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Malignant metastatic melanoma to the gallbladder: Report of a peculiar case

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ABSTRACT

INTRODUCTION: Melanoma is one of the most aggressive and one of the fastest growing types of cancer. The occurrence of a malignant melanoma in the gastrointestinal tract, either primary or metastatic, is a rare event. Metastasis from cutaneous malignant melanoma to the gallbladder are a highly uncommon finding, usually associated with diffuse metastatic disease and observed during autopsy. The event of a solitary metastasis of malignant melanoma to gallbladder is barely reported.

CASE REPORT: We report a case of a 35-year old Caucasian woman with isolated metastasis of gallbladder from cutaneous primary malignant melanoma managed with laparoscopic cholecystectomy.

DISCUSSION: Gallbladder metastasis as a first site of recurrence represents a rare condition for all cancers. Since the occurrence of an isolated gallbladder metastasis of cutaneous melanoma is an uncommon circumstance, no therapeutic guidelines have yet been proposed. Nevertheless cholecystectomy appears to be the standard of care for the treatment of this unusual condition, especially when symptomatic and for palliative purpose. The surgical approach is still debated, with no unanimous consent between mini-invasive surgery and open technique.

CONCLUSION: In our case, we decided to carry out a three-port laparoscopic cholecystectomy, preferring a mini-invasive approach considering the good performance status of our patient and her young age.

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1. Introduction

Melanoma is one of the most aggressive and one of the fastest growing types of cancer. It originates from melanocytes; these dendritic cells produce melanin and are located in the basal layer of the epidermis, but also in the eye, the mucosa of upper respiratory tract and gastrointestinal tract. Primary melanoma has an 11% mortality rate, while metastatic melanoma patients typically have a low survival rate due to the poor response to current cancer therapies [1]. The occurrence of a malignant melanoma in the gastrointestinal tract, either primary or metastatic, is a rare event. The incidence of metastatic cutaneous melanoma in gastrointestinal tract accounts from 2 to 4% [2] and the most common sites are small bowel, colon and stomach [3]. The gallbladder involvement from a metastatic cutaneous malignant melanoma is a highly

uncommon finding, usually associated with diffuse metastatic disease and observed during autopsy. Metastasis to the gallbladder are rare for all cancers [4]. The event of a solitary metastasis of malignant melanoma to gallbladder is barely described [5]. We report a case of a 35-year old Caucasian woman with isolated metastasis of gallbladder from cutaneous primary malignant melanoma in line with the SCARE criteria [6,7].

2. Case report

In November 2019 a 35-year old Caucasian woman underwent local surgical excision of ulcerated nodular melanoma located at the base of neck (Breslow thickness 4 mm; Clark's level IV with no evidence of metastases in the sentinel lymph node nor distant sites; pT3bN0M0; negative resection margins). On April 2020 she was studied with an ultrasound for follow up. Cutaneous and subcutaneous regions of neck, axillary cavity, supraclavicular fossae, inguinal region and abdomen were explored. An ovoid formation was seen alongside the surgical scar of the neck. As well, an echosolid pedunculated mass of 1.8 cm × 1.5 cm protruding into the lumen of gallbladder was found. She underwent a second local excision of the ovoid formation located at the base of the neck, and the histopathological findings pointed out a recurrence of the

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primary disease. The possibility of metastatic involvement of gallbladder was considered, which led to a PET/CT scan which showed an increased uptake of fluorodeoxyglucose (FDG) in the gallbladder (SUV 12.5). No other areas of increased uptake of FDG were identified in the liver or in the other organs. Thus, we proposed a laparoscopic three-port cholecystectomy [8]. After administration of general anaesthesia, an optical 10-mm trocar was placed at the umbilical cicatrix [9,10] via Hasson technique, and other two 5-mm trocars were placed in left hypochondriac region and in right flank. The exploration of the abdominal cavity showed neither peritoneal fluid nor macroscopic lesions of the organs. We found a distended gallbladder but no abnormalities of its peritoneal surface were found. In the lymph nodal station 12b we detected a lymph node of increased size and soft consistency at palpation with laparoscopic grasper [11]. Both the lymph node 12b and the removed gallbladder were pulled out carefully into an endobag to prevent dissemination. The histopathological findings confirmed the diagnosis of gallbladder metastasis of melanoma (immunohistochemistry positive for Melan-A, HMB-45 and S-100). No regional metastases were detected in the lymph node of 12b station, describing only a reactive tissue with no evidence of metastatic colonization. Postoperative course was uneventful and the patient was discharged on POD 2.

