CASE REPORT

UDC: 618.19-006-033.2-07
DOI: https://doi.org/10.2298/VSP210212040D

Facial nerve palsy as the first sign of late breast cancer metastasis to the temporal bone

Paraliza facijalnog nerva kao prvi znak kasne metastaze karcinoma dojke u temporalnu kost

Zoran Dudvarski*†, Nenad Arsović*†, Milovan Dimitrijević*†, Saša Jakovljević†, Novica Boričić*‡, Ivan Boričić*‡

***University of Belgrade, Faculty of Medicine, Belgrade, Serbia; †University Clinical Center of Serbia, Clinic of Otorhinolaryngology and Maxillofacial Surgery, Belgrade, Serbia; ‡Institute of Pathology, Belgrade, Serbia**

Abstract

Introduction. Late metastases of malignant tumors in the temporal bone are very rare lesions. They can be asymptomatic for a long time and usually manifest themselves in the form of hearing loss, dizziness, tinnitus, and paralysis of the facial nerve. Modern radiological diagnostics and explorative surgery with biopsy are essential for diagnosis. **Case report.** We present a rare and unusual case of a 66-year-old female patient with facial nerve paralysis that appeared as the first sign of metastatic breast cancer in the temporal bone 10 years after treatment. A sudden hearing loss and dizziness occurred six months later, and the value of CA 15-3 was elevated. Scintigraphy pointed to susceptible metastatic deposits of the axial skeleton without lesions in the temporal bone. Finally, repeated computed tomography revealed osteolytic changes in the temporal bone six months after that. Immunohistochemical analysis of mastoid tissue samples confirmed that it was a breast cancer metastasis. One year after palliative radiotherapy and oral hormone therapy, a patient had a good general condition with a better function of the facial nerve. **Conclusion.** A high degree of clinical suspicion sometimes requires repeated radiological diagnostics in order to detect osteolytic metastatic changes in the temporal bone but also in other bone structures within the hematogenous dissemination of the malignant disease.

Key words:
breast neoplasms; facial nerve diseases; immunohistochemistry; neoplasm metastasis; temporal bone; tomography, x-ray computed; treatment outcome.

Apstrakt

Uvod. Kasne metastaze malignih tumora u temporalnoj kosti su veoma retke lezije. One dugo mogu biti asimptomatske i obično se manifestuju gubitkom sluha, vrtoglavicom, zujanjem u ušima i paralizom facijalnog nerva. Savremena radiološka dijagnostika i eksplorativna hirurgija sa biopsijom neophodni su za dijagnozu. **Prikaz bolesnika.** Prikazujemo redak i neobičan slučaj 66-godišnje bolesnice sa paralizom facijalnog nerva koja se pojavila kao prvi znak metastatskog karcinoma dojke u temporalnoj kosti 10 godina nakon lečenja. Nagli gubitak sluha i vrtoglavica pojavili su se šest meseci kasnije, a vrednost CA 15-3 bila je povišena. Scintigrafija je ukazala na moguće metastatske depozite osovinskog skeleta, bez lezija u temporalnoj kosti. Konačno, ponovljena kompjuterizovana tomografija otkrila je osteolitičke promene temporalne kosti, šest meseci nakon toga. Imunohistohemijska analiza uzoraka tkiva iz mastoida potvrdila je da se radilo o metastazi karcinoma dojke. Godinu dana nakon palijativne radioterapije i oralne hormonske terapije, bolesnica je bila dobrog opšteg stanja, sa boljom funkcijom facijalnog nerva. **Zaključak.** Visok stepen kliničke sumnje ponekad zahteva ponavljanu radiološku dijagnostiku kako bi se otkrile osteolitičke metastatske promene u temporalnoj kosti, ali i na ostalim koštanim strukturama, u okviru hematogene diseminacije maligne bolesti.

Ključne reči:
dojka, neoplazme; facijalni nerv, bolesti; imunohistohemija; neoplazme, metastaze; temporalna kost; tomografija, kompjuterizovana, rendgenska; lečenje, ishod.

