Primary Mucinous Carcinoma of the Facial Skin : A Case Report and Literature Review

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－ ABSTRACT －

Primary mucinous carcinoma of the facial skin is a rare adnexal tumor that arises from sweat glands. These tumor are diagnosed by their clinical, histopathologic, and immunohistochemical features, and by exclusion of metastasis from mucinous carcinoma at other sites. Currently, positron emission tomography-computed tomography (PET-CT) is known to be a useful tool to identify for early lesions in various carcinomas. However, PET-CT is not always specific for head and neck mucinous carcinoma lesions because of high mucin content of the tumor mass. This report describes a patient with primary mucinous carcinoma of the facial skin, who was treated surgically. Ten months after wide excision with negative resection margins, there have been no signs of tumor recurrence. **(J Clinical Otolaryngol 2017;28:110-115)**

KEY WORDS：Mucinous carcinoma · Skin neoplasm · Sweat gland neoplasms · Positron-emission tomography.

Introduction

Primary mucinous carcinoma of the skin (PMCS), also called adenocystic carcinoma, colloid carcinoma, gelatinous carcinoma, and mucin secreting carcinoma, is an extremely rare cutaneous cancer that arises from the sweat glands.[1)] PMCS must be differentiated from cutaneous metastasis of mucinous adenocarcinomas at other sites. This report describes a PMCS in a 45-year-old man. Ten months after wide excision with negative resection margins, there has been no evidence of recurrence or nodal metastasis.

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Case Report

The patient was a 45-year-old man with a 1 year history of a slowly growing, nontender nodule on his left cheek. The patient denied any trauma or irradiation of the affected area. The patient had a biopsy at an outside hospital. However, the pathology report showed a mucinous carcinoma. Thus, the patient was referred to our hospital.

Initial examination showed an about 1.5 cm-sized scar on his left cheek (Fig. 1A). Re-examination of the specimen slides again showed mucinous carcinoma. The possibility of metastasis was assessed by performing PET-CT, gastroscopy, colonoscopy, and CT scans of the chest and abdomen. These modalities failed to identify any primary tumors or significant lymph nodes. Preoperative MRI (Magnetic Resonance Imaging) showed an irregularly shaped, enhanced soft tissue lesion, of longest transverse axis about 1.6 cm in size (Fig. 2A). However, PET-CT was not showed FDG (Fluorode-

oxy-D-Glucose) uptake (Fig 2B). The tumor was located in the subcutaneous fat layer between the overlying skin and the partial orbicularis oculi muscle. The lesion was again resected with safety margins of 12 mm.

Examination of an intraoperative frozen biopsy showed that all margins were free of tumor cells. Plastic surgeons reconstructed the elliptical defect with a pedicled superficial temporalis fascial flap (Fig. 1B). The patient's postoperative course was unremarkable. The final pathologic report indicated no residual tumor.

Histopathology showed a tumor circumscribed by large amounts of mucin compartmentalized by fibrous septa and scattered floating islands of tumors cells in the dermis (Fig. 3).

Immunohistochemical examinations showed that the tumor cells were positive for cytokeratin 7 (CK7) (Fig. 4A), estrogen receptor (Fig. 4C), and progesterone receptor (Fig. 4D), but were negative for cytokeratin 20 (CK20) (Fig. 4B). Taken together, these findings indicated a diagnosis of PMCS. Ten months after sur-

