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Collision tumor of choriocarcinoma and small cell carcinoma of the stomach: A case report

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ABSTRACT

INTRODUCTION: Both gastric choriocarcinoma and small cell carcinoma are extremely rare, both accounting for approximately 0.1% of all gastric cancers. Therefore, simultaneous occurrence of gastric choriocarcinoma and small cell carcinoma is even rarer.

PRESENTATION OF CASE: An 84-year-old Japanese man was referred to our hospital with the chief complaint of dysphagia. Laboratory data showed iron deficiency anemia. Contrast-enhanced computed tomography of the abdomen revealed thickened wall of the stomach at the fundus and several enlarged abdominal lymph nodes. Upper gastrointestinal endoscopy showed a friable gastric tumor with necrosis in the gastric cardia extending to the abdominal esophagus. Small cell carcinoma was diagnosed based on pathological examination of biopsy specimens. The anemia, which was probably because of tumor bleeding, progressed despite repeated transfusion; therefore, a semi-urgent laparotomy was performed to control hemorrhage. Finally, total gastrectomy and lymph node resection were performed. Based on pathological findings, a diagnosis of collision tumor of choriocarcinoma and small cell carcinoma of the stomach was confirmed.

DISCUSSION: When encountering large tumors with necrosis or hemorrhage in the stomach, the possibility of choriocarcinoma component should be considered. Moreover, when small cell carcinoma is morphologically suspected, even if slightly, additional immunohistochemical staining must be performed.

CONCLUSION: This report detailed an extremely rare case of collision tumor of choriocarcinoma and small cell carcinoma of the stomach.

1. Introduction

Although most choriocarcinomas occur in the uterus in relation to pregnancy, some may occur without any relation to it, arising in the ovary or testes and rarely in the stomach [1–3]. Small cell carcinomas occur primarily in the lungs and rarely at extra-pulmonary sites, including the stomach [4,5]. Both gastric choriocarcinoma and small cell carcinoma are aggressive neoplasms and the prognoses of these tumors are poorer than that of the common-type gastric cancer [3,5]. Several theories have been reported to explain the pathogenesis of gastric choriocarcinoma and small cell carcinoma. Among them, one of the most widely accepted is the dedifferentiation theory: gastric choriocarcinoma and small cell carcinoma are proposed to arise by overgrowth and elimination of the original adenocarcinoma [6,7].

Both gastric choriocarcinoma and small cell carcinoma are extremely rare, both accounting for approximately 0.1% of all gastric cancers [6,8,9]. Therefore, simultaneous occurrence of gastric choriocarcinoma and small cell carcinoma is even rarer. Here, we report such an extremely rare case. The work has been reported in line with the SCARE criteria [10].

2. Presentation of case

An 84-year-old Japanese man was referred to our hospital with the chief complaint of dysphagia. The patient reported a 10-kg

Abbreviations: AFP, α-fetoprotein; CD56, cluster of differentiation 56; CT, computed tomography; hCG, human chorionic gonadotropin; NSE, neuron-specific enolase.

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weight loss in 3 months. He was an ex-smoker of 1 pack per year for 25 years and was a social drinker. He also had a history of diabetes mellitus, hypertension, hyperlipidemia, and angina pectoris. His blood pressure was 108/49 mmHg, pulse was 75 beats per minute, and body temperature was 36.9 °C. Physical examination showed no swelling of superficial lymph nodes. Laboratory data showed the presence of iron deficiency anemia (hemoglobin, 7.3 g/dL). Tumor markers, including carcinoembryonic antigen and carbohydrate antigen 19–9, were within normal ranges, but α-fetoprotein (AFP) level was elevated by 166.2 ng/mL (normal level, <10 ng/mL).

Contrast-enhanced computed tomography (CT) scan of the abdomen revealed thickened wall of the stomach at the fundus and several enlarged abdominal lymph nodes. Upper gastrointestinal endoscopy revealed a friable gastric tumor with necrosis in the gastric cardia extending to the abdominal esophagus (Fig. 1). Microscopic examination of the endoscopic biopsy specimens showed solid growth of small cells with hyperchromatic nuclei and scant cytoplasm (Fig. 2a). Small cell carcinoma was suspected morphologically, and additional immunohistochemical staining of chromogranin A, synaptophysin, cluster of differentiation 56 (CD56), and neuron-specific enolase (NSE) were performed. Positive staining for chromogranin A and synaptophysin and negative staining for CD56 and NSE in the cytoplasm of cancer cells were noted, and a diagnosis of small cell carcinoma was established (Fig. 2b–e).