Correspondence to: Zoran Dudvarski, University Clinical Center of Serbia, Clinic of Otorhinolaryngology and Maxillofacial Surgery, Pasterova 2, 11 000 Belgrade, Serbia. E-mail: dudvarski1809@gmail.com

Introduction

Temporal bone metastases are rare lesions, and they usually originate from malignant breast, lung, kidney, stomach, and prostate tumors [1, 2]. The metastases found 10 years after the initial treatment of the malignant disease are especially rare, and then they are defined as late metastases [3]. The most common way of metastases formation is the hematogenous dissemination of malignant cells to the temporal bone marrow, while disease spreading mechanisms through cerebrospinal fluid, lymphatic and perineural pathways, or directly from the surrounding areas have been described as well [2, 4–6]. The petrous apex, internal auditory meatus, and mastoid cavity are the areas of the temporal bone most commonly affected by metastatic changes [2, 4].

In addition to potentially being asymptomatic for a long time, temporal bone metastases usually manifest themselves in symptoms and signs corresponding to different diseases of the ear and the adjacent areas [2, 4, 5, 7, 8]. Contemporary imaging methods like high-resolution computed tomography (HRCT) and magnetic resonance imaging (MRI) uncover pathological changes in the temporal bone and the adjoining areas. However, differentiation of tumorous and inflammatory changes based on radiological findings sometimes proves to be very difficult, while differential diagnostic dilemma can be eliminated only through biopsy, histopathological and immunohistochemical analyses of the tissue samples [5, 8–10].

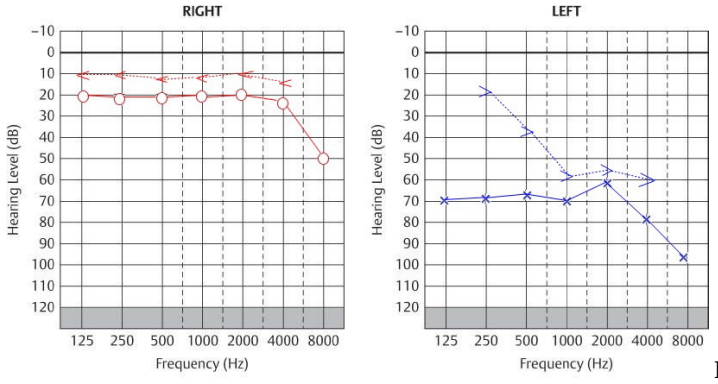
We present a rare and unusual case of a 66-year-old female patient with facial nerve palsy as the first sign of breast cancer metastasis to the temporal bone 10 years after initial treatment.

Case report

A 66-year-old female patient was admitted to the Clinic of Otorhinolaryngology and Maxillofacial Surgery of the Univeristy Clinical Center of Serbia in Belgrade due to facial nerve paralysis on the left that had appeared 12 months earlier. From the patient's medical history, we found out that the left ear was previously operated on twice (Tympanoplasty type 1) due to chronic tubotympanic otitis media. We also found out that the patient had undergone radical surgery using the Madden technique due to right breast cancer 11 years earlier (*Carcinoma lobulare*, high grade, G III NG III). It was then discovered intraoperatively that the primary tumor had broadly infiltrated the fat tissue of the lateral portion of the breast with a pronounced multifocality. No signs of regional metastases were detected in the axillary lymph nodes (0/27). Six cycles of chemotherapy with cyclophosphamide, 5-fluorouracil sodium, and epirubicin were given postoperatively as well as radiotherapy (RT). The patient was then given oral hormone therapy with tamoxifen for five years. She had regular control checkups for 10 years without signs of relapse of the malignant disease.

The current problems started 12 months earlier with the appearance of pain in the retroauricular area and sudden complete paralysis of the facial nerve on the left (Grade VI on the House-Brackmann scale). There were no signs of inflammation or any data on the possible trauma or herpes infection. HRCT of the temporal bones and endocranium was conducted, and the findings were normal. The patient was treated with corticosteroids and physical therapy, however, without improvement.

