Case Report

Giant Cell Reparative Granuloma Concurrent with Squamous Cell Carcinoma of the Temporal Bone: A Case Report and Review of the Literature

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A case of giant cell reparative granuloma concurrent with squamous cell carcinoma of the right temporal bone in a 44-year-old man with clinically presenting otorrhea from the mass of the right acoustic canal with hearing loss is reported. The histopathological examination of the lesion characterizes by multinucleated giant cells with in a fibroblastic stroma and area of keratinizing squamous cell carcinoma. GCRG may have been a local reaction provoked by the squamous cell carcinoma. Clinical and pathological features with briefly reviewed relevant literatures of temporal GCRG describing 24 cases are discussed. The patients have the mean age of 34.8 years. The ages of the patients ranged from 4 months to 72 years old. Temporal bone GCRG shows a male predilection of approximately 3:1. The frequently presenting symptoms of temporal bone GCRG are hearing loss, mass, tinnitus, otalgia, otorrhea, vertigo, headache, facial weakness, and diplopia. This is the first reported description in the literature of temporal bone GCRG concurrent with squamous cell carcinoma.

Keywords: *Giant cell reparative granuloma, Central giant cell lesion, Squamous cell carcinoma, Temporal bone*

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Giant cell reparative granuloma (GCRG) is a relatively uncommon non-neoplastic reactive tumefaction demonstrating multinucleate giant cells and spindle-shaped cells associated with foci of hemorrhage[1,2]. The various appellations have included central giant cell lesion, giant cell reaction, and solid variant of aneurysmal bone cyst[1,2]. GCRG has been described most frequently in the jaw. Its occurrence in the long bone, tubular bone, paranasal sinus, orbital region, cranial vault, and temporal bone has also been reported[1,2]. GCRG is not truly reparative and, is in fact destruction, and will progress if not treated.

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To the authors' knowledge, 23 cases of temporal GCRG in 20 English literatures have been reported[3-22]. The purpose of the present report was to illustrate the first published case of the right temporal bone GCRG concurrent with squamous cell carcinoma on the imaging findings and histopathological features. The lesion stimulates the pathologists to be aware not to be misled and over diagnose as a giant cell tumor, osteosarcoma, and sarcomatoid carcinoma.

Case Report

A 44-year-old Thai married male patient living in Nontaburi, Thailand was admitted to Ramathibodi Hospital in July 2004, because of otorrhea from the mass of the right acoustic canal and hearing loss of two months' duration. There was a 10-year history of

one-pack-a-day cigarette smoking. He had been diagnosed with otitis media 30 years earlier, which was treated with right mastoidectomy. The patient had a history of stroke and hyperlipidemia for one year. The computed topography revealed lacunar infarction of the right pons. There was no evidence of osteolytic and exophytic lesion in the temporal region. He was placed on acetylsalicylic acid, atorvastatin calcium, and folic acid. Ten months later, he developed otorrhea with hearing loss. Physical examination revealed pus per the right ear. There was a large firm mass totally occupying the right acoustic canal with contact bleeding. Right tympanic membrane could not be visualized. The left ear was normal. The cervical lymph node could not be palpated. Liver and spleen were not palpable. Relevant laboratory examination revealed normal serum calcium and phosphate valves, liver function tests, serum alkaline phosphatase, and chest radiograph. Anti-human immunodeficiency virus was negative by ELISA technique. The right audiograms revealed mixed sensory and neural hearing loss. The computer tomography of the temporal bone showed extensive irregular heterogeneous enhancing soft tissue density mass occupying within the entire right mastoid antrum, external auditory canal and middle ear cavity associated with destruction of the adjacent medial and lateral walls of the mastoid antrum, posterior and superior walls of the external auditory canal, ossicles and scutum (Fig. 1). Biopsy of the right auditory mass was performed. The pathological diagnosis was atypical fibro-osseous lesion. Right suboccipital craniectomy with subtotal tumor removal was done. The final pathological diagnosis was SCC concurrent with GCRG of the temporal bone. The post operative course was uneventful. The patient received 3,000 rads in divided doses for palliative treatment of SCC. He expired at ten months after the operation. Local invasion and systemic metastasis were detected. No autopsy was performed.