The anemia, which was possibly because of tumor bleeding, progressed despite repeated transfusion. A semi-urgent laparotomy was performed to control bleeding. Accumulation of serous ascites was observed under the left diaphragm and in the pouch of Douglas. Exploration of the abdomen at the time of surgery revealed no evidence of metastasis to the liver or peritoneum. Finally, total gastrectomy and lymph node resection was performed.

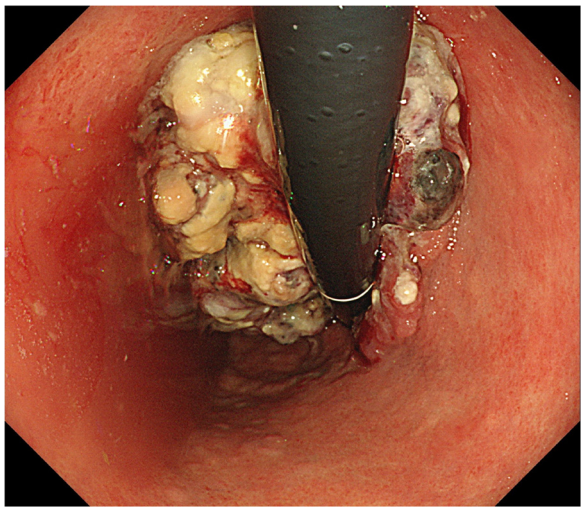

Fig. 1. Upper gastrointestinal endoscopy showing a friable gastric tumor with necrosis in the gastric cardia and extending to the abdominal esophagus.

Size of the resected tumor was 90 × 75 mm, and it was accompanied by necrosis and hemorrhage (Fig. 3). Microscopic evaluation following hematoxylin–eosin staining showed that the hemorrhagic and necrotic areas showed two histological types: cytotrophoblastic cells with single oval nuclei and syncytiotrophoblastic cells with multiple bizarre nuclei (Fig. 4a).