A sudden hearing loss in the left ear and the appearance of vertigo occurred six months later. Audiological and vestibulological examination showed a severe mixed hearing impairment and severe damage to the sense of balance in the left ear while hearing in the right ear was normal (Figure 1). Scintigraphy of the skeleton with the technetium-99m-labelled 3,3-diphosphono-1,2-propanodicarboxylic acid (99mTc-DPD) indicated increased accumulation in the right shoulder joint area, left clavicle, left humerus, both femurs, left ischium, and sacral bone. The distribution of the radiopharmaceuticals in all segments of the vertebral column was noticeably non-homogeneous, with increased accumulation in the thoracic vertebrae bodies. Based on the scintigraphic features, the changes described may have corresponded to the secondary deposits (Figure 2). The value of tumor marker CA 15-3 was elevated and amounted to 54.5 U/mL (normal range: < 25 U/mL). The laboratory analyses recorded reduced values of the following parameters: erythrocytes 3.24 × 1,012/L (normal range: 3.80–5.00 ×



A) **B)**

Fig. 1 – A pure tone audiogram showed normal hearing in the right ear and severe mixed hearing loss in the left ear; frequency in hertz (Hz) is shown on the abscissa and hearing level in decibels (dB) is shown on the ordinate.

1,012/L), hemoglobin 96 g/L (normal range: 110–180 g/L), and hematocrit 0.31 L/L (normal range: 0.35–0.47 L/L). Moreover, elevated values of the following parameters were recorded: erythrocyte sedimentation rate 102 mm/h (normal range: < 30 mm/h), alkaline phosphatase (ALP) 876 U/L (normal range: 64–153 U/L), and lactate dehydrogenase (LDH) 313 U/L (normal range: < 241 U/L). MRI findings of temporal bones and endocranium were normal again. Lung radiography and echosonography examination of the left breast, both axillae, and abdomen did not reveal pathological changes. Physical therapy was continued with another cycle of corticosteroid therapy, followed by a temporary improvement in the facial nerve function for two months.

HRCT of the temporal bone, which was repeated 12 months after the initial paralysis of the facial nerve, uncovered osteolytic changes in the base of the skull, the petrous apex of both pyramids, *tegmen tympani* on the left with non-homogeneous shading in the mastoid cavity, perifacial and perilabirynthine cells (Figure 3).

The preoperative otomicroscopy finding indicated that it was an inactive tubotympanic otitis on the left, with a small perforation in the rear lower quadrant of the eardrum. An explorative mastoidectomy with epitympanotomy was performed. Intraoperatively, it was noted that the bone was osteolytic, sequestered, and dehiscent in the *tegmen* antri region with the presence of fibrous and adherent tumor tissue in the peridural region, around the labyrinth, and along the course of the facial nerve. Histopathological and immunohistochemical analyses of tissue samples have shown that it was metastatic breast cancer. Tumor cells were positive for cytokeratin 7 (CK7), GATA-3, estrogen receptor (ER) (Figure 4), progesterone receptor (PR) and negative for CK20, CDX-2, TTF-1, PAX-8, WT-1, mamoglobin, p40, CK5/6, TM, p63 (not shown). Rare single cells are positive for GCDFP15 (not shown).

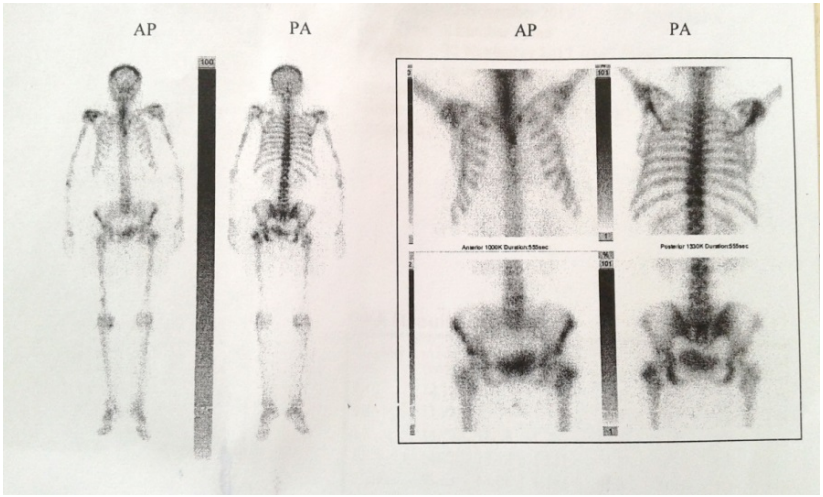


Fig. 2 – Scintigraphy of the skeleton with the suspected metastatic changes in the right shoulder joint area, left clavicle, left humerus, both femurs, left ischium, and sacral bone.