Pathologic finding

Several fragments of soft hemorrhagic tissue measuring 14 x 9.5 x 9 cm were obtained at the first operation. The sections of the right temporal bone tumor revealed randomly scattered multinucleated giant cells within a collagen stroma of connective tissue and spindle-shaped cells (Fig. 2). Foci of hemorrhage with hemosiderin pigments and areas of the newly formed bone spicules and osteoid were usually presented. No other mesenchymal elements, malignant osteoid, or epithelial cells were noted. There was no evidence of atypical mitosis in the stromal cells. Immunohistochemical stains showed that giant tumor cells were non-immunoreactive for CD 68, macrophage markers. Spindle-shaped cells were positive reactivity for vimentin. Spindle-shaped cells and giant cells were negative reactivity for osteocalcin, epithelial membrane antigen (EMA), pancytokeratin, and desmin.

The following specimen of the suboccipital craniectomy with subtotal tumor removal revealed multiple fragments of light brown soft and bony tissues measuring 10 x 10 x 5 cm. The sections of the right temporal tumor revealed infiltrative squamous epithelial component (Fig. 3), which showed large pleomorphic nuclei with prominent nucleoli and eosinophilic cytoplasm. The stroma showed spindle cellular component with few pleomorphic nuclei. The final pathological diagnosis was SCC concurrent with GCRG of the right temporal bone (Fig. 4).

Discussion

GCRG is the rare non-neoplastic reactive tumefaction revealing the histology and gross presentation of the bona-fide, true giant cell neoplasm of the bone[1,2]. Including the presented patients; 24 cases of temporal bone GCRG were reported (Table 1). Temporal bone GCRG shows a male predilection of approximately

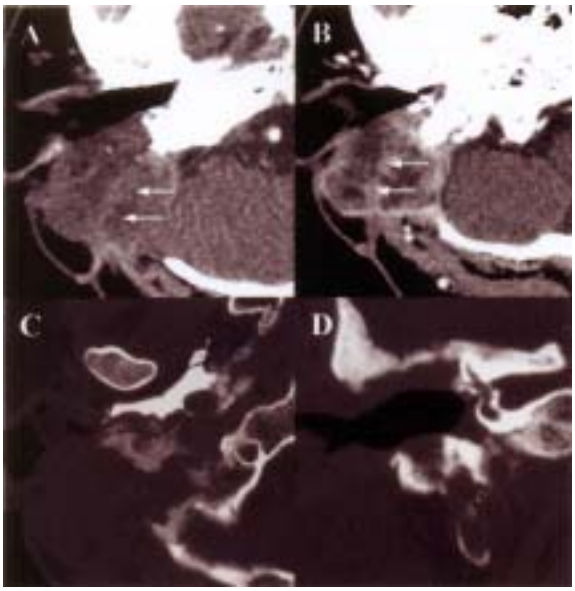

Fig. 1 CT images. Noncontrasted CT (A), contrasted CT (B), bone window (C, D) show large heterogenous enhancing mass at the right mastoid antrum and external ear (arrow) with destruction of the adjacent bones

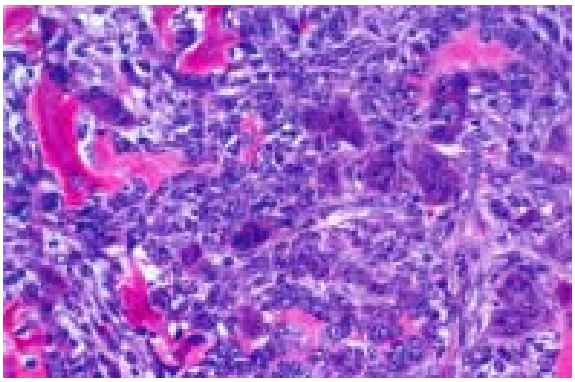

Fig. 2 The section of the right temporal bone tumor reveals randomly scattered multinucleated giant cells within a collagen stroma of connective tissue and spindle-shaped cells. H&E, X200

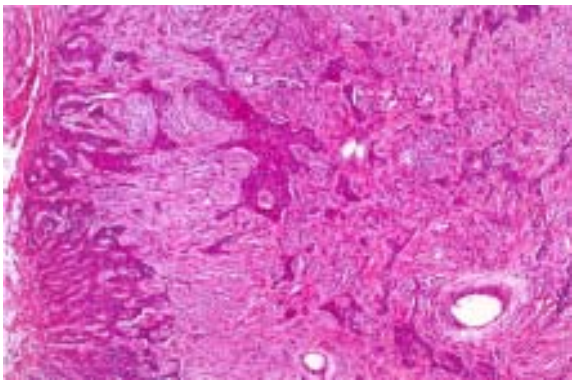

Fig. 3 The section of the right temporal tumor reveals infiltrative squamous epithelial component. H&E, X40

