Iranian Journal of Pathology | ISSN: 2345-3656

Salivary Duct Carcinoma with Late Distant Brain and Cutaneous Metastasis: A Case Report

Hassan Mirmohammad Sadeghi[1], Abbas Karimi[2], Amirsina Rahpeima[3], Samira Derakhshan[4*]

1. *Oral & Maxillofacial Surgery Department, Taleghani Hospital, School of Dentistry, Shahid Beheshti University of Medical Sciences, Tehran, Iran*
2. *Oral & Maxillofacial Surgery Department, Shariati Hospital, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran*
3. *School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran*
4. *Oral and Maxillofacial Pathology Department, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran*

Scan to discover online

Main Subjects:
Head & Neck Pathology

Received 05 Feb 2019;
Accepted 09 Mar 2020;
Published Online 09 May 2020;

10.30699/ijp.2020.103326.2039

ABSTRACT

Salivary duct carcinoma (SDC) is a rare and highly aggressive salivary gland tumor with poor prognosis, rapid growth, distant metastasis, early regional metastasis, and a high rate of recurrence. The parotid gland is the most common site of involvement, and the lungs and the bones are the most common sites of distant metastasis of SDC. Herein, we present a case of SDC of the parotid gland in a 62-year-old male patient with an unusual metastasis to the skin of the primary site and brain 6 years after primary treatment, which comprised of total parotidectomy and radical neck dissection followed by radiotherapy. It is noteworthy that in few cases of SDC with infiltration, (and not in low-grade intraductal carcinoma of the salivary glands), routine treatment may not suffice, and long-term follow-up is highly recommended.

KEYWORDS: Brain, Metastasis**,** Parotid, Salivary duct carcinoma, Skin, Treatment

Corresponding Information: **Samira Derakhshan**; Oral and Maxillofacial Pathology Department, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran Email: sderakhshan@sina.tums.ac.ir

Introduction

Salivary duct carcinoma (SDC) is an extremely rare and highly aggressive salivary gland malignancy with poor prognosis. Kleinsasser *et al.*, were the first to report SDC in 1968 (1). SDC is estimated to account for 1-3% of all salivary gland malignancies (2,3,4). It has a poor prognosis due to its rapid growth, distant metastasis, early regional metastasis, and high rate of recurrence (2). The parotid gland is the most common site of involvement (2-5). SDC may also be observed in the submandibular and minor salivary glands, predominantly in the palate (2). Surgical resection of the tumor and ipsilateral neck dissection followed by chemotherapy and radiotherapy is currently the most common treatment protocol for SDC (4).

The local recurrence, lymph node metastasis and distant metastasis rates of SDC are 30%, 60%, and 30% to 70%, respectively (5). The lungs and the bones are the most common sites of distant metastasis; however, metastasis to the liver, skin and brain has also been reported with lower frequency (6).

Herein, we present a case of SDC of the parotid gland in a 62-year-old male patient with unusual skin and brain metastases 6 years after total parotidectomy and radical neck dissection of the primary tumor.

Case Report

A 56-year-old male patient was referred to the oral and maxillofacial surgery department for evaluation of a large painless swelling in his right parotid gland region. Facial asymmetry due to the lesion was noticeable. There was no pain, paresthesia or lymphadenopathy. No pus drainage was evident in extraoral and intraoral examination; the regional skin and the tissue mass were intact. The patient's past medical history was unremarkable. The patient reported swelling since 3 months ago. The patient underwent computed tomography of the head and neck, which revealed an ill-defined lesion in the right parotid gland that was attached to the superficial skin (Figure 1).

An incisional biopsy was performed and histopathological examination revealed a malignant salivary gland tumor composed of islands and sheets of large epithelial cells with numerous ductal structures and comedo necrosis (Figure 2).