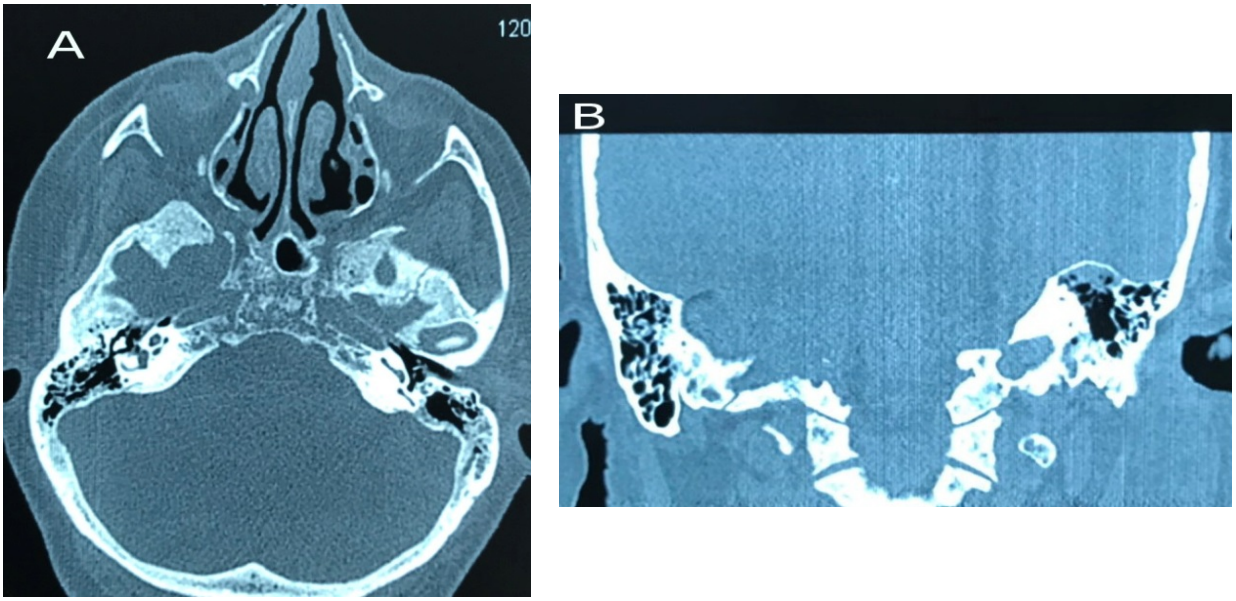


Fig. 3 – Computed tomography (CT) scan in axial (A) and coronal (B) plane showed osteolytic changes in the skull base, petrous apexes, and the left temporal bone.