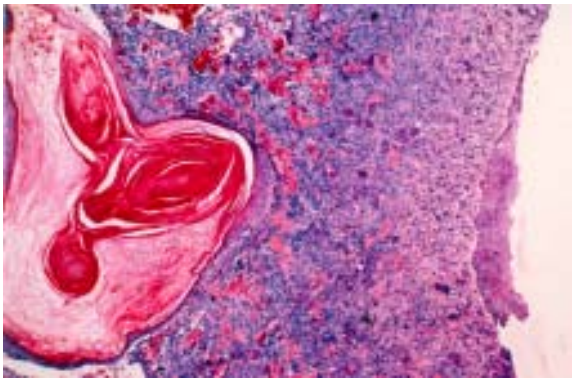

Fig 4. The section of the right temporal bone reveals SCC concurrent with GCRG. H&E, X40

3:1[3-22]. The patients have the mean and median ages of 34.8 and 36 years, respectively[3-22]. The ages of patients ranged from 4 months to 72 years old[3-22]. The most frequently presenting symptoms of temporal bone GCRG are hearing loss (67%), mass (29%), tinnitus (21%), otalgia (17%), otorrhea (8%), vertigo (8%), headache (8%), facial palsy (4%), and diplopia (4%)[3-22]. The routine initial laboratory investigations are non-contributory. The imaging procedures such as computer topography and magnetic resonance image may allow early recognition of primary temporal bone tumors. There has not been a documented case of metastasis from GCRG. GCRG can be locally aggressive and it recurs following incomplete excision.

The peculiarities of GCRG of the temporal bone that were highlighted by the presented case report and the reviewed literature are as follows:

1. The age at onset of GCRGs of the temporal bone most commonly manifests itself in the third and fourth decade of life. However, GCRG usually appears in persons between the age of 10 and 25[1,2]. The median and mean ages of the onset of GCRGs of the temporal bone are older than those with GCRGs of the maxillofacial region.

2. There is a male predominance in the temporal bone GCRG. By contrast, the GCRG of the maxillofacial region has a female predilection[1,2]. The male to female ratio of temporal and maxillofacial GCRG were 3:1 and 1:2, respectively

3. The temporal bone GCRGs usually clinically affect the vestibulocochlear nerve more than the facial nerve.

The macroscopic finding of GCRG is soft, spongy, reddish, friable tissue[1-3]. The histopathologic findings consist of a fairly loose vascular stroma composed of small, spindle-shaped cells and much hemorrhagic extravasations[1,2]. The multinucleate giant cells present are sparse, small, and unevenly distributed. They are often clumped in areas of hemorrhage[1,2]. There are occasional edema and even cystification. Some delicate trabebulae of newly formed osteoid or bone can be seen between microscopic lobules of tumor[1,2].

The histological differential diagnoses of mesenchymal neoplasms of the temporal bone include giant cell reparative tumor, giant cell tumor (GCT), brown tumor of hyperparathyroidism, and osteosarcoma[1,2]. GCT composes of moderately vascularized stroma associated with rather plump spindle-shaped void cells regularly interspersed with multinucleated giant cells containing 50-100 nuclei[23]. More uneven

Table 1. Summary of 24 reported cases of Giant cell reparative granuloma of the temporal bone