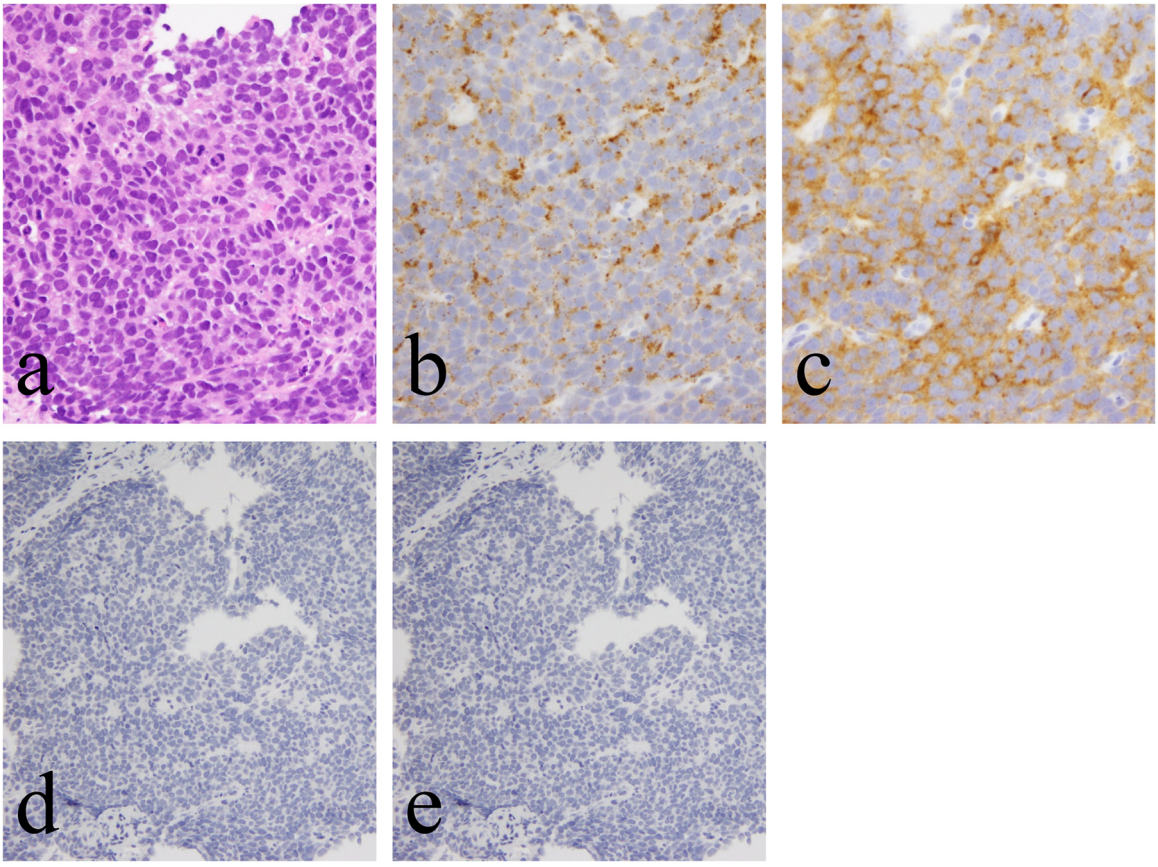

Fig. 2. (a) Microscopic evaluation of biopsy specimens showing solid growth of small cells with hyperchromatic nuclei and scant cytoplasm. (b)–(e) Immunohistochemical staining showing cancer cells stained positive for chromogranin A (b) and synaptophysin (c) and negative for cluster of differentiation 56 (d) and neuron-specific enolase (e) in the cytoplasm.

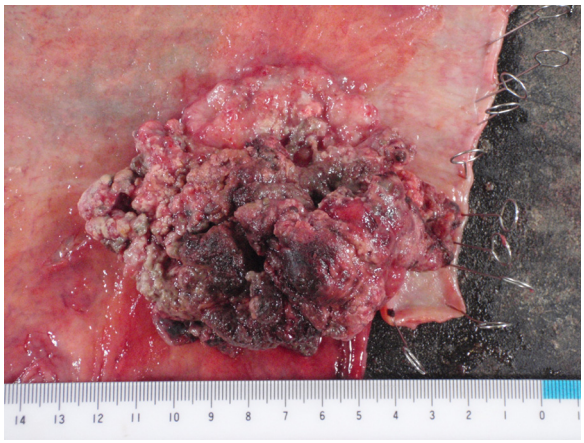

Fig. 3. Resected tumor with accompanying necrosis and hemorrhage. Size, 90 × 75 mm.

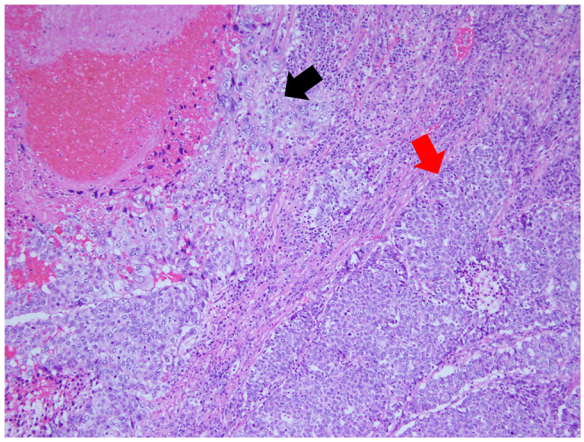

Fig. 5. The tumor was predominantly composed of two distinct components: choriocarcinoma (black arrow) and small cell carcinoma (red arrow), with a clear point of collision.

Immunohistochemical staining revealed that the tumor stained positive for anti-human chorionic gonadotropin (hCG) antibody, but negative for chromogranin A and synaptophysin (Fig. 4b). Furthermore, tumor cells that were identical to the preoperative biopsy specimens were noted in the tumor; these were positive for chromogranin A and synaptophysin and negative for anti-hCG antibody. The tumor was thus predominantly composed of two distinct components: choriocarcinoma and small cell carcinoma, with a clear point of collision (Fig. 5); the adenocarcinoma component was minor. Immunohistochemical staining of HER2 was strongly positive for choriocarcinoma, but negative for small cell carcinoma. Furthermore, immunohistochemical staining of AFP was negative in all cancer cells. The resected regional lymph nodes showed no evidence of metastasis. The resection margins were free of tumor cells. The patient was diagnosed with a collision tumor of choriocarcinoma and small cell carcinoma of the stomach with a grading of Stage IIA (T3N0M0) according to the Union for International Cancer Control TNM classification of malignant tumors (7th edition). Choriocarcinoma generally produces hCG [6]; therefore, serum hCG levels were postoperatively measured and were found to have increased to 6.4 ng/mL (normal level, <0.1 ng/mL), whereas those of AFP decreased to 8.0 ng/mL.