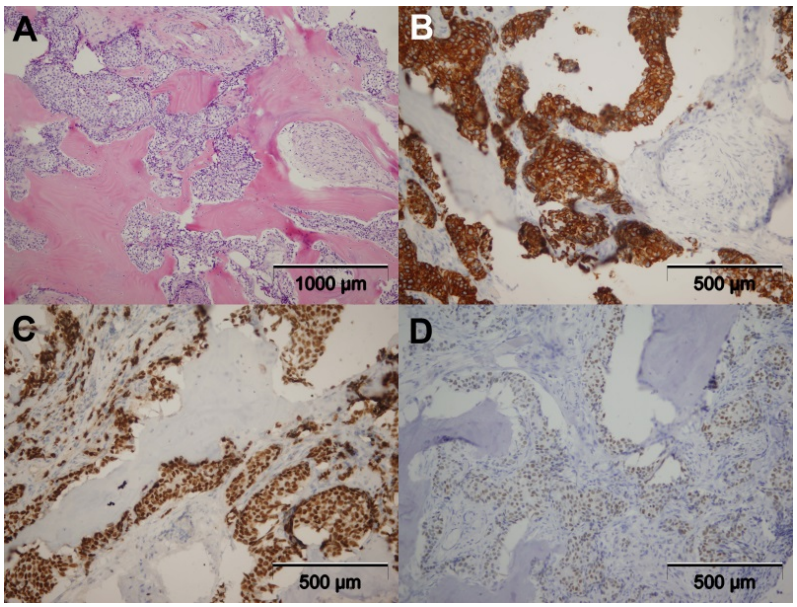


Fig. 4 – Histopathological and immunohistochemical findings of mastoid tissue samples. Bone marrow is infiltrated with medium sized cells with indistinct borders, abundant, eosinophilic, or clear cytoplasm. Nuclear polymorphism is mild. Chromatin is evenly dispersed, with small nucleoli in some tumor cells. Tumor growth is diffused with formation of rare tubules. Hematoxylin-eosin (A); Tumor cells are positive for cytokeratin 7 (CK7) (B), GATA-3 (C) and estrogen receptor (ER) (D).

By the decision of the Oncology Consilium for malignant breast disease, palliative RT with therapeutic dose (TD) 40 Gy was applied to the area of the left temporal bone with further application of oral hormone therapy (anastrozole). Following the RT, there was a gradual improvement in the function of the mimic facial muscles, and 12 months later, during the last control examination, we established a facial nerve paresis Grade III on the House-Brackmann scale.

Discussion

Reviewing the world literature from 1902 to 1994, Streitmann and Sismanis [2] recorded 139 cases of metastatic tumors in the temporal bone, and about 25% of metastases originated from breast cancer. Metastatic disease in the temporal bone may be asymptomatic for a long time and undetected for several reasons. Routine examination of the ear, audiological screening, and radiological diagnostics of the temporal bone are not commonly carried out during the evaluation and monitoring of patients with malignant diseases. In addition, it is well known that the otic capsule is the strongest bone in the human body, and the facial nerve is protected by the Fallopian canal. Based on autopsy results, Gloria-Cruz et al. [4] have detected metastases in the temporal bone in 22% of patients who primarily had no disseminated malignant disease. Although metastatic changes were found in both temporal bones in 62% of the cases, as many as 36% of the patients had no otological symptoms. Streitmann and Sismanis [2] also state that approximately 30% of the patients with unilateral metastases in the internal auditory meatus had no symptoms, and the disease was detected accidentally either by radiological methods or by autopsy. Since histopathological examination of the temporal bone is not routinely performed during the autopsy in patients treated for malignant diseases, some authors believe that the prevalence of metastatic tumors in the temporal bone is underestimated [2, 4].

Symptoms and signs of metastatic disease in the temporal bone are non-specific and may correspond to various inflammatory, systemic, or specific illnesses. Therefore, it is very important to take a detailed anamnesis and perform a complete physical examination. According to some studies, hearing loss is one of the most common symptoms of metastatic disease in the temporal bone, which is present in 40% of patients [4]. Metastases in the temporal bone can also be manifested by vertiginous disorders, as well as very unusual symptoms and signs that resemble temporal arteritis [7, 8]. Extremely rare, metastases of malignant tumors manifest themselves as a soft-tissue mass in the external ear canal [9].

There are numerous causes of facial nerve palsy, most notably Bell's palsy, herpes zoster oticus, chronic suppurative otitis media, and cholesteatoma. According to literature data, the incidence of facial nerve paralysis in the temporal bone metastases ranges from 15% to 50% [4, 11, 12]. Studies have shown that tumor invasion of the Fallopian canal does not necessarily lead to facial nerve paralysis, and the clinical presentation correlates well with the degree of tumor infiltration into the nerve fibers [13, 14]. Some histological studies have shown that the complete paralysis of the facial nerve was present only in the tumor invasion through the epineural layer, which was reported in about 50% of cases [13, 14]. It is also

important to pay attention to the clinical presentation of the facial nerve paralysis that does not necessarily have a sudden onset and progressive character. Breadon et al. [15] describe two cases of breast cancer metastases in the temporal bone that had been clinically manifested in the form of recurrent paralysis of the facial nerve.