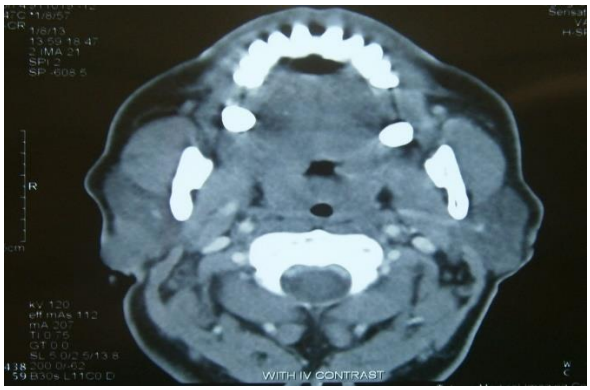
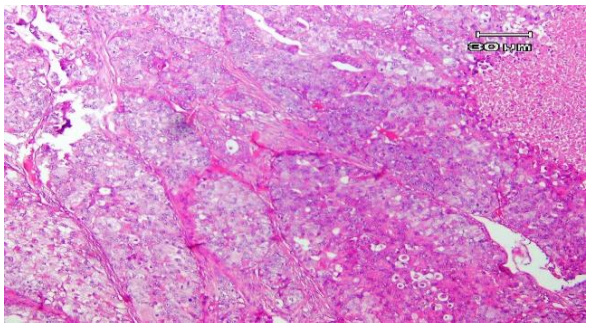
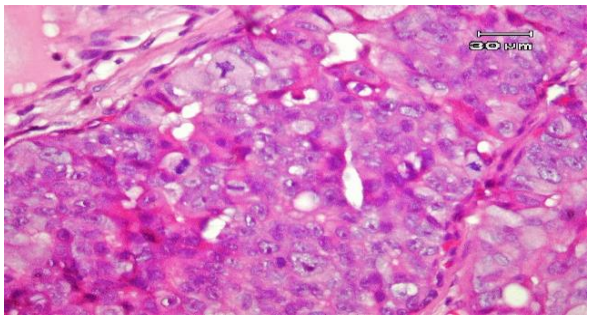


Fig. 1. Radiographic view showing an ill-defined lesion in the right parotid gland, which is attached to the superficial skin.



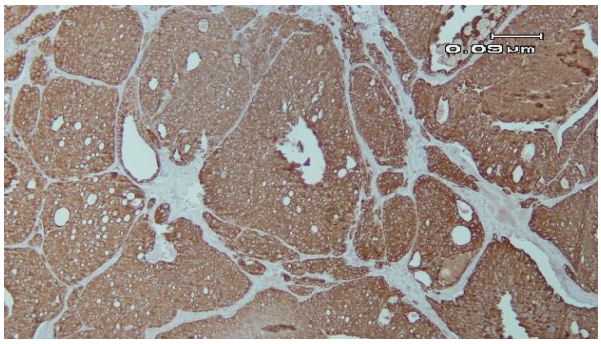
2a



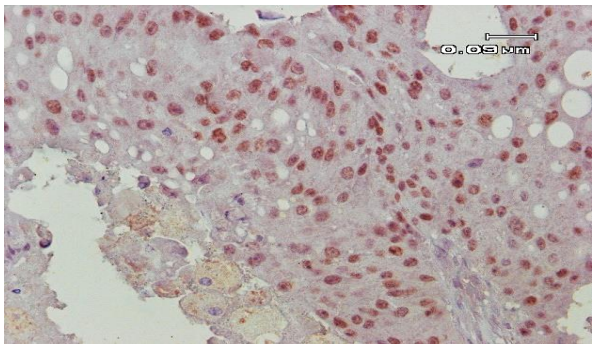
2b

Fig. 2. Microscopic features of the tumor. (a) Sheets of dysplastic cells with ductal structures. Note the comedo necrosis in the top right side (H & E staining, ×100). (b) Atypical mitotic features in tumoral cells (H & E staining, ×400)

Severe pleomorphism and atypical mitotic features were also seen. The most probable diagnosis was high-grade carcinoma most compatible with high-grade SDC. Immunohistochemical staining was performed to confirm the diagnosis. The tumoral cells showed positive staining for CK7 and androgen receptor (AR) (Figure 3).