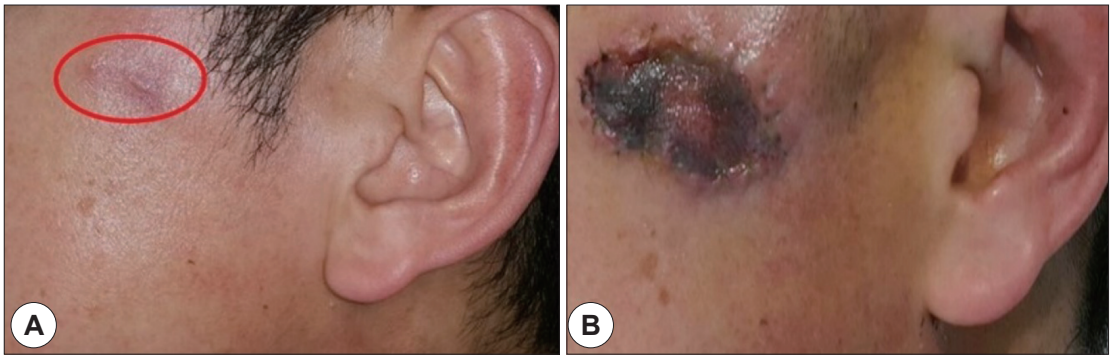

Fig. 1. Preoperative and postoperative pictures. Preoperative picture showing a 1.5 cm-sized biopsy scar on the left cheek (A). Postoperative picture showing wide excision of the lesion in the left cheek area with resection margins of 12 mm. The scar was reconstructed with a pedicled superficial temporalis fascial flap (B).

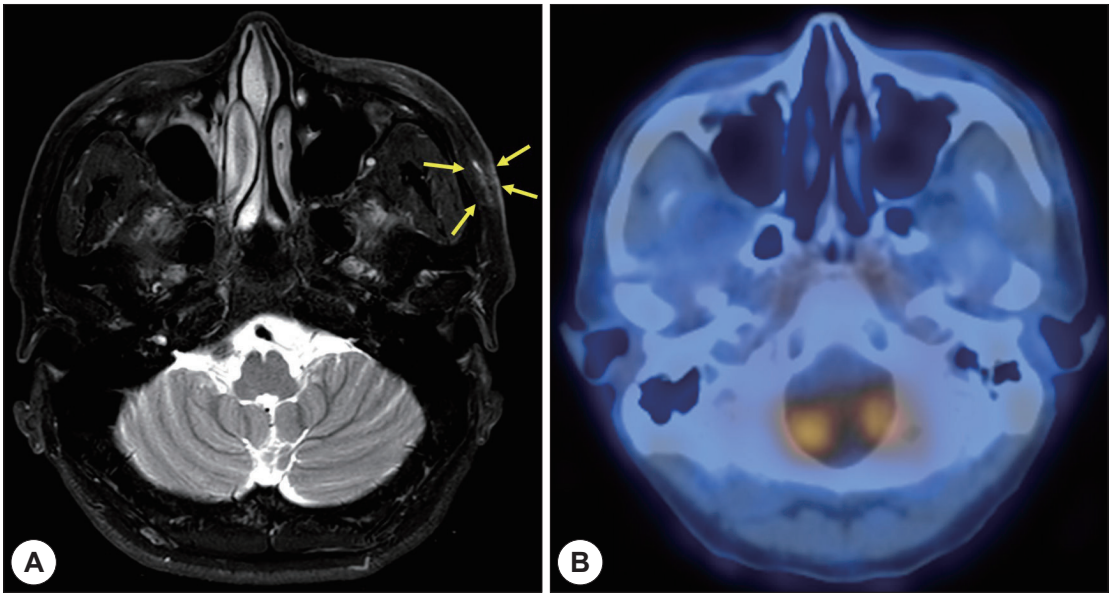

Fig. 2. Preoperative MRI and PET-CT imaging. T2 MRI. Arrows indicates the area of the tumor in the left side of zygomatic region (A). No uptake of FDG in the PET-CT scan in the area of left zygomatic tumor (B).

gery, there has been no evidence of tumor recurrence (Fig. 5).

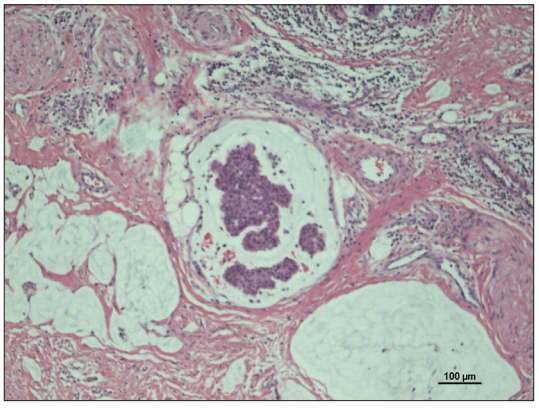

Fig. 3. Histopathology showing a circumscribed tumor with large amounts of mucin compartmentalized by fibrous septa and scattered floating islands of tumor cells in the dermis (hematoxylin and eosin stain, 100×).