According to some authors, facial nerve paralysis with otalgia and periauricular edema represents a highly suspicious triad of symptoms that can indicate the presence of metastases in the temporal bone [11]. Thus, the occurrence of the individual or associated symptoms and their clinical course depend on the localization and extension of the metastatic lesion in the temporal bone, as well as whether it is a unilateral or bilateral presentation of the disease [2].

The finding of temporal bone destruction on the CT scan is always highly suspicious but not pathognomonic for malignant tumors and may correspond to other pathological conditions, such as cholesteatoma, necrotizing otitis externa, or paraganglioma. In suspicion of metastatic disease, attention should be paid to the typical localization of osteolytic lesions in correlation with a medical history, laboratory, clinical, and audiological findings. MRI is a superior method for differentiating the soft-tissue changes in the temporal bone and detection of endocranial propagation of the pathological process. In addition, it is possible to display the entire intratemporal course of the facial nerve in detail. Therefore, MRI is recommended in the unusual clinical course of facial nerve palsy. Scintigraphy of the skeleton and positron emission tomography are also very important in detecting metastases and disseminated malignant diseases [7].

The case of our patient is interesting for many reasons. Namely, she had a history of chronic suppurative otitis media on her left side, and she had previously undergone two operations in other institutions. The facial nerve paralysis had appeared on the same side. However, as it was an inactive process, the possibility of otogenic facial nerve paralysis was excluded. Furthermore, there were no other known etiological factors, and CT findings of the temporal bone were normal. Despite the emergence of new symptoms in the form of dizziness and hearing impairment, elevated values of CA 15-3, ALP, and LDH, repeated imaging diagnostics did not reveal pathological changes in the temporal bone even six months later. The finding of scintigraphy was highly suspected of metastatic disease of the axial skeleton but did not indicate any temporal bone lesion. In addition, our patient did not have any of the skeletal-related events such as bone pain, pathological fracture, spinal cord compression, or tumor-induced hypercalcemia [16]. Interestingly, there was a temporary improvement in facial nerve function afterward, as described by some authors in the literature [10, 15]. Although everything indicated a likely late hematogenous dissemination of the malignant disease, it was necessary to conduct HRCT of the temporal bone repeatedly in order to detect osteolytic metastatic changes in typical localization.

Treatment of patients with breast cancer relapse in the form of metastases in the temporal bone depends on the locoregional status, systemic expansion of the malignant disease, the general condition of the patient, histopathological findings, and previous therapy. The temporal bone region is mostly treated with palliative RT in combination with chemotherapy and hormone therapy [5, 17].

Literature data point to the absence of temporal bone metastases if the primary malignant tumor is discovered early and treated adequately [4]. Our patient had a local advanced malignant tumor of the breast, and the histopathological type of invasive lobular carcinoma is, according to some studies, an independent risk factor for the appearance of metastases in the bones [18]. Detection of metastatic disease in the temporal bone is often an indicator of the presence of distant metastases in other locations within hematogenous dissemination [4, 5, 7], which was confirmed by scintigraphy of the skeleton in our case. Our patient had been in complete remission for ten years. In the literature, there are cases of recorded metastatic breast cancer in the temporal bone as much as 33 years after the initial treatment [8]. Therefore, some authors emphasize that the follow-up period for patients treated for breast cancer must continue even after the routine period of ten years, with regular control of tumor markers [3].

Conclusion

Although late metastatic tumors in the temporal bone are very rare, they should be considered as a differential diagnosis in cases of otological symptomatology, which is refractory to therapy, and facial nerve paralysis that has a prolonged or unusual clinical presentation. This particularly applies to the elderly population and patients who have a positive history of malignancy, regardless of how long the treatment period has elapsed. A high degree of clinical suspicion sometimes requires repeated imaging diagnostics in order to detect osteolytic metastatic changes in the temporal bone, but also in the other bone structures within the hematogenous dissemination of the malignant disease. The occurrence of otologic symptoms that are usually a late sign of the systemic metastatic disease, as well as the time that is sometimes needed to establish a definitive diagnosis are only some of the factors that negatively affect the overall prognosis of these patients.