3a

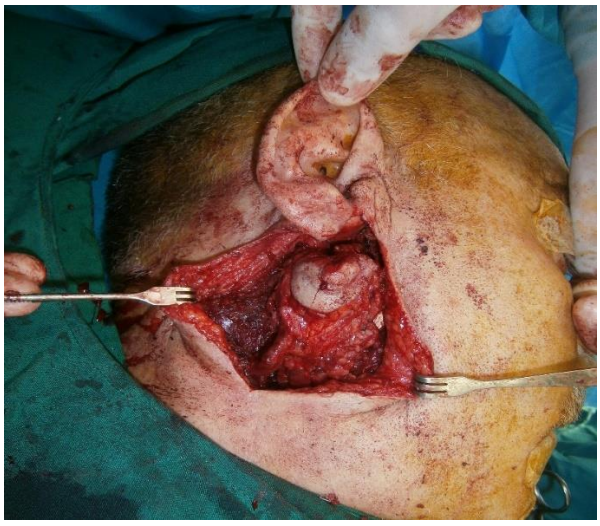


3b

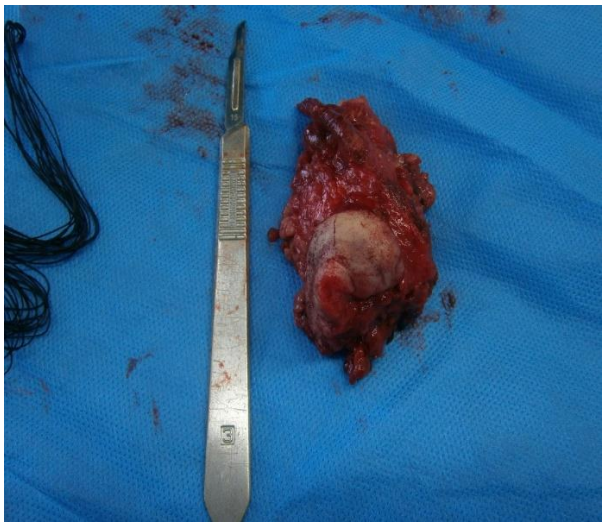
Fig. 3. Immunohistochemical staining. (a) Strong positive immunostaining for CK7 (×100). (b) Strong nuclear immunostaining for AR (×400)

Over 40% of tumoral cells showed positive staining for Ki67. The tumoral cells were negative for S100, estrogen receptor and progesterone receptor. These findings were in favor of high-grade SDC of the parotid gland. Thus, total parotidectomy was carried out followed by adjacent radiotherapy (Figure 4).

The patient had no noticeable complication at the 6-year follow-up; however, in his next follow-up session, an exophytic ulcerated small lesion was detected at the previous surgical site. The entire lesion was surgically excised with 2 mm of safe margin (Figure 5). Microscopic examination of the lesion revealed the same features as the previous lesion with free surgical margins. Considering the history of total parotidectomy and development of a new skin lesion at the same site 6 years later, we presumed that the new lesion more probably was a delayed metastatic skin lesion. Although the lesion could be a late local recurrence possibly due to implantation or seeding of the tumoral cells during the previous surgical procedure, but local recurrence was expected to happen earlier than 6 years. The patient underwent full body examination to find any other possible distant metastatic lesion. Computed tomography of the head and neck revealed one ill-defied lesion in the brain (Figure 5). Unfortunately, the patient died 2 weeks after surgical resection of the brain lesion.