Authors & Year	Age	Sex	Initial symptoms	Trauma	Treatment	Follow up (years)
Katz A et al, 1974[3]	36	F	Hearing loss	Yes	Biopsy & radiation (2500 cGy)	Well at 17 mo
Colclasure JB et al, 1981[4]	10	M	Hearing loss	NR	Total resection	Well at 6 yr
	22	M	Hearing loss, mass	NR	Total resection & radiation (600 cGy)	Well at 7 yr
Tesluk H et al, 1989[5]	56	M	Mass, otalgia	No	Total resection	Well at 1 yr
Ciappetta P et al, 1990[6]	25	M	Headache, protrusion, diplopia	Yes	Total resection	Well at 15 yr
Cohen D et al, 1993[7]	0.3	F	Mass	No	Total resection	NR
Lewis ML et al, 1994[8]	32	F	Hearing loss	Yes	Total resection	Well, duration NR
Nemoto Y et al, 1995[9]	36	M	Hearing loss, mass, otalgia	No	Total resection	NR
	28	M	Tinnitus, hearing loss	No	Total resection	NR
Maruno M et al, 1997[10]	3	F	Facial palsy, hearing loss	No	Total resection	Recurrence at16 mo
Ung F et al, 1998[11]	36	F	Hearing loss	No	Total resection	Recurrence at 4 yr
Liu J et al, 2001[12]	44	M	Hearing loss, tinnitus	No	Total resection & radiation (5000cGy)	Well at 3 yr
	72	M	Hearing loss	No	Total resection	Well at 21 mo
Khodaei I et al, 2001[13]	36	M	Tinnitus, otalgia, vertigo	NR	Total resection	Well at 3 yr
Sharma RR et al, 2002[14]	12	M	Hearing loss, vertigo, tinnitus, otalgia	Yes	Total resection	Well at 10 mo
Matsui T et al, 2002[15]	41	M	Mass	NR	Total resection	NR
Yoshimura J et al, 2002[16]	38	M	NR	NR	Total resection	Well at 4 yr
Montero EH et al, 2003[17]	60	M	Hearing loss, otorrhea	NR	Total resection	Well at 2 yr
Kim HJ et al, 2003[18]	50	M	Hearing loss, tinnitus	No	Total resection	Well at 5 mo
Tian X et al, 2003[19]	32	M	Mass	No	Total resection	Well at 26 mo
Boedeker CC et al, 2003[20]	17	F	Hearing loss	No	Total resection	Well at 25 mo
Dimitakopoulos I et al, 2006[21]	43	M	Mass, headache	Yes	Total resection	Well at 36 mo
Souter MA et al, 2006 [22]	62	M	Hearing loss	NR	Calcitonin injection	Well at 24 mo
Larbcharoensub N, et al (The present report)	44	M	Hearing loss, otorrhea	Yes	Partial resection & radiation * (3000cGy)	Dead at 10 mo (clinical local invasion and systemic metastasis)

M = Male, F = Female, R = Right, L = Left, yr = year, mo = month, NR = not reported, * treatment of squamous cell carcinoma

and patchy distribution of giant cells and greater tendency for nuclei to agglomerate in giant cells are typically found in GCT. GCT usually demonstrates mitotic activity in the stromal cells. These findings were not found in the presented patient. Brown tumor of hyperparathyroidism caused by hormonal imbalance usually occurs in later life. The radiologic findings typically show multiple osteolytic lesions with generalized osteopenia and subperiosteal resorption. Brown tumor of hyperparathyroidism is discarded due to normal serum calcium level and lack of characteristic radiologic findings in the presented patient. The osseous component in the lesion comprises of woven-bone arranging in trabecular sheets surrounded by active osteoblasts and focally differentiates toward more mature bone. There is no evidence of malignant osteoid. The osseous area should be compatible with reactive bone rather than osteosarcoma. Absence of immunoreactivity for epithelial marker of the stromal spindle and giant cells are against the interpretation of sarcomatoid squamous cell carcinoma.

The pathogenesis of GCRG remains enigmatic, although initially the GCRG was thought to represent a reactive traumatic process. However, two thirds of the temporal bone GCRGs are not clearly related to trauma[3-22], they may represent chronic response or delayed presentation related to remote or undetected trauma. Currently, it is generally agreed that a granulomatous reaction to intraosseous hemorrhage is the primary cause of GCRG. There are few reports in the literature suggesting the presence of an unidentified circulating parathyroid (PTH) related peptide associated with GCRG[24]. Other causes that have been proposed including infection and developmental anomalies, but no single hypothesis has gained wide acceptance. Furthermore, patients previously reported with GCRG of the ethmoid bone had been associated with epidermoid carcinoma of nasal sinus[25]. In the presented case, SCC may have caused spontaneous intra-acoustic temporal bone hemorrhage after trivial trauma, resulting in a GCRG. The GCRG may have been a local reaction provoked by the squamous cell carcinoma. However, the authors do not conclude that SCC is definitely on etiology factor in the presented case, but the causal relationship between squamous cell carcinoma and temporal bone GCRG is not altogether clear, especially in a patient who had no history of radiotherapy. This is the first report of documentation purposes in the temporal bone.