REFERENCES

1. *Castillo MN, Serdà RF, Molins BA, Martí PJ, Claramunt CF, Scherdel PE*. Facial paralysis of metastatic origin. Review of metastatic lesions of the temporal bone. An Otorrinolaringol Ibero Am 2000; 27(3): 255–63. (Spanish)
2. *Streitmann MJ, Sismanis A*. Metastatic carcinoma of the temporal bone. Am J Otol 1996; 17(5): 780–3.
3. *Gabrovski N, Poptodorov G, Velinov N, Gabrovski S*. Late metastases from breast cancer-report of two cases. Khirurgiia (Sofiia) 2010; (1): 62–6. (Bulgarian)
4. *Gloria-Cruz TI, Schachern PA, Paparella MM, Adams GL, Fulton SE*. Metastases to temporal bones from primary nonsystemic malignant neoplasms. Arch Otolaryngol Head Neck Surg 2000; 126(2): 209–14.

5. *Lan MY, Shiao AS, Li WY*. Facial paralysis caused by metastasis of breast carcinoma to the temporal bone. J Chin Med Assoc 2004; 67(11): 587–90.
6. *Berlinger NT, Koutroupas S, Adams G, Maisel R*. Patterns of involvement of the temporal bone in metastatic and systemic malignancy. Laryngoscope 1980; 90(4): 619–27.
7. *Jalava-Karvinen P, Kemppainen J, Saario R, Kotilainen P*. Metastasis in the temporal bone mimicking temporal arteritis. J Clin Rheumatol 2010; 16(1): 19–21.
8. *Tsunoda A, Tanaka Y, Sato T, Kirimura S, Kitamura K*. Vertigo by Breast Cancer Metastasis 33 Years after Treatment. Intern Med 2016; 55(3): 311–3.
9. *Sari S, Battal BV, Akgun V, Salih Deveci MS*. Metastasis of Breast Carcinoma to the External Auditory Canal: Report of an Unusual Case and Literature Review. J Belg Soc Radiol 2015; 99(1): 53–7.
10. *Ferri GG, Castellucci A, Vecchio VD, Brandolini C*. Skull Base Metastasis of a Breast Carcinoma. Clin Surg 2016; 1: 1105.
11. *Maddox HE 3rd*. Metastatic tumors of the temporal bone. Ann Oto Rhinol Larygol 1967; 76(1): 149–65.
12. *Schuknecht HF, Allam AF, Murakami Y*. Pathology of secondary malignant tumors of the temporal bone. Ann Otol Rhinol Laryngol 1968; 77(1): 5–22.
13. *Jung TT, Jun BH, Shea D, Paparella MM*. Primary and secondary tumors of the facial nerve. A temporal bone study. Arch Otolaryngol Head Neck Surg 1986; 112(12): 1269–73.
14. *Saito H, Chinzei K, Furuta M*. Pathological features of peripheral facial paralysis caused by malignant tumour. Acta Otolaryngol Suppl 1988; 446: 165–71.
15. *Breadon GE, Cody DT, Weiland LH*. Facial palsy: unusual etiology. Laryngoscope 1977; 87(1): 26–34.
16. *Svendsen ML, Gammelager H, Sværke C, Yong M, Chia VM, Christiansen CF*, et al. Hospital visits among women with skeletal-related events secondary to breast cancer and bone metastases: a nationwide population-based cohort study in Denmark. Clin Epidemiol 2013; 5: 97–103.
17. *Zhang H, Zhu W, Biskup E, Yang W, Yang Z, Wang H*, et al. Incidence, risk factors and prognostic characteristics of bone metastases and skeletal-related events (SREs) in breast cancer patients: a systematic review of the real world data. J Bone Oncol 2018; 11: 38–50.
18. *Harries M, Taylor A, Holmberg L, Agbaje O, Garmo H, Kabilan S*, et al. Incidence of bone metastases and survival after a diagnosis of bone metastases in breast cancer patients. Cancer Epidemiol 2014; 38(4): 427–34.

Received on February 12, 2021
Accepted on March 24, 2021
Online First April 2021