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Signet Ring Cell Carcinoma of the Gallbladder with Skin Metastasis: A Case Report

Cilt Metastazı Yapan Safra Kesesinin Taşlı Yüzük Hücreli Karsinomu: Olgu Sunumu

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ABSTRACT

The aim of this case report is to attract the attention of related clinicians to similar cases because of their rarity. We believe this case and other similar cases in the literature could initiate studies that may explain the pathways of metastasis.

A 50-year-old female patient underwent laparoscopic cholecystectomy because of symptomatic cholelithiasis. Postoperative pathologic examination of the specimen led to a diagnosis of signet ring carcinoma in the wall of gallbladder. After this incidental diagnosis, this patient underwent a second operation, which was a radical cholecystectomy. After pathological examination of the second operation material, we decided to call this patient for periodic controls, as the tumor was graded as stage I. A cutaneous lesion 33 months after the second operation was diagnosed as metastasis of signet ring cell carcinoma.

Signet ring carcinoma of the gallbladder is a rarely seen malignancy. Cutaneous metastasis of this rare malignancy is also quite rare. There are only a few reports of cutaneous metastasis of signet ring carcinoma of the gallbladder. It is necessary to explain the reasons of this unusual metastasis with further studies.

Key Words: Gallbladder neoplasms, Signet ring cell carcinoma, Skin nodule, Metastasis

ÖZ

Bu olgunun sunulmasının amacı nadir görülmesi sebebiyle ilgili klinisyenlerin dikkatini çekmektir. Bu olgunun, literatürde ortaya çıkan diğer benzer vakalarla birlikte değerlendirilerek metastaz basamaklarını açıklayacak çalışmalara ön ayak olabileceği düşünülmüştür.

50 yaşındaki kadın hasta semptomatik kolelitiyazis nedeniyle laparoskopik kolesistektomi ameliyatına alındı. Hastaya, ameliyat sonrası patolojik incelemede insidental olarak saptanan safra kesesinin taşlı yüzük hücreli karsinomu tanısı konuldu. Hasta 2. kez ameliyata alınarak radikal kolesistektomi yapıldı. Spesmenin patolojik incelemesi sonrası tümör evre I olduğu için takip kararı verildi. Ameliyat sonrası 33. ayda ciltte ortaya çıkan lezyona yapılan eksizyonel biyopsi sonrası taşlı yüzük hücreli karsinomun cilt metastazı saptandı.

Taşlı yüzük hücreli karsinom safra kesesinde nadir görülen bir malignitedir. Bu nadir malignitenin kutanöz metastazı da oldukça nadirdir. Literatürde safra kesesi karsinomunun alışılmadık şekilde cilde metastazını bildiren yalnızca bir kaç vaka sunumu mevcuttur. Yeni çalışmalarla bu tümörlerde görülen alışılmadık yerlerdeki metastazların nedeninin açıklanması gerekli gözükmektedir.

Anahtar Sözcükler: Safra kesesi neoplazmları, Taşlı yüzük hücreli karsinom, Deri nodülü, Metastaz

INTRODUCTION

Gallbladder carcinoma is rare and is seen with gallbladder stones in about 90% of the cases (1). It has an aggressive course except for early cases found incidentally during cholecystectomy for cholelithiasis. Signet ring cell carcinoma is a rare form of mucinous adenocarcinoma and has a worse prognosis. Skin metastasis of signet ring cell carcinoma is rare and there are only a few reported cases (2,3).

CASE REPORT

A 50-year-old female presented at the out patients department with dyspectic complaints. Her history was unremarkable except for hypertension. Physical examination revealed right upper quadrant abdominal tenderness only. Routine biochemistry tests and full blood count were normal. Upper abdominal ultrasonography revealed multiple stones in the gallbladder lumen with the largest 2 cm in diameter. Upper gastrointestinal system endoscopy showed alkaline