Surgical excision and local curettage remains the cornerstone of management of GCRGs. GCRGs generally behave in an indolent manner and generally do not recur after complete surgical excision. However, some lesions appear to be more aggressive and may recur. The adjunctive possible therapy includes intralesional steroid injections, calcitonin therapy, which had been reported resolving mandibular GCRGs[22,26,27]. Radiotherapy is generally avoided, except in advanced inoperative cases because of the risk of sarcomatous and carcinomatous transformation. To the authors' knowledge, this is the first reported case of temporal bone GCRG concurrent with SCC.

References

1. Nager GT, Hyams VJ. Mesenchymal neoplastic processes. In: Nager GT, editor. Pathology of the ear and temporal bone. Maryland: Williams & Wilkins; 1993: 467-8.
2. Sciubba JJ, Fantasia JE, Kahn LB. Nonodontogenic lesions. In: Sciubba JJ, Fantasia JE, Kahn LB, editors. Atlas of tumor pathology: tumors and cysts of the jaw. 3rd Series, Fascicle 29. Washington, DC: Armed Forces Institute of Pathology; 2001: 161-7, 181-201.
3. Katz A, Hirschl S. Giant cell reparative granuloma in the temporal bone. Arch Otolaryngol 1974; 100: 380-2.
4. Colclasure JB, Shea MC Jr, Graham SS. Giant cell lesions of the temporal bone. Am J Otol 1981; 2: 188-92.
5. Tesluk H, Senders CW, Dublin AB. Case report 562: Giant cell reparative granuloma of temporal bone. Skeletal Radiol 1989; 18: 599-602.
6. Ciappetta P, Salvati M, Bernardi C, Raco A, Di Lorenzo N. Giant cell reparative granuloma of the skull base mimicking an intracranial tumor. Case report and review of the literature. Surg Neurol 1990; 33: 52-6.
7. Cohen D, Granda-Ricart MC. Giant cell reparative granuloma of the base of the skull in a 4-month-old infant - CT findings. Pediatr Radiol 1993; 23: 319-20.
8. Lewis ML, Weber AL, McKenna MJ. Reparative cell granuloma of the temporal bone. Ann Otol Rhinol Laryngol 1994; 103: 826-8.
9. Nemoto Y, Inoue Y, Tashiro T, Mochizuki T, Katsuyama J, Hakuba A, et al. Central giant cell granuloma of the temporal bone. AJNR Am J Neuroradiol 1995; 16(4 Suppl): 982-5.
10. Maruno M, Yoshimine T, Kubo T, Hayakawa T. A case of giant cell reparative granuloma of the petrous bone: demonstration of the proliferative

