Very delayed liver metastasis from small bowel gastrointestinal stromal tumor (32 years after resection of the small bowel GIST): Report of a case

Masahiro Ishizaki a,*, Futoshi Uno a, Ryosuke Yoshida a, Shunsaku Miyauchi a, Osamu Honda b

a Department of Surgery, Okayama Rosai Hospital, Okayama, Japan
b Department of Radiology, Okayama Rosai Hospital, Okayama, Japan

1. Introduction

Gastrointestinal stromal tumors (GIST) are tumors derived from the interstitial cells of Cajal cells of the gastrointestinal tract [1], and were previously known as leiomyoma or leiomyosarcoma. Most postoperative recurrences occur within 2 years after surgery [2]. Metastatic disease is most commonly observed in the liver, at an average of 16–38 months after resection of the primary tumor [3,4].

We report a case of delayed liver metastasis of GIST, which was diagnosed as leiomyosarcoma of the small intestine 32 years ago. We also discuss other cases of delayed liver metastasis of GIST.

This paper has been reported in line with the SCARE criteria [5].

2. Presentation of case

A 72-year-old woman with no symptoms was referred to our department for a tumor in the liver detected on CT-scan during the follow up for urinary stone. She had a history of resection of the small intestine 32 years ago for a tumor (Details of the disease were unknown). A slightly smaller lesion was seen in the previous CT scans taken at our hospital. Hemato-biochemical findings showed no abnormalities. There was no increase in the tumor markers for gastrointestinal cancer or hepatocellular carcinoma. Abdominal ultrasonography showed a tumor in segment 7 of the liver, which was hypoechogenic but was difficult to diagnose on radiology. Abdominal contrast-enhanced CT showed a mass 2.4 cm in size with slight enhancement in segment 7 of the liver (Fig. 1). There were no findings suggestive of advanced cancer in the stomach or large intestine that could cause metastasis. Abdominal magnetic resonance imaging (MRI) showed hyperintense mass on diffusion-weighted imaging and a slightly hyperintense mass on fat-suppressed T2WI in segment 7 of the liver (Fig. 1). On re-

* Corresponding author at: Department of Surgery, Okayama Rosai Hospital, 1-10-25, Chikkou-midorimachi, Minami ward, Okayama city, 702-8055, Japan. E-mail address: hca013333@okayamanishi.ohsas.go.jp (M. Ishizaki).
evaluating the CT images taken at our institute in the past, we found that the lesions were not visible on the CT scan 4 years ago, but were slightly visible on the CT scans performed 2 years ago, and had gradually increased in size (Fig. 2).

Although HCC and metastatic liver cancer were suspected based on the above findings, there were no lesions suggestive of a primary lesion on gastroscopy and colonoscopy. Hence, a needle biopsy of the liver was performed, which revealed a mesenchymal lesion that is not usually seen in the liver.

Therefore, a surgery was planned. The tumor was located in segment 7 of the liver, and partial resection of segment 7 of the liver was performed (Fig. 3). The post-operative course was uneventful.

Pathological findings of the resected specimen showed a characteristic appearance of GIST with convoluted spindle-shaped tumor cells, and HCC and metastatic gastrointestinal cancer were ruled out. Immunohistochemical staining revealed CK7(-), CK 20(-), CAM 5.2(-), Alpha-SMA (-), Vimentin (+), CD 34 (-), C-kit (+), Desmin (-) (Fig. 4).

Based on the above results, her past medical records were obtained from the institute where she was operated 32 years ago, and it was found that the small intestine was resected based on the diagnosis of a leiomyosarcoma of the small intestine, and the block specimen from that time was available. The results of the block specimen were compared with those of the resected lesion at our institute, and the results were almost identical. Since primary GIST in the liver is extremely rare and PET CT scan showed no other GIST lesion that could have caused liver metastasis, the lesion was finally diagnosed as liver metastasis of small intestinal GIST that occurred 32 years ago. Adjuvant therapy was also considered, but it was not administered at the patient’s request, and the patient has been free from recurrence for 5 years.

3. Discussion

GISTs account for 0.2–0.5% of all tumors of the digestive tract and have the highest incidence (approximately 80%) among mesenchymal tumors [6,7]. These tumors are derived from the Cajal intercalated cells proposed by Rosai in 1996 [1], and have been attributed to function mutations in the c-kit and PDGFRα genes [7]. In addition to the stomach, small intestine, large intestine, and esophagus, non-gastrointestinal sites such as omentum and mesenteric retroperitoneum have been reported [8,9].

In this case, the possibility of GIST was suspected from the pathological analysis of the specimen obtained on biopsy of the
liver lesion. However, primary GIST of liver has been rarely reported in the past [10,11]. An identical histopathological match with the specimen diagnosed as leiomyosarcoma 32 years ago, enabled us to diagnose liver metastasis of GIST. During the earlier times, there was no concept of GIST, and we were able to arrive at a diagnosis because the block of specimens from her previous surgery were available. The GIST had occurred 32 years ago, and the patient herself did not recognize the relationship with the tumor of small intestine.