The patient's respiration worsened on postoperative day 6, with CT scan showing ground-glass opacity and consolidation in both lungs without obvious traction bronchiectasis. A diagnosis of acute exacerbation of interstitial pneumonia was established and steroid pulse therapy was initiated; however, the patient died on postoperative day 24 due to multiple organ failure.

3. Discussion

Collision tumors are neoplasms comprising two different histological cells that coexist in a side-by-side pattern with no transition zone [11,12]. Gastric collision tumors are rare and usually comprise neuroendocrine carcinoma and adenocarcinoma, lymphoma and adenocarcinoma, squamous cell carcinoma and adenocarcinoma, and gastrointestinal stromal tumor and adenocarcinoma [13]. Gastric collision tumors involving choriocarcinoma and small cell carcinoma are extremely rare. Because our case met the above-mentioned criteria, the patient was diagnosed with a collision tumor of choriocarcinoma and small cell carcinoma of the stomach. To the best of our knowledge, Hirano et al. reported the first case of simultaneous occurrence of choriocarcinoma and small cell carcinoma of the stomach [14], and ours is the second case. We were able to show a histologically clear point of collision between the two carcinomas, with distinct immunohistochemical profiles of each component.

Choriocarcinoma is a germ cell tumor that rarely occurs in the stomach [15]. It involves rapidly growing, highly invasive,

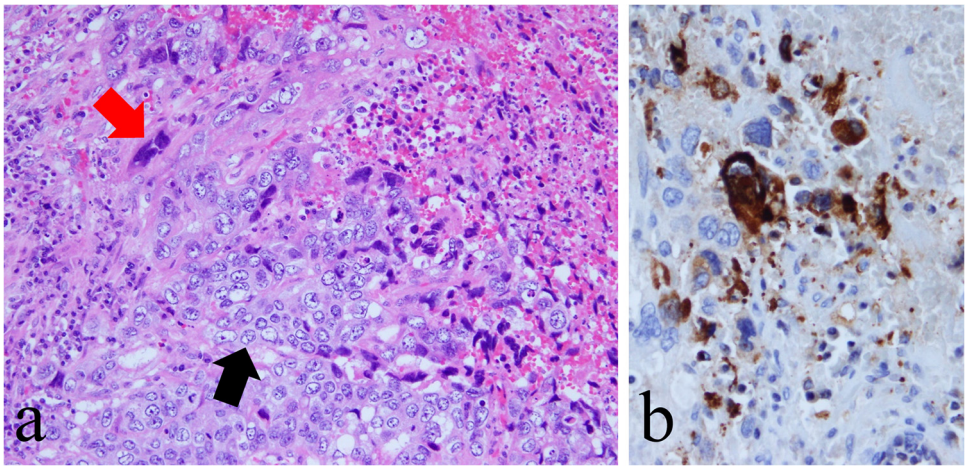

Fig. 4. (a) Hematoxylin–eosin staining revealing that the hemorrhagic and necrotic areas were composed of two histological types: cytotrophoblastic cells with single oval nuclei (black arrow) and syncytiotrophoblastic cells with multiple bizarre nuclei (red arrow). (b) Immunohistochemical staining revealing that the tumor cells stained positive for anti-human chorionic gonadotropin antibody.

and widely metastatic tumors [3,16]. As abovementioned, the specific findings of choriocarcinoma by hematoxylin–eosin staining are components of two histological types: single oval nuclei (cytotrophoblastic cells) and multiple bizarre nuclei (syncytiotrophoblastic cells), which generally have necrosis or hemorrhage. Clinical presentation of choriocarcinoma is similar to that of gastric adenocarcinoma; however, the former frequently causes gastrointestinal bleeding because of its striking vascularity [3,6]. Endoscopy shows that necrosis or hemorrhage is present in most patients with gastric choriocarcinoma [8]. In the present study, endoscopy revealed necrosis within the large gastric tumor; however, on the basis of pathological examination of biopsy specimens, the patient was preoperatively diagnosed with small cell carcinoma but not with choriocarcinoma. When encountering large tumors with necrosis or hemorrhage in the stomach, the possibility of choriocarcinoma component should be considered and sufficient biopsy samples should be obtained for accurate pathological examination. In reality, the rarity of gastric choriocarcinoma makes it difficult to precisely diagnose it preoperatively; therefore, decision of the optimal timing of surgery may be more important. When large gastric tumors with necrosis or hemorrhage show progressed anemia resembling that reported in our case, a prompt decision of surgery is necessary.