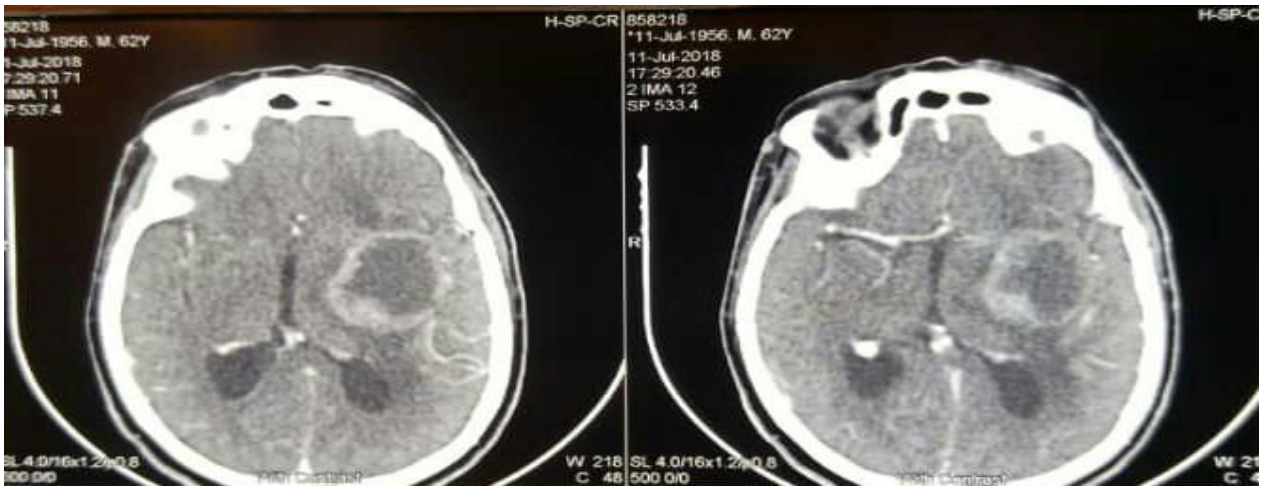
4a



4b

Fig. 4. Surgical excision of the lesion. a) Pre- and retro-auricular incision for total parotidectomy. (b) Complete excision of tumor

5a



5b

Fig. 5. Distant metastasis of the tumor. (a) Excised skin lesion with 2 mm of safe margin (b) Brain metastasis

Discussion

SDC of the parotid gland is a malignant tumor with an aggressive clinical course and occasional lung metastasis. Detection of SDC cells in the skin tissue several years after total tumorectomy is an extremely rare occurrence. SDC has a tendency to invade the

surrounding tissue and has a high metastatic potential via the hematogenous and lymphatic pathways (4,7). SDC shows an aggressive clinical course with poor prognosis, and over 70% of patients die within 3 years after the primary diagnosis (7). Although our patient survived for more than 6 years after the primary diagnosis, he died due to late distant metastasis.

SDC is usually a high-grade malignant tumor, but low-grade SDC and intraductal SDC have also been reported (8). High-grade SDC is histopathologically characterized by proliferation of dysplastic cells containing large round to oval nuclei with conspicuous nucleoli and rich eosinophilic cytoplasm, occasionally accompanied by comedo necrosis, which resembles high-grade breast carcinoma. The immunohistochemical characteristics of SDC cells include positive staining for human epidermal growth factor receptor (HER) 2, AR and CK7 (2,4). Since most salivary gland malignancies have positive immunoreactivity for CK7, immunoexpression of this protein may provide valuable information to differentiate primary salivary gland carcinomas from metastatic tumors (9). SDC usually shows negative results for expression of S-100, p63 and smooth muscle myosin (8). Our patient showed positive immunostaining for CK7 and AR.

SDC shows a high frequency of lymph node metastasis and distant metastasis to the lungs, liver, brain, and bones. In this study, we presented a case of SDC of the parotid gland in a 62 year-old man with unusual metastases to the skin and brain 6 years after primary treatment. Based on this fact that metastasis of SDC to the skin tissue is very uncommon and the cutaneous lesion happened in the primary site of the lesion, late local recurrence could be considered. On the other hand, local recurrence was expected to happen sooner than 6 years. It seemed that an unusual cutaneous metastasis was the most probable diagnosis. The above-mentioned points indicate the aggressiveness and poor prognosis of SDC.

Although complete surgical resection and ipsilateral neck dissection followed by postoperative radiation comprise the standard treatment for SDC (10-12), the reported survival rate is 43% for the 5-year disease-specific survival and 36% for the disease-free survival (2,13). Johnston *et al.* reported that 37.5% of the patients with local and regional recurrence of SDC showed distant metastases (14). The majority of them received palliative therapy and supportive care, although some of them underwent salvage surgery with additional radiation therapy (14).

In this case, we highlighted the importance of having a high insight in evaluation of highly aggressive tumors such as SDC for atypical findings during periodic follow-ups especially in long-term. It seems that routine surgical treatment may not be enough even in cases with no distant metastasis at the time of initial diagnosis. Considering the aggressive nature of SDC, chemotherapy accompanied by surgical treatment may be the best approach for patients with SDC. Although systemic chemotherapy should be considered to minimize the risk of distant metastasis of SDC, there is no convincing evidence supporting the optimal efficacy of chemotherapy for SDC. On the other hand, a previous study claimed that chemotherapy was not effective for SDC, and SDC cells were resistant to chemotherapy (14). Recently, Kawahara *et al.* reported that although cetuximab monochemotherapy was not sufficient to control tumor growth in SDC, cisplatin/5-FU chemotherapy plus cetuximab was effective for treatment of lung metastasis of SDC (3).