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reflux gastritis. Laparoscopic cholecystectomy was planned with a diagnosis of symptomatic cholelithiasis. During surgery, the gallbladder was found to be firm, thick and edematous. Malignancy was not suspected and the surgery was finished laparoscopically. Pathological examination of the gallbladder revealed malignant neoplastic infiltration as single cells and small cell groups along the complete wall of the gallbladder including the surgical margin, in addition to the stones in the gallbladder lumen. The tumor cells were denser in the areas close to the mucosal surface and became sparse further away. Cytoplasmic mucin was found in some of the cells with an eccentric nucleus (signet ring cell carcinoma) with mucin histochemistry (Figure 1). The colonoscopy, and thoracic and abdominal CT that followed were normal. The patient was reoperated to perform radical cholecystectomy. The trocar insertion site in the subxiphoid region where the gallbladder had been removed from the abdomen was excised to include the skin-subcutaneous tissue-fascia and peritoneum. The cystic stump was excised and sent for frozen section and no tumor was found on the distal part. The radical cholecystectomy was then completed. The patient was discharged uneventfully on the 7th postoperative day. Pathological investigation of the specimen showed signet ring cell carcinoma infiltration in the cystic canal stump although there was no tumor in the surgical margin. Reactive changes were seen in sections of the skin, subcutaneous tissue, peritoneum and falciform ligament. No metastasis was found in the 3 lymph nodes dissected from the paraduodenal and paracholedochal regions. The patient was referred to Oncology and followed-up with no treatment recommendiation. The patient underwent routine follow-up with no signs or symptoms but presented at the outpatients department 33 months after the surgery with a 2x2 cm mass on the skin over the left scapula. The mass was excised under local anesthesia. Pathological investigation of this mass revealed signet ring cell carcinoma and clean surgical margins (Figure 2). Positron emission tomography was performed and revealed a 2 cm area in the bony tissue of the occipital region that was consistent with metastasis. Chemotherapy was decided on and the patient underwent 12 cycles. Shoulder magnetic resonance imaging was performed for shoulder pain and showed findings consistent with metastasis. Bone scintigraphy also showed widespread metastases and radiotherapy was initiated. The patient currently continues to receive treatment on the 40th month following the surgery.

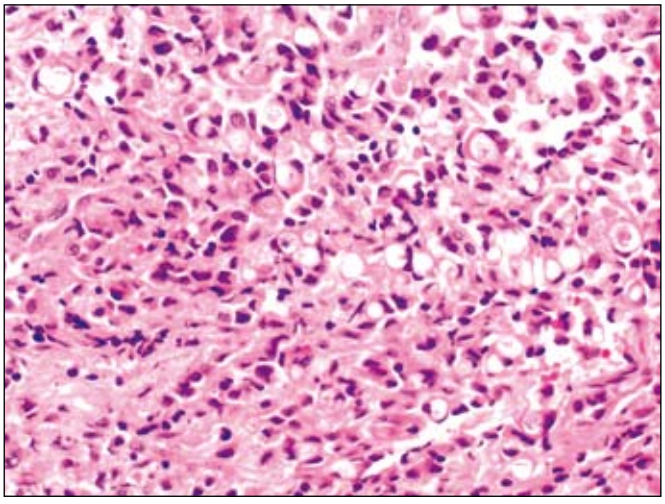

Figure 1: Signet ring cell carcinoma infiltration of gallbladder wall (H&E, x400).

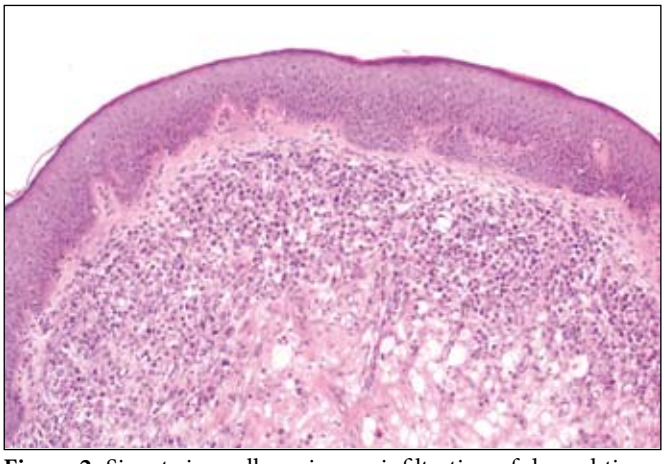

Figure 2: Signet ring cell carcinoma infiltration of dermal tissue (the dermis) (H&E, x100).

DISCUSSION

Signet ring cell carcinoma is a rare type of mucinous adenocarcinoma and has a poor prognosis (4). When a diagnosis of gallbladder cancer is made, usually 50% of cases have local regional spread or regional lymph node metastasis. Lymphatic spread is to the hepatic artery and celiac axis or portal system (4). The rate of skin metastasis from intraabdominal malignancies is 1 to 9% (5). Skin metastasis of signet ring cell carcinoma is rare. There are few well-documented cases in the literature (2,3). The 5-year survival for gallbladder cancer is less than 5% despite aggressive treatment (4). Our case was Grade I (T1N0M0). The expected 5-year survival for grade I patients is reported as 75 to 100% (6,7). The treatment for early grade incidental cancers is a matter of debate. Some authors provide long survival periods following cholecystectomy, saying this surgery is sufficient without a need for reoperation while others feel reoperation and radical cholecystectomy are the only way to obtain cure (8-10).