Histological diagnosis of gastric small cell carcinoma with preoperative biopsy is generally difficult; differential diagnosis is malignant lymphoma, undifferentiated carcinoma, and common-type gastric cancer [9,17]. Reportedly, only 10.5% small cell carcinomas are correctly diagnosed with preoperative biopsy [17]. This is possibly attributable to the challenge of distinguishing small cell carcinoma from poorly differentiated adenocarcinoma, its specific proliferation pattern under the mucosal layer, and potential inclusion an adenocarcinoma component [4,18,19]. Small cell carcinoma is usually diagnosed with immunohistochemical staining of chromogranin A, synaptophysin, CD56, or NSE, but not with hematoxylin–eosin staining alone [19,20]. Therefore, when small cell carcinoma is morphologically suspected, even if slightly, additional immunohistochemical staining of chromogranin A, synaptophysin, CD56, or NSE must be performed. In the present study, we observed a specific morphology of small cell carcinoma, including solid growth of small cells with hyperchromatic nuclei and scant cytoplasm, and additional immunohistochemical positive staining of chromogranin A and synaptophysin lead to the diagnosis of small cell carcinoma.

Standard treatment and prognosis of gastric choriocarcinoma and small cell carcinoma remain unclear owing to the rarity of the tumors [21,22]. In this case, the prognosis of collision tumor of choriocarcinoma and small cell carcinoma of the stomach is not determined, because the patient died occurring severe acute lung injury. As previously reported, curative resection and adequate chemotherapy have been found to promote long-term survival in gastric choriocarcinoma and small cell carcinoma [5,8,16]. Both gastric choriocarcinoma and small cell carcinoma are highly aggressive diseases and often spread to other organs. Kobayashi et al. reported that curative resection could not be performed on 31 of 53 patients (58.5%) with gastric choriocarcinoma and non-curative resection has a poorer prognosis than curative resection [8]. Furthermore, Toyokawa et al. reported that curative resection could not be performed on 2 of 7 patients (28.6%) with gastric small cell carcinoma and 2 of 5 patients (40.0%) with curative resection survived for more than 4 years [9]. Therefore, for achieving curative resection, early detection might be essential in improving the prognosis of gastric collision tumors comprising choriocarcinoma and small cell carcinoma.

4. Conclusion

The present report detailed an extremely rare case of collision tumor of choriocarcinoma and small cell carcinoma of the stomach. The accumulation of prospective evidence from multiple case reports under special protocols and performance of further investigations is necessary to evaluate its pathogenesis and optimal treatment strategy. Learning points of this case report are 1) when encountering large tumors with necrosis or hemorrhage in the stomach, the possibility of choriocarcinoma component should be considered and sufficient biopsy samples should be obtained for accurate pathological examination and 2) when small cell carcinoma is morphologically suspected, even if slightly, additional immunohistochemical staining of chromogranin A, synaptophysin, CD56, or NSE must be performed.

Conflicts of interest

None.

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Ethical approval

This study was approved by the Ethics Committee of our institution (approval number: 17-21).

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

SF designed the study and drafted the manuscript. SF and YF performed the operation. TW and YO performed the histopathological examination. KI, KK, HI, MT, MY, and MI participated in the manuscript revision process. All authors read and approved the final manuscript.

Registration of research studies

Not applicable.

Guarantor

The guarantor of this manuscript is Shuichi Fukuda, corresponding author.

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References

[1] S. Hayashi, Y. Abe, S. Tomita, Y. Nakanishi, S. Miwa, T. Nakajima, et al., Primary non-gestational pure choriocarcinoma arising in the ovary: a case report and literature review, Oncol. Lett. 9 (2015) 2109–2111.

[2] I. Alvarado-Cabrero, N. Hernández-Toriz, G.P. Paner, Clinicopathologic analysis of choriocarcinoma as a pure or predominant component of germ cell tumor of the testis, Am. J. Surg. Pathol. 38 (2014) 111–118.