Discussion

Primary mucinous carcinomas are sweat gland-derived tumors.[2] PMCS mainly affects elderly patients, with higher rates in men than in women.[3] These tumors generally grow slowly, with high rates of local recurrence but low rates of distant metastasis.[4] PMCS is usually located in the head and neck region, with the eyelids (41%) being the most common site of presentation.5,6) Additional locations include the scalp (17%), face (14%), axilla (9%), chest/abdomen (7%), vulva (4%), neck (2%), extremity (2%), canthus (2%), groin (1%), and ear (1%).[5,6]

PMCS is often misdiagnosed clinically because it has an uncharacteristic gross appearance and may microscopically resemble cutaneous metastasis from other mucinous carcinomas, including those of the breast,

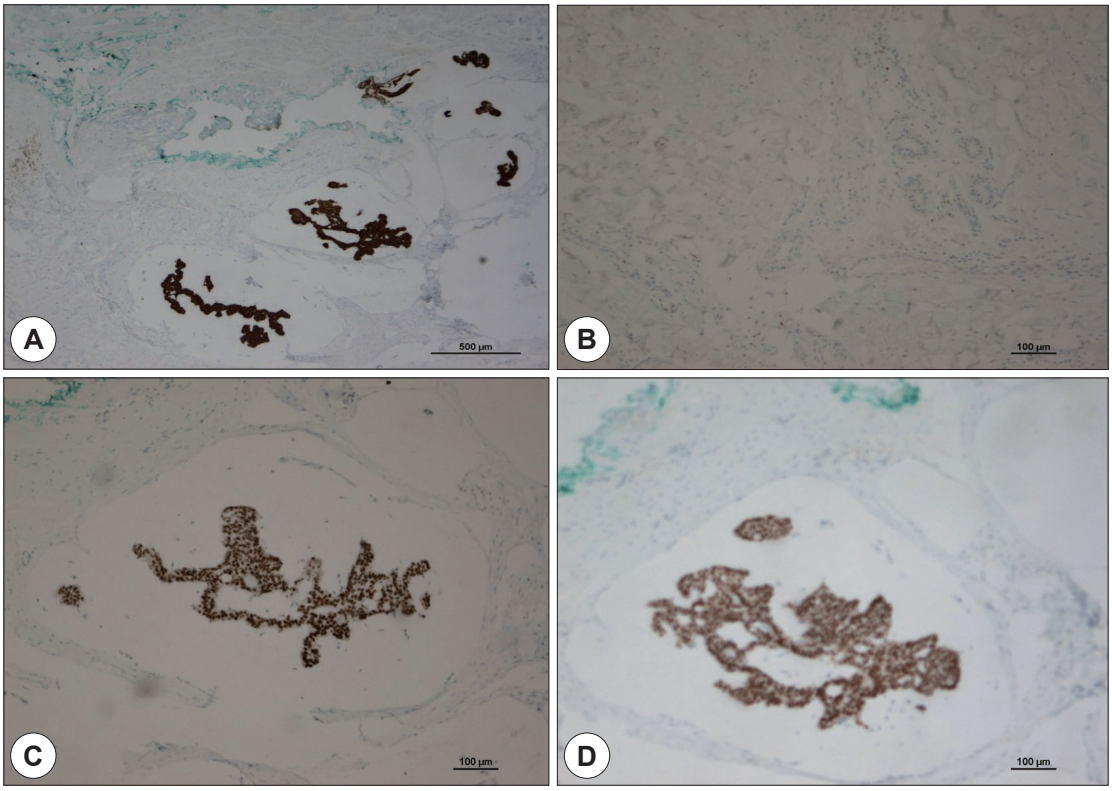

Fig. 4. Immunohistochemistry findings. A : Positive for CK7 (40×). B : negative for CK20 (100×). C : Positive for estrogen receptors (100×). D : Positive for progesterone receptors (100×).