3. Discussion

Malignant cutaneous melanoma is a skin cancer characterized by the highest mortality due to its high potential for wide spread metastasis, with unpredictable and variable biology. One of its more important features is the Breslow thickness, which is directly proportional to the risk of disease spreading. Over 90% of melanomas are observed in the skin [12]. This tumour can virtually metastasize to any organ of the body even years after diagnosis and it is characterized by various morphologic patterns that can mimic any type of neoplastic disease ranging from benign to malignant ones [13]. Metastasis usually spread via lymphatic system draining in the areas around the primary melanoma and via blood stream to distant sites, such as skin and soft tissues, lung, liver, brain and gastrointestinal tract [2,14]. Isolated metastasis of gallbladder are barely described, and mostly present in a widespread metastatic disease. Nevertheless, in few cases the gallbladder may represent the first metastatic site [2]. The dissemination of melanoma neoplastic cells to the gallbladder may occur via blood stream but also as a mucosal implants from the bile via the liver [15]. These lesions are usually asymptomatic and mostly detected at follow-up imaging or autopsy. In a minority of cases, metastasis to the gallbladder are symptomatic. The most common presentations are epigastric and right upper quadrant pain mimicking acute cholecystitis, obstructive jaundice, and more rarely haemobilia and external biliary fistula formation [16]. Radiological findings are fundamental to help in diagnostic process. The location and nature of a gallbladder mass should be studied at first instance with ultrasonography [17], thanks to its high sensitivity and specificity. Masses of gallbladder have a lower density than gallstones and are characterized by a minimal or absent acoustic shadowing. It is also possible to identify the presence of focal thickening of gallbladder wall or intraluminal masses, or a ductal distension if the mass involves the biliary tree. Metastatic disease of gallbladder may appear as a flat and infiltrative lesion or as a single polypoid tumour. Doppler is useful to highlight the presence of pathological blood flow [18]. CT abdominal scan can reveal the presence of solid masses originating from biliary tract. Finally, positivity at fluorodeoxyglucose PET scan may show the occurrence of unsuspected metastatic sites and help in differential diagnosis of gallbladder lesions. Due to the rarity of this condition, no therapeutic guidelines have yet been proposed, but evidences show that patients with solitary melanoma

metastasis to the gallbladder may benefit from resection of the lesion with improved quality of life and survival [19–22]. Surgical treatment is indicated considering the extension of the disease and the clinical status of the patient [23]. Even in cases of disseminated disease, surgical removal seems to be valuable procedure for palliative purpose. Surgical approach is still controversial, since there are some studies preferring open surgery to mini-invasive techniques in order to minimize port site recurrence [24]. Other studies support laparoscopic surgery for all benefits of the mini-invasive technique (lesser surgical trauma and postoperative pain, better intraoperative view, faster discharge). Moreover because the melanoma metastasis of gallbladder are usually intraluminal and lymphadenectomy of hepato-duodenal ligament is not recommended laparoscopic cholecystectomy appears to be appropriate [25,26].

4. Conclusion

In conclusion, we know that isolated melanoma metastasis to gallbladder is certainly a rare entity. To date there is no an unanimous consent about the appropriate treatment of this condition, even if the few available evidences show that surgical approach appears to be beneficial in term of prognosis and improvement of quality of life. In our case, we preferred to carry out a mini-invasive laparoscopic approach considering the good performance status of our patient and the young age. On the basis of experience in oncological and laparoscopic surgery the risk of spread of disease was avoided by careful intraoperative manipulation of gallbladder and its extraction with endobag [27–29]. Further studies and evidences are required in order to better manage this rare circumstance.

Declaration of Competing Interest

The authors report no declarations of interest.

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Ethical Approval was not necessary for this study.
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Consent

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Author contribution

Di Buono Giuseppe: study design, data collections, data analysis and writing.

Maienza Elisa: study design, data collections, data analysis and writing.

Rinaldi Gaetana: data collections.

Buscemi Salvatore: data collections.

Romano Giorgio: study design, data collections, data analysis and writing.

Agrusa Antonino: study design, data collections, data analysis and writing.

