Okada O, Demitsu T, Manabe M, et al. A case of multiple subungual glomus tumors associated with neurofibromatosis type 1. *J Dermatol*. 1999;26:535–537.
10. Kumar MG, Emnett RJ, Bayliss SJ, et al. Glomus tumors in individuals with neurofibromatosis type 1. *J Am Acad Dermatol*. 2014;71(1):44–48.
11. Shari RL and Richard KS. Subungual glomus tumors: Underrecognized clinical findings in neurofibromatosis 1. *J am Acad Deramtol*. 2021;84(6):269.
12. Reed RJ and Pulitzer DR. Neurofibromatosis (phenotypic divercity expressed genetically determined hamartomas and neoptasms). In: David EE (ed.) *Lever's histopathology of the skin*. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2008, pp. 1100–1116.
13. Bridget H, Amy MM, Ryan C, et al. The association between glomus tumors and neurofibromatosis. *J Hund Surg*. 2013;38(A):1571–1574.
14. Morohashi A, Shingyouchi Y and Hattori H. Multiple subungual glomus tumours associated with neurofibromatosis type 1. *J Hand Surg Eur* 2015;40(2):212–213.
15. Ly KI and Blaceley JO. The diagnosis and management of neurofibromatosis type 1. *Med Cln N Am* 2019;103:1035–1054.