Cases of liver metastases from gastrointestinal GIST more than 10 years later have sometimes been reported in the Japanese and other literature (Table 1) [12–26]. Although some cases of metastasis have been reported 20 years after the initial gastrointestinal surgery, our search revealed that this case had the longest disease-free interval between resection of the primary tumor and resection of liver metastasis. The details of 16 cases of delayed metastasis were examined. The age at detection of the liver metastases was 58–84 years (median 66), 12 patients were males and 4 were females. The stomach was the most common site of the primary tumor, followed by the duodenum. The size of the primary lesion was more than 5 cm in 8 cases. Only 3 cases had a mitotic index of 10/50 or more, and 8 cases were classified as "High risk group" according to the Modified-Fletcher classification [1,27]. These cases indicate that late liver metastasis can occur in the low risk group. Our case was in the low risk group according to the Modified-Fletcher classification.

Considering the long-interval before recurrence, the period for follow-up of GIST after surgery needs to be determined. Japanese guideline [28] of GIST recommends the follow up within 10 years after resection of the primary tumor, even in the high risk group. However, considering the cases in Table 1, some cases of liver metastasis have been reported after ten years; patients should be informed about the possibility of late or very delayed recurrence even after ten years.

In this case, adjuvant chemotherapy after resection of the hepatic metastasis was not performed because of the patient's
reluctance. Nunobe et al. [29] reported that the prognosis of patients with liver metastasis when the interval before recurrence was more than 5 years was better than that of patients in whom recurrence occurred in less than 5 years. The Japanese guidelines do not specifically recommend postoperative adjuvant therapy in such cases; hence, adjuvant chemotherapy was not administered. In fact, five patients in Table 1 were alive without recurrence for more than 2 years, and at least early hepatic recurrence within 6 months was not described in any of these articles. Thus the prognosis appears to be relatively good after resection of liver recurrence after more than 10 years. Our patient has been well without liver recurrence for more than five years.

4. Conclusion

We experienced a case of liver metastasis 32 years after surgery for the first small intestinal GIST. Recurrence of late liver metastasis can occur sometimes, and it is necessary for the attending physician to be aware of it and to educate the patient accordingly.

Declaration of Competing Interest

The authors report no declarations of interest.

Funding

No source of funding.

Ethical approval

We have reported a single case, not a clinical study, with no requirement for ethical approval.

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

Dr Masahiro Ishizaki: Investigation, Writing-original draft, Writing-Review and Editing, Visualization.
Dr Futoshi Uno: Review and Editing.
Dr Ryosuke Yoshida: Review and Editing.
Dr Shunsaku Miyachi: Collecting datas, Review and Editing.
Dr Osamu Honda: Review and Editing about radiological materials.

Registration of research studies

Not applicable.

Guarantor

Dr Masahiro Ishizaki.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Acknowledgements

The authors would like to express their gratitude to Dr Hiroshi Sonobe, Director of Department of Pathology, Okayama Rosai Hospital for pathological diagnosis for this article.

References

[1] C.D.M. Fletcher, J.J. Berman, C. Corless, F. Gorstein, J. Lasota, B.J. Longley, M. Miettinen, T.J. O’Leary, H. Remotti, R.B. Rubin, S. Shmookler, L.H. Sobin, S.W. Weiss, Diagnosis of gastrointestinal stromal tumors: a consensus approach, Hum. Pathol. 33 (2002) 459–465, http://dx.doi.org/10.1016/s0046-8177(02)01485-4.
[2] M. Miettinen, M. Majidi, J. Lasota, Pathology and diagnostic criteria of gastrointestinal stromal tumors (GISTs): a review, Eur. J. Cancer 38 (Suppl. 5) (2002) S39–S41, http://dx.doi.org/10.1016/s0959-8049(02)80802-5.
[3] H. Chen, A. Pruitt, T.L. Nicol, S. Gorgulu, M.A. Choti, Complete hepatic resection of metastases from leiomyosarcoma prolongs survival, J. Gastrointest. Surg. 2 (1998) 151–155, http://dx.doi.org/10.1016/S1090-0983(98)00006-1.
[4] R.P. DeMatteo, A. Shah, Y. Feng, W.R. Narangin, L.H. Blumgart, M.F. Brennan, Results of hepatic resection for sarcoma metastatic to liver, Ann. Surg. 234 (2001) 540–548, http://dx.doi.org/10.1097/00000658-200101000-00013.
[5] R.A. Agha, M.R. Borrelli, R. Farwana, K. Koshy, A.J. Fowler, D.P. Orgill, The SCARE 2018 statement: updating consensus Surgical Case REPORT (SCARE) guidelines, Int. J. Surg. 60 (2018) 132–136, http://dx.doi.org/10.1016/j.ijjsu. 2018.10.026.
[6] R.P. DeMatteo, J.J. Lewis, D. Leung, S.S. Mudan, J.M. Woodruff, M.F. Brennan, Two hundred gastrointestinal stromal tumors: recurrence patterns and prognostic factors for survival, Ann. Surg. 231 (2000) 51–58, http://dx.doi.org/10.1097/00000658-200001000-00008.
[7] S. Hirata, K. Itozaki, Y. Moriyama, K. Hashimoto, T. Nishida, S. Ishiguro, K. Kawano, M. Hanada, A. Kurata, M. Takeda, G. Muhammad Tunio