Skin tumors of signet ring cell morphology may be metastatic or primary. The skin metastases of signet ring cell carcinomas usually originate from the stomach, pancreas, colon, rectum, breast, prostate, gallbladder and bladder that are the most common mucin-secreting adenocarcinomas. If the signet ring cell carcinoma of the skin is primary, such cases have been reported with primary signet cell ring carcinoma of the skin, squamous cell carcinoma, basal cell carcinoma, signet ring cell lymphoma, trichilemmal carcinoma and malignant melanoma (3,11). Although the skin metastasis of signet ring cell carcinoma usually appears as a nodule and a plaque with central necrosis, herpetiform lesions have also been reported recently (12). Excess mucin is collected in signet ring cell carcinomas as there are no normal secretion or excretion mechanisms. The nucleus is compressed in one part of the cell and looks like a crescent, giving rise to the signet ring name. The mucinous content looks clear with routine stains while it stains positive with Periodic acid-Schiff, negative with diastase and positive with mucicarmen (11). Immunohistochemical investigation may help differentiate the origin of signet ring cell carcinoma. Cytokeratin 7 is positive in tumors of gallbladder, hepatic canal and pancreatic canal origin. Cytokeratin 20 is positive in gastric/intestinal mucosa or gallbladder and skin primary signet ring cell carcinoma (13). Skin metastases of signet ring cell carcinomas are mostly seen in regions rich in apocrine glands and this is attributed to the collection and growth of metastatic signet ring cells in areas with regional stromal support. This stromal support is emphasized in recurrent and metastatic disease in recent reports (14).

We presented a case that had undergone elective laparoscopic cholecystectomy for cholelithiasis and was incidentally diagnosed with grade I gallbladder cancer in this case report. A skin metastasis, which is not an expected metastasis site for signet ring cell gallbladder carcinoma, appeared during the patient's follow-up. It is difficult to explain the skin metastasis 33 months and the bone metastasis 38 months after the surgical treatment without intraabdominal organ involvement. It is necessary to explain these metastases at unusual sites of these tumors with new studies.

REFERENCES

1. ***Nagorney DM, McPherson GA:*** Carcinoma of the gallbladder and extrahepatic bile ducts. Semin Oncol 1998, 15:106-115
2. ***Krunic AL, Chen HM, Lopatka K:*** Signet-ring cell carcinoma of the gallbladder with skin metastases. Australas J Dermatol 2007, 48:187-189
3. ***Bastian BC, Kutzner H, Yen Ts, LeBoit PE:*** Signet-ring cell formation in cutaneous neoplasms. J Am Acad Dermatol 1999, 41:606-613
4. ***Henson DE, Albores-Saavedra J, Corle D:*** Carcinoma of the gallbladder. Histologic types, stage of disease, grade, and survival rates. Cancer 1992, 70:1493-1497
5. ***Lookingbill DP, Spangler N, Helm KF:*** Cutaneous metastases in patients with metastatic carcinoma: a retrospective study of 4020 patients. J Am Acad Dermatol 1993, 29:228-236
6. ***Taçyıldız İH, Aban N, Boylu Ş, Bozdağ AD, Keleş C:*** Safra kesesi kanseri. Ulusal Cerrahi Dergisi 1996, 12:217-223
7. ***Muratore A, Polastri R, Bouzari H, Vergara V, Capussotti L:*** Radical surgery for gallbladder cancer: a worthwhile operation? Eur J Surg Oncol 2000, 26:160-163
8. ***Orth K, Beger HG:*** Gallbladder carcinoma and surgical treatment. Langenbeck's Arch Surg 2000, 385:501-518
9. ***Gençosmanoğlu R, Tahan V, Yapıcıer ÖK:*** Safra kesesi kanseri: etyopatogenez, tanı yöntemleri, evreleme, tedavi modaliteleri ve prognoza güncel bakış. Güncel Gastroenteroloji 2003, 7:157-169
10. ***Wakai T, Shirai Y, Yokoyama N, Nagakura S, Watanebe H, Hatakeyama K:*** Early gallbladder carcinoma does not warrant radical resection. Br J Surg 2001, 88:675-678
11. ***Aroni K, Lazaris AC, Nikolaou I, Saetta A, Kavantzas N, Davaris PS:*** Signet ring basal cell carcinoma. A case study emphasizing the differential diagnosis of neoplasms with signet ring cell formation. Pathol Res Pract 2001, 197:853-856
12. ***Torné J, Bonaut B, Sanz C, Martínez C, Torrero MV, Miranda-Romero A:*** Cutaneous metastases of rectal adenocarcinoma in a herpetiform distribution. Actas Dermosifiliogr 2006, 97:206-207
13. ***Kiyohara T, Kumakiri M, Kouraba S, Tokuriki A, Ansai S:*** Primary cutaneous signet ring cell carcinoma expressing cytokeratin 20 immunoreactivity. J Am Acad Dermatol 2006, 54:532-536
14. ***Ayala G, Tuxhorn JA, Wheeler TM, Frolov A, Scardino PT, Ohori M, Wheeler M, Spitler J, Rowley DR:*** Reactive stroma as a predictor of biochemical-free recurrence in prostate cancer. Clin Cancer Res 2003, 9:4792-4801