[3] T. Noguchi, S. Takeno, T. Sato, Y. Takahashi, Y. Uchida, S. Yokoyama, A patient with primary gastric choriocarcinoma who received a correct preoperative diagnosis and achieved prolonged survival, Gastric Cancer 5 (2002) 112–117.
[4] T. Namikawa, M. Kobayashi, T. Okabayashi, S. Ozaki, S. Nakamura, K. Yamashita, et al., Primary gastric small cell carcinoma: report of a case and review of the literature, Med. Mol. Morphol. 38 (2005) 256–261.
[5] J. Huang, Y. Zhou, X. Zhao, H. Zhang, X. Yuan, J. Wang, Primary small cell carcinoma of the stomach: an experience of two decades (1990–2011) in a Chinese cancer institute, J. Surg. Oncol. 106 (2012) 994–998.
[6] V.F. Martins, F. Moreno, J.R. Vizcaíno, J. Santos, Primary gastric choriocarcinoma: a rare case, Int. J. Surg. Case Rep. 14 (2015) 44–47.
[7] M. Ishida, S. Sekine, T. Fukagawa, M. Ohashi, S. Morita, H. Taniguchi, et al., Neuroendocrine carcinoma of the stomach: morphologic and immunohistochemical characteristics and prognosis, Am. J. Surg. Pathol. 37 (2013) 949–959.
[8] I. Kobayashi, T. Hasebe, Y. Endo, S. Sasaki, M. Konishi, M. Sugito, et al., Primary gastric choriocarcioma: two case reports and a pooled analysis of 53 cases, Gastric Cancer 8 (2005) 178–185.
[9] T. Toyokawa, H. Tanaka, K. Muguruma, T. Tamura, K. Sakurai, N. Kubo, et al., Primary gastric small cell carcinoma: a series of seven cases, Anticancer Res. 35 (2015) 563–567.
[10] 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.
[11] D.V. Spagnolo, P.J. Heenan, Collision carcinoma at the esophagogastric junction: report of two cases, Cancer 46 (1980) 2702–2708.
[12] A.M. Minaya-Bravo, J.C. Garcia Mahillo, F. Mendoza Moreno, F. Noguelares Fraguas, J. Granell, Large cell neuroendocrine – adenocarcinoma mixed tumour of colon: collision tumour with peculiar behavior. What do we know about these tumours? Ann. Med. Surg. (Lond.) 4 (2015) 399–403.
[13] A. Michalinos, A. Constantinidou, M. Kontos, Gastric collision tumors: an insight into their origin and clinical significance, Gastroenterol. Res. Pract. 2015 (2015) 314158.
[14] Y. Hirano, T. Hara, H. Nozawa, K. Oyama, N. Ohta, K. Omura, et al., Combined choriocarcinoma, neuroendocrine cell carcinoma and tubular adenocarcinoma in the stomach, World J. Gastroenterol. 14 (2008) 3269–3272.
[15] J.H. Yoon, M.S. Kim, E.H. Kook, S.H. Ahn, S.Y. Jeong, M.S. Han, et al., Primary gastric choriocarcinoma: two case reports and review of the literatures, Cancer Res. Treat. 40 (2008) 145–150.
[16] B.W. Eom, S.Y. Jung, H. Yoon, M.C. Kook, K.W. Ryu, J.H. Lee, et al., Gastric choriocarcinoma admixed with an alpha-fetoprotein-producing adenocarcinoma and separated adenocarcinoma, World J. Gastroenterol. 15 (2009) 5106–5108.
[17] H. Tanemura, H. Ohshita, A. Kanno, M. Kusakabe, E. Tomita, Y. Nishigaki, et al., A patient with small-cell carcinoma of the stomach with long survival after percutaneous microwave coagulating therapy (PMCT) for liver metastasis, Int. J. Clin. Oncol. 7 (2002) 128–132.
[18] K. Nishikura, H. Watanabe, M. Iwafuchi, T. Fujiwara, K. Kojima, Y. Ajioka, Carcinogenesis of gastric endocrine cell carcinoma: analysis of histopathology and p53 gene alteration, Gastric Cancer 6 (2003) 203–209.
[19] D. Richards, D. Davis, P. Yan, S. Guha, Unusual case of small cell gastric carcinoma: case report and literature review, Dig. Dis. Sci. 56 (2011) 951–957.
[20] N. Chiba, T. Suwa, M. Hori, M. Sakuma, M. Kitajima, Advanced gastric endocrine cell carcinoma with distant lymph node metastasis: a case report and clinicopathological characteristics of the disease, Gastric Cancer 7 (2004) 122–127.
[21] K. Takahashi, S. Tsukamoto, K. Saito, N. Ohkohchi, K. Hirayama, Complete response to multidisciplinary therapy in a patient with primary gastric choriocarcinoma, World J. Gastroenterol. 19 (2013) 5187–5194.
[22] B. Brenner, L.H. Tang, D.S. Klimstra, D.P. Kelsen, Small-cell carcinomas of the gastrointestinal tract: a review, J. Clin. Oncol. 22 (2004) 2730–2739.