Registration of research studies

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References

- [1] Y. Liu, M.S. Sheikh, Melanoma: molecular pathogenesis and therapeutic management, *Mol. Cell. Pharmacol.* 6 (3) (2014) 228.
- [2] I. Giannini, D.A. Cutrignelli, L. Resta, A. Gentile, L. Vincenti, Metastatic melanoma of the gallbladder: report of two cases and a review of the literature, *Clin. Exp. Med.* 16 (3) (2016) 295–300, <http://dx.doi.org/10.1007/s10238-015-0353-6>.
- [3] G.R. Ercolino, G. Guglielmi, L. Paziienza, F. Urbano, D. Palladino, Simeone, Gallbladder and small bowel metastasis of regressive melanoma: a case report, *BJR Case Rep.* 5 (2018), <http://dx.doi.org/10.1259/bjrcr.20180032>, p. 20180032.
- [4] M. Romero, L. Bianchi, R. Vilana, Metástasis de melanoma en la vesícula biliar [Melanoma metastasis to the gallbladder], *Radiologia* 48 (5) (2006) 321–323, [http://dx.doi.org/10.1016/s0033-8338\(06\)75143-8](http://dx.doi.org/10.1016/s0033-8338(06)75143-8).
- [5] G. Riva, M. Villanova, A. Eccher, et al., Metastatic malignant melanoma to the gallbladder. Case report and review of the literature, *Pathologica* 110 (1) (2018) 68–71, PMID: 30259913.
- [6] R.A. Agha, A.J. Fowler, A. Saetta, I. Barai, S. Rajmohan, D.P. Orgill, for the SCARE Group, The SCARE statement: consensus-based surgical case report guidelines, *Int. J. Surg.* 34 (2016) 180–186.
- [7] R.A. Agha, M.R. Borrelli, R. Farwana, K. Koshy, A. Fowler, D.P. Orgill, For the SCARE Group, The SCARE 2018 statement: updating consensus Surgical Case Report (SCARE) guidelines, *Int. J. Surg.* 60 (2018) 132–136.
- [8] A. Agrusa, G. Romano, G. Cucinella, G. Cocorullo, S. Bonventre, G. Salamone, G. Di Buono, G. De Vita, D. Frazzetta, D. Chianetta, V. Sorce, G. Bellanica, G. Gulotta, Laparoscopic, three-port and SILS cholecystectomy: a retrospective study, *G. Chir.* 34 (September–October (9–10)) (2013) 249–253.
- [9] G. Cucinella, A. Perino, G. Romano, G. Di Buono, G. Calagna, V. Sorce, L. Gulotta, M. Triolo, V. Billone, G. Gulotta, A. Agrusa, Endometrial cancer: robotic versus laparoscopic treatment. Preliminary report, *GIOG* 37 (November–December (6)) (2015), 283–273.
- [10] G. Cucinella, G. Calagna, G. Romano, G. Di Buono, G. Gugliotta, S. Saitta, G. Adile, M. Manzone, G. Accardi, A. Perino, A. Agrusa, Robotic versus laparoscopic sacrocolpopexy for apical prolapse: a case-control study, *G. Chir.* 37 (May–June (3)) (2016) 113–117.
- [11] G. Romano, A. Agrusa, M. Galia, G. Di Buono, D. Chianetta, V. Sorce, L. Gulotta, G. Brancatelli, G. Gulotta, Whipple's pancreaticoduodenectomy: surgical technique and perioperative clinical outcomes in a single center, *Int. J. Surg.* 21 (September (Suppl. 1)) (2015) S68–71, <http://dx.doi.org/10.1016/j.ijsu.2015.06.062>, Epub 2015 Jun 26.
- [12] H. Ettahri, F. Elomrani, M. Elkabous, et al., Duodenal and gallbladder metastasis of regressive melanoma: a case report and review of the literature, *J. Gastrointest. Oncol.* 6 (5) (2015) E77–E81, <http://dx.doi.org/10.3978/j.issn.2078-6891.2015.048>.
- [13] A.A. Lo, J. Peevey, E.C. Lo, J. Guitart, M.S. Rao, G.Y. Yang, Isolated gallbladder intramucosal metastatic melanoma with features mimicking lymphoepithelial carcinoma, *Int. J. Surg. Pathol.* 23 (5) (2015) 409–413, <http://dx.doi.org/10.1177/1066896915588932>.
- [14] N.B. Saraswat, W.B. DeVoe, Metastatic melanoma of the gallbladder presenting as polyp in acute cholecystitis, *J. Surg. Case Rep.* 11 (December) (2019), <http://dx.doi.org/10.1093/jscr/rjz324>, p. rjz324.