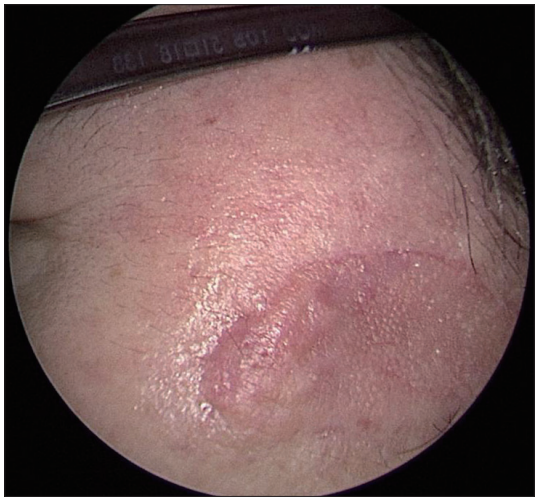

Fig. 5. Photo of postoperative ten months with no evidence of recurrence.

gastrointestinal tract, lungs, ovaries, prostate, salivary glands, and lacrimal glands.[4] CT scans of the chest, abdomen, and pelvis are recommended, and upper and lower gastrointestinal endoscopic examinations should also be considered.[7] Although PET-CT may be useful, false negative results have been reported in patients with mucin-producing carcinomas due to the hypocellularity of these tumors.[8] Concerning the histological characteristics of PMCS, FDG uptake may be positively associated with tumor cellularity, and negatively associated with the mucin content of the tumor mass, which accounts for the low detectability of FDG PET-CT.[9,10] MRI (Magnetic resonance imaging) is very helpful modality to plan the surgical margin. Mucinous carcinoma is generally believed to show high signal intensity on T2-weighted images because of its large mucin component.[11]

Immunohistochemical staining has been reported to be helpful in the diagnosis of PMCS. Immunohistochemistry is used to understand the distribution and localization of biomarkers and differentially expressed proteins in different parts of biological tissue.[12] Because most colorectal cancers express CK20, the absence of CK20 may help in excluding a diagnosis of metastasis from colorectal cancers.[13] PMCS is CK7 positive and CK20 negative, similar to breast cancer but different from gastrointestinal adenocarcinoma, which is CK7 negative and CK20 positive. Use of CK7 and CK20 immunohistochemical stains thus allows approximately one-half of cases of mucinous carcinomas (ie, those from the gastrointestinal tract) to be effectively eliminated from consideration. Other CK7-positive and CK20-negative tumors such as adenocarcinoma of the lung and gallbladder may metastasize to the skin; these can be differentiated from a primary skin tumor based largely on clinical investigation with potential assistance from other immunohistochemical stains. And, although there are controversies, the expression of p63 also have a diagnostic utility. The p63 immunostaining highlights a peripheral layer of myoepithelial cells, this is considered diagnostic of an in situ component of the tumor and conclusive evidence of an origin in the skin.[5,14,15] Although immunohistochemistry may help in establishing the primary site of the tumor, a final diagnosis requires thorough clinical investigation to exclude the likelihood of more common primary mucinous carcinomas, including those of the breast, lungs, gastrointestinal tract, prostate, and ovaries.[4]

The primary treatment of PMCS consists of wide local excision with clear margins and lymph node dissection for clinically positive nodes.[6] Because of the recurring nature of the tumor, adequate excision with wide margins (at least 1 cm) is advocated.[16-18] Mohs procedure is also preferable for PMCS.[19] Mohs surgery is a precise surgical technique used to treat skin cancer. During Mohs surgery, thin layers of cancer-containing skin are progressively removed and examined until only cancer-free tissue remains. The goal of Mohs surgery is to remove as much of the skin cancer as possible, while doing minimal damage to surrounding healthy tissue. Mohs surgery has been well-established as the gold standard for the treatment of basal cell carcinomas and squamous cell carcinomas with lower recurrence rate and better normal tissue conservation.[20] Many reports suggest that it may play and equally important role in the management of several other cutaneous malignancies.[21] In 1988, Weber et al first reported the use of Mohs micrographic surgery for the treatment of pri-

mary mucinous carcinoma of the eyelid.[22] John et al reviewed 23 cases of primary mucinous carcinoma of the eyelid treated with Mohs procedure.[5] The rate of reported recurrence derived from the cases in which follow-up is provided is 26% (6 of 23 cases), with an average follow-up period of 26.3 months (range, 1−158 months).[5] This recurrence rate is significantly less than that reported previously for primary mucinous carcinoma of the eyelid with conventional surgical excision (recurrence rate 40%).[23,24] However, in this case, we did not perform the surgery with Mohs procedure. We could estimate the size, location and depth of the tumor through MRI scan and the features of exposed skin lesion. And, the tumor was located in the zygomatic area without involving functional structures or cosmetically important regions in the face, such as eyelids, intercanthal region, nasal columella, and lips. We could remove the tumor with relatively lower limitation of resection margin with conventional surgical excision.