component. Surg Neurol 1997; 48: 64-8.
11. Ung F, Li KK, Keith DA, McKenna MJ. Giant cell reparative granuloma of the temporal bone: case report and review of the literature. Otolaryngol Head Neck Surg 1998; 118: 525-9.
12. Liu J, Zhong DR, Liu LF, Han DY, Yang WY, Jiang SC. Giant cell reparative granuloma of the temporal bone. Acta Otolaryngol 2001; 121: 523-8.
13. Khodaei I, Rowley H, Farrell M, Collins CM, Vianni L, Rawluk D. An unusual cause for tinnitus. Ir Med J 2001; 94: 312-3.
14. Sharma RR, Verma A, Pawar SJ, Dev E, Devadas RV, Shiv VK, et al. Pediatric giant cell granuloma of the temporal bone: a case report and brief review of the literature. J Clin Neurosci 2002; 9: 459-62.
15. Matsui T, Iwamuro K, Ishikawa T, Asano T, Itoyama S, Tabe H. Large giant cell reparative granuloma of the petrous bone - case report. Neurol Med Chir (Tokyo) 2002; 42: 232-6.
16. Yoshimura J, Onda K, Tanaka R, Takahashi H. Giant cell reparative granuloma of the temporal bone: neuroradiological and immunohistochemical findings. Neurol Med Chir (Tokyo) 2002; 42: 510-5.
17. Montero EH, Navarro JS, Pueyo JL, Garca FM, Samperiz LC, Garca AO. Giant-cell reparative granuloma in the temporal bone. Am J Otolaryngol 2003; 24: 191-3.
18. Kim HJ, Lee HK, Suh DC, Choi CG, Kim JK, Lee JH, et al. Giant cell reparative granuloma of the temporal bone: MR findings with pathologic correlation. AJNR Am J Neuroradiol 2003; 24: 1136-8.
19. Tian XF, Li TJ, Yu SF. Giant cell granuloma of the temporal bone: a case report with immunohistochemical, enzyme histochemical, and in vitro studies. Arch Pathol Lab Med 2003; 127: 1217-20.
20. Boedeker CC, Kayser G, Ridder GJ, Maier W, Schipper J. Giant-cell reparative granuloma of the temporal bone: a case report and review of the literature. Ear Nose Throat J 2003; 82: 926-4, 936.
21. Dimitrakopoulos I, Lazaridis N, Sakellariou P, Asimaki A. Giant-cell granuloma in the temporal bone: a case report and review of the literature. J Oral Maxillofac Surg 2006; 64: 531-6.
22. Souter MA, Bird PA, Worthington JP. Giant cell reparative granuloma of the temporal bone treated with calcitonin. Otol Neurotol 2006; 27: 999-1002.
23. Reid R, Banerjee SS, Sciot R. Giant cell tumour. In: Fletcher CD, Unni KK, Mertens F, editors. Pathology & genetics: tumours of soft tissue and bone. Lyon: IARC Press; 2002: 310-2.
24. Davis JP, Archer DJ, Fisher C, Wimalawansa SJ, Baldwin D. Multiple recurrent giant cell lesions associated with high circulating levels of parathyroid hormone-related peptide in a young adult. Br J Oral Maxillofac Surg 1991; 29: 102-5.
25. Damjanov I, Aras D, Krstulovic B. Giant cell reparative granuloma of ethmoid concurrent with carcinoma of nasal sinuses. Ear Nose Throat J 1976; 55: 38-41.
26. Carlos R, Sedano HO. Intralesional corticosteroids as an alternative treatment for central giant cell granuloma. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2002; 93: 161-6.
27. de Lange J, Rosenberg AJ, van den Akker HP, Koole R, Wirds JJ, van den BH. Treatment of central giant cell granuloma of the jaw with calcitonin. Int J Oral Maxillofac Surg 1999; 28: 372-6.

รายงานผู้ป่วย giant cell reparative granuloma เกิดร่วมกับมะเร็งเยื่อบุผิวชนิด squamous ที่กระดูกขมับ

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รายงานผู้ป่วย giant cell reparative granuloma เกิดร่วมกับมะเร็งเยื่อบุผิวชนิด squamous ที่กระดูกขมับ ในผู้ป่วยชายไทยอายุ 44 ปี มีอาการน้ำไหลออกจากก้อนที่หูขวาร่วมกับการสูญเสียการได้ยิน ตรวจทางกล้องจุลทรรศน์พบเป็น เซลล์ยักษ์หลายนิวเคลียส, เซลล์ fibroblast และเซลล์มะเร็งเยื่อบุผิวชนิด squamous โดยกลุ่มของ giant cell reparative granuloma สันนิษฐานว่าถูกก่อให้เกิดโดยมะเร็งเยื่อบุผิวชนิด squamous ทางคณะผู้นิพนธ์ได้รายงานเรื่อง giant cell reparative granuloma ที่กระดูกขมับร่วมกับทบทวนจดหมายเหตุทางแพทย์ บรรยายลักษณะโรค 24 ราย ผู้ป่วยมีอายุเฉลี่ย 34.8 ปี (อายุระหว่าง 4 เดือน ถึง 72 ปี) อัตราส่วนในเพศชายต่อเพศหญิงเป็น 3 ต่อ 1 โดยอาการแสดงที่พบได้แก่ หูดับ, ก้อนทูม, เสียงในหู, ปวดหู, น้ำไหลจากหู, เวียนศีรษะ, ปวดศีรษะ, อัมพาตของเส้นประสาทสมองคู่ที่ 7, และมองเห็นภาพซ้อน พบเป็นกรณีศึกษาแรกของประเทศไทย โดยรวบรวมวิเคราะห์การแสดงออกทางคลินิกและพยาธิวิทยา