Some prognostic factors have been suggested for SDC prognosis. In major salivary glands, tumor size > 3 cm, patient's age over 50 years, lymph node involvement, high tumor grade, perineural invasion, positive surgical margins, and regional and distant metastases may indicate poor prognosis (2,15,16). In addition, overexpression of HER2/neu and p53 has been reported as a poor prognostic factor for early regional recurrence, distant metastasis, and eventually lower survival rate (17). Considering the overexpression of HER2/neu in SDC, anti-HER2 monoclonal antibodies (trastuzumab) have been suggested for targeted therapy of advanced SDC HER2/neu-positive tumors (18). Williams *et al.* found that both AR and estrogen receptor β-negative SDC were significantly correlated with a lower survival rate (17). This finding may explain the poor prognosis of our reported AR-positive case with delay distant metastasis. For AR-positive SDCs, androgen deprivation therapy has also been evaluated as a treatment option (19,20). Along with these studies, we suggest that AR positivity in SDC may be correlated with poor prognosis and can be used for targeted therapy of AR-positive SDCs. Further studies are required to assess the effectiveness of targeted therapy for advanced SDCs.

Conclusion

We reported a 62-year-old male patient with SDC of the parotid gland with unusual metastases to the skin of the primary site and brain 6 years after the primary treatment. Despite the comprehensive treatment composed of total parotidectomy and radiotherapy, the patient died 6 years after surgery because of late distant metastasis to the brain. These findings highlight the aggressiveness, poor prognosis and low rate of disease-specific and disease-free survival of SDC and also the need for long term follow up and further knowledge about the available treatment options for management of this tumor.

Acknowledgements

We would like to express our gratitude to Dr. Pouyan Aminishakib for valuable comments in various aspects that really improved the manuscript.

Conflict of Interest

The authors declared that there is no conflict of interest regarding the publication of this article.