The presence of estrogen and progesterone receptors in our case of PMCS, and some previously published similar reports,[2,25-27] support the potential usefulness of anti-estrogenic drugs like tamoxifen to treat PMCS as there is a high rate of local recurrence after surgical excision, especially in anatomical areas where adequate wide excision is not possible.[25] Recurrence in patients with estrogen receptor positive tumors may be reduced by adjuvant hormone treatment with tamoxifen.[26] Other treatments, such as chemotherapy and radiation, are generally not employed in the management of PMCS.[17] PMCS is generally resistant to radiotherapy and chemotherapy, surgical excision is the therapeutic mainstay in most cases.[16,28] However, by the literature review, postoperative adjuvant radiotherapy was applied in the recurrent cases of PMCS.[3,7,29] Elective lymph node dissection is performed with clinically positive nodes.[6] Prophylactic lymph node dissection should be considered for recurrent, locally aggressive, or poorly differentiated tumors.[6] In our case, there were no significant lymph nodes in head and neck regions. Thus, we did not have elective neck dissection.

Because PMCS is slow growing and painless, its diagnosis may be delayed or it may be misdiagnosed as a benign lesion. Lesions that persist for several months must be further assessed, even if these lesions look benign. Generally, PET-CT is useful diagnostic tool to find out the primary and metastatic region of tumors. However, PET-CT is limited in the evaluation of mucinous carcinomas, particularly in hypocellular lesions with abundant mucin. Thus, it is important to correlate with other diagnostic modalities such as MRI of tumor site, abdomen-chest-pelvis CT, and upper-lower gastrointestinal endoscopic examinations.

Patients with skin metastasis from a primary tumor usually have a poor prognosis. By contrast, patients with PMCS generally have a good prognosis, with cure often achieved by wide excision.[3] Patients should be counseled about the importance of periodic follow-ups for evaluation of local recurrence or development of regional lymphadenopathy.

REFERENCES

1) Balin AK, Fine RM, Golitz LE. *Mucinous carcinoma. J Dermatol Surg Oncol 1988;14(5):521-4.*
2) Bellezza G, Sidoni A, Bucciarelli E. *Primary mucinous carcinoma of the skin. Am J Dermatopathol 2000;22(2): 166-70.*
3) Miyasaka M, Tanaka R, Hirabayashi K, Yamazaki A, Shinohara H, Taira H, *et al. Primary mucinous carcinoma of the skin: a case of metastasis after 10 years of disease-free interval. Eur J Plast Surg 2009;32(4):189-93.*
4) Breiting L, Christensen L, Dahlstrøm K, Breiting V, Winther JF. *Primary mucinous carcinoma of the skin: a population-based study. Int J Dermatol 2008;47(3):242-5.*
5) Papalas JA, Proia AD. *Primary mucinous carcinoma of the eyelid: a clinicopathologic and immunohistochemical study of 4 cases and an update on recurrence rates. Arch Ophthalmol 2010;128(9):1160-5.*
6) Steve R. *Martinez MD. Primary mucinous carcinoma of the skin: a review. The internet Journal of Oncology 2004;2.*
7) Anderson PJ, Dobson CM, Berry RB. *Mucinous adenocarcinoma of the face. A case report. Int J Oral Maxillofac Surg 2004;33(6):610-2.*
8) Berger KL, Nicholson SA, Dehdashti F, Siegel BA. *FDG PET evaluation of mucinous neoplasms: correlation of FDG uptake with histopathologic features. AJR Am J Roentgenol 2000;174(4):1005-8.*
9) Lee JW, Lee SM, Lee MS, Shin HC. *Role of ^{18}F-FDG PET/CT in the prediction of gastric cancer recurrence after curative surgical resection. Eur J Nucl Med Mol Imaging 2012;39(9):1425-34.*