- [15] D.G. Ostick, M.T. Haqqani, Obstructive cholecystitis due to metastatic melanoma, *Postgrad. Med. J.* 52 (613) (1976) 710–712, <http://dx.doi.org/10.1136/pgmj.52.613.710>.
- [16] H. Onozawa, M. Saito, S. Yoshida, et al., Multiple metastatic malignant melanoma presenting intraluminal gallbladder bleeding, *Int. Surg.* 99 (5) (2014) 600–605, <http://dx.doi.org/10.9738/INTSURG-D-13-00143.1>.
- [17] M.K. Samplaski, E.L. Rosato, A.K. Witkiewicz, M.J. Mastrangelo, A.C. Berger, Malignant melanoma of the gallbladder: a report of two cases and review of the literature, *J. Gastrointest. Surg.* 12 (6) (2008) 1123–1126, <http://dx.doi.org/10.1007/s11605-007-0432-4>.
- [18] S. Vernadakis, G. Rallis, N. Danias, et al., Metastatic melanoma of the gallbladder: an unusual clinical presentation of acute cholecystitis, *World J. Gastroenterol.* 15 (27) (2009) 3434–3436, <http://dx.doi.org/10.3748/wjg.15.3434>.
- [19] M.L. Barretta, O. Catalano, S.V. Setola, V. Granata, U. Marone, A. D'Errico Gallipoli, Gallbladder metastasis: spectrum of imaging findings, *Abdom. Imaging* 36 (6) (2011) 729–734, <http://dx.doi.org/10.1007/s00261-011-9696-y>.
- [20] G.G. D'Urso Vilar, F. Iriarte, D. Speisky, M.L. Bregante, S.D. Quidrian, Isolated gallbladder metastasis of melanoma: case report, *Int. J. Surg. Case Rep.* 71 (14 May) (2020) 311–314, <http://dx.doi.org/10.1016/j.ijscr.2020.04.086>.
- [21] K. Furumoto, Y. Miyauchi, D. Ito, T. Kitai, M. Kogire, Solitary metastatic gallbladder malignant melanoma originated from the nasal cavity: a case report, *Int. J. Surg. Case Rep.* 4 (11) (2013) 965–968, <http://dx.doi.org/10.1016/j.ijscr.2013.08.005>.
- [22] J. Gogas, D. Mantas, H. Gogas, E. Kouskos, C. Markopoulos, S. Vgenopoulou, Metastatic melanoma in the gallbladder: report of a case, *Surg. Today* 33 (2) (2003) 135–137, <http://dx.doi.org/10.1007/s005950300030>.
- [23] U. Marone, C. Caracò, S. Losito, et al., Laparoscopic cholecystectomy for melanoma metastatic to the gallbladder: is it an adequate surgical procedure? Report of a case and review of the literature, *World J. Surg. Oncol.* 5 (141) (2007), <http://dx.doi.org/10.1186/1477-7819-5-141>, 11 Dec.
- [24] A. Khan, S. Patel, D.J. Zaccarini, M. McGrath, Metastatic melanoma of the gallbladder in an asymptomatic patient, *Case Rep. Gastrointest. Med.* (2017), <http://dx.doi.org/10.1155/2017/1767418>.
- [25] U. Köhler, T. Jacobi, G. Sebastian, M. Nagel, Laparoskopische Cholecystektomie bei einer isolierten Gallenblasenmetastase eines malignen Melanoms, *Chirurg* 71 (12) (2000) 1517–1520, <http://dx.doi.org/10.1007/s001040051255>.
- [26] M.H. Seelig, K. Schönleben, Laparoscopic cholecystectomy for a metastasis of a malignant melanoma in the gallbladder, *Z. Gastroenterol.* 35 (9) (1997) 673–675.
- [27] A. Agrusa, G. Di Buono, S. Buscemi, G. Cucinella, G. Romano, G. Gulotta, 3D laparoscopic surgery: a prospective clinical trial, *Oncotarget* 9 (April (25)) (2018) 17325–17333, <http://dx.doi.org/10.18632/oncotarget.24669>, eCollection 2018 Apr 3.
- [28] A. Agrusa, G. Romano, L.J. Dominguez, G. Amato, R. Citarrella, L. Vernuccio, G. Di Buono, V. Sorce, L. Gulotta, M. Galia, P. Mansueto, G. Gulotta, Adrenal cavernous hemangioma: which correct decision making process? *Acta Medica Mediterranea* 32 (2016) 385–389.
- [29] G. Di Buono, S. Buscemi, A.I. Lo Monte, G. Geraci, V. Sorce, R. Citarrella, E. Gulotta, V.D. Palumbo, S. Fazzotta, L. Gulotta, D. Albano, M. Galia, G. Romano, A. Agrusa, Laparoscopic adrenalectomy: preoperative data, surgical technique and clinical outcomes, *BMC Surg.* 18 (April (Suppl. 1)) (2019) 128, <http://dx.doi.org/10.1186/s12893-018-0456-6>.

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