References

1. Kleinsasser O, Klein HJ, Hűbner G. Salivary duct carcinoma: a grope of salivary gland tumors analogous to mammary duct carcinoma. Arch Klin Exp Ohren Nasen Kehlkopfheilkd. 1968; 192: 100-105. [DOI:10.1007/BF00301495] [PMID]
2. Hsu CC, Li WY, Chu PY. Salivary duct carcinoma of the supraglottis with a distinct presentation: A case report and literature review. Medicine. 2018 Mar;97(11). [DOI:10.1097/MD.0000000000010095] [PMID] [PMCID]
3. Kawahara K, Hiraki A, Yoshida R, Arita H, Matsuoka Y, Yamashita T, Koga KI, Nagata M, Hirosue A, Fukuma D, Nakayama H. Salivary duct carcinoma treated with cetuximab-based targeted therapy: A case report. Molecular and clinical oncology. 2017 Jun 1;6(6):886-92. [DOI:10.3892/mco.2017.1226] [PMID] [PMCID]
4. Zainab H, Sultana A, Jahagirdar P. Denovo High Grade Salivary Duct Carcinoma: A Case Report and Review of Literature. Journal of clinical and diagnostic research: JCDR. 2017 Jul;11(7):ZD10. [DOI:10.7860/JCDR/2017/29195.10210] [PMID] [PMCID]
5. Otsuru M, Aoki T, Kondo Y, Ota Y, Sasaki M, Suzuki T, Ogura G, Kumaki N. Salivary Duct Carcinoma with Invasive Micropapillary and Rhabdoid Feature Arising in the Submandibular Gland. The Tokai journal of experimental and clinical medicine. 2017 Apr 20;42(1):30-6.
6. Boon E, Bel M, van Boxtel W, van der Graaf WT, van Es RJ, Eerenstein SE, Baatenburg de Jong RJ, van den Brekel MW, van der Velden LA, Witjes MJ, Hoeben A. A clinicopathological study and prognostic factor analysis of 177 salivary duct carcinoma patients from The N etherlands. International journal of cancer. 2018 Mar 1. [DOI:10.1002/ijc.31353] [PMID] [PMCID]
7. Gondak RO, Mariano FV, Alves FA, Almeida OP, Lopes MA. Salivary duct carcinoma in minor salivary glands: report of two cases with different clinical behavior. J Clin Exp Pathol. 2014;4(2):1-6. [DOI:10.4172/2161-0681.1000164]
8. Xie S, Yang H, Bredell M, Shen S, Huijun Y, Jin L, et al. Salivary duct carcinoma of the parotid gland: A case report and review of the literature. Oncology letters. 2015;9:371-74. [DOI:10.3892/ol.2014.2655] [PMID] [PMCID]
9. Chandrasekar C, Salati N, Rao L, Radhakrishnan R. Salivary duct carcinoma in the mandibular anterior region: The role of immunohistochemical markers in its definitive diagnosis. J Oral Maxillofac Pathol. 2016;20:505-09. [DOI:10.4103/0973-029X.190955] [PMID] [PMCID]
10. Jaehne M, Roeser K, Jaekel T, Schepers JD, Albert N and Löning T: Clinical and immunohistologic typing of salivary duct carcinoma: A report of 50 cases. Cancer. 2005;103: 2526 2533. [DOI:10.1002/cncr.21116] [PMID]
11. McHugh JB, Visscher DW and Barnes EL: Update on selected salivary gland neoplasms. Arch Pathol Lab Med. 2009;133: 1763 1774.
12. Shinoto M, Shioyama Y, Nakamura K, Nakashima T, Kunitake N, Higaki Y, Sasaki T, Ohga S, Yoshitake T, Ohnishi K, et al: Postoperative radiotherapy in patients with salivary duct carci¬noma: Clinical outcomes and prognostic factors. J Radiat Res. 2013;54: 925 930. [DOI:10.1093/jrr/rrt026] [PMID] [PMCID]
13. Luk PP, Weston JD, Yu B, et al. Salivary duct carcinoma: clinicopathologicfeatures, morphologic spectrum, and somatic mutations. Head Neck. 2016;38(suppl 1):E1838-47. [DOI:10.1002/hed.24332] [PMID]
14. Johnston ML, Huang SH, Waldron JN, Atenafu EG, Chan K, Cummings BJ, Gilbert RW, Goldstein D, Gullane PJ, Irish JC, et al: Salivary duct carcinoma: Treatment, outcomes, and patterns of failure. Head Neck. 2016;8 (Suppl 1): E820 E826. [DOI:10.1002/hed.24107] [PMID]
15. Jayaprakash V, Merzianu M, Warren GW, et al. Survival rates and prognostic factors for infiltrating salivary duct carcinoma: analysis of 228 cases from the Surveillance, Epidemiology, and End Results database. Head Neck 2014;36:694-701. [DOI:10.1002/hed.23350] [PMID] [PMCID]
16. Pons Y, Alves A, Clement P, et al. Salivary duct carcinoma of the parotid. Eur Ann Otorhinolaryngol Head Neck Dis. 2011;128:194-6. [DOI:10.1016/j.anorl.2010.12.008] [PMID]
17. Williams MD, Roberts D, Blumenschein GRJr, et al. Differential expression of hormonal and growth factor receptors in salivary duct carcinomas: biologic significance and potential role in therapeutic stratification of patients. Am J Surg Pathol. 2007;31:1645-52. [DOI:10.1097/PAS.0b013e3180caa099] [PMID]
18. Kaidar-Person O, Billan S, Kuten A. Targeted therapy with trastuzumab for advanced salivary ductal carcinoma: case report and literature review. Med Oncol. 2012;29:704-6. [DOI:10.1007/s12032-011-9884-1] [PMID]
19. Simpson RH. Salivary duct carcinoma: new developments-morphological variants including pure in situ high grade lesions; proposed molecular classification. Head Neck Pathol. 2013;7(suppl 1):S48-58. [DOI:10.1007/s12105-013-0456-x] [PMID] [PMCID]
20. Luk PP, Weston JD, Yu B, et al. Salivary duct carcinoma: clinicopathologic features, morphologic spectrum, and somatic mutations. Head Neck. 2016;38(suppl 1):E1838-47. [DOI:10.1002/hed.24332] [PMID]

How to Cite This Article

Mir Mohammad Sadeghi, H., Karimi, A., Rahpeima, A., Derakhshan, S. Salivary Duct Carcinoma with Late Distant Brain and Cutaneous Metastasis: A Case Report. *Iranian Journal of Pathology*, 2020; 15(3): 251-255. doi: 10.30699/ijp.2020.103326.2039