10) Jih MH, Friedman PM, Kimyai-Asadi A, Goldberg LH. *A rare case of fatal primary cutaneous mucinous carcinoma of the scalp with multiple in-transit and pulmonary metastases. J Am Acad Dermatol 2005;52(5 Suppl 1):S76-80.*
11) Kawashima M, Tamaki Y, Nonaka T, Higuchi K, Kimura M, Koida T, *et al. MR imaging of mucinous carcinoma of the breast. AJR Am J Roentgenol 2002;179(1):179-83.*
12) Kandalaft PL, Gown AM. *Practical Applications in Immunohistochemistry: Carcinomas of Unknown Primary Site. Arch Pathol Lab Med 2016;140(6):508-23.*
13) Kalebi A, Hale M. *Primary mucinous carcinoma of the skin: usefulness of p63 in excluding metastasis and first report of psammoma bodies. Am J Dermatopathol 2008;30 (5):510.*
14) Kazakov DV, Suster S, LeBoit PE, Calonje E, Bisceglia M, Kutzner H, *et al. Mucinous carcinoma of the skin, primary, and secondary: a clinicopathologic study of 63 cases with emphasis on the morphologic spectrum of primary cutaneous forms: homologies with mucinous lesions in the breast. Am J Surg Pathol 2005;29(6):764-82.*
15) Qureshi HS, Salama ME, Chitale D, Bansal I, Ma CK, Raju U, *et al. Primary cutaneous mucinous carcinoma: presence of myoepithelial cells as a clue to the cutaneous origin. Am J Dermatopathol 2004;26(5):353-8.*
16) Beteddini OS, Sheikh S, Shareefi F, Shahab R. *Primary mucinous adenocarcinoma of the scalp: a case report and literature review. Int J Surg Case Rep 2015;10:241-4.*
17) Mardi K, Diwana VK. *Primary cutaneous mucinous carcinoma: a rare entity. Indian Dermatol Online J 2011;2(2): 82-4.*
18) Maerki J, Ahmed S, Lee E. *Primary mucinous carcinoma of the skin. Eplasty 2013;13:ic47.*
19) Ortiz KJ, Gaughan MD, Bang RH, Padilla RS, Crooks LA. *A case of primary mucinous carcinoma of the scalp treated with mohs surgery. Dermatol Surg 2002;28(8):751-4;discussion 4.*
20) Rowe DE, Carroll RJ, Day CL. *Long-term recurrence rates in previously untreated (primary) basal cell carcinoma: implications for patient follow-up. J Dermatol Surg Oncol 1989;15(3):315-28.*
21) Pennington BE, Leffell DJ. *Mohs micrographic surgery: established uses and emerging trends. Oncology (Williston Park) 2005;19(9):1165-71;discussion 71-2, 75.*
22) Weber PJ, Hevia O, Gretzula JC, Rabinovitz HC. *Primary mucinous carcinoma. J Dermatol Surg Oncol 1988;14(2): 170-2.*
23) Snow SN, Reizner GT. *Mucinous eccrine carcinoma of the eyelid. Cancer 1992;70(8):2099-104.*
24) Wright JD, Font RL. *Mucinous sweat gland adenocarcinoma of eyelid: a clinicopathologic study of 21 cases with histochemical and electron microscopic observations. Cancer 1979;44 (5):1757-68.*
25) Kwatra KS, Prabhakar BR, Jain S. *Oestrogen and progesterone receptors in primary mucinous carcinoma of skin. Australas J Dermatol 2005;46(4):246-9.*
26) Hanby AM, McKee P, Jeffery M, Grayson W, Dublin E, Poulsom R, *et al. Primary mucinous carcinomas of the skin express TFF1, TFF3, estrogen receptor, and progesterone receptors. Am J Surg Pathol 1998;22(9):1125-31.*
27) Carson HJ, Gattuso P, Raslan WF, Reddy V. *Mucinous carcinoma of the eyelid. An immunohistochemical study. Am J Dermatopathol 1995;17(5):494-8.*
28) Kelly BC, Koay J, Driscoll MS, Raimer SS, Colome-Grimmer MI. *Report of a case: primary mucinous carcinoma of the skin. Dermatol Online J 2008;14(6):4.*
29) Laco J, Simáková E, Svobodová J, Ryska A. *Recurrent mucinous carcinoma of skin mimicking primary mucinous carcinoma of parotid gland: a diagnostic pitfall. Cesk Patol 2009;45(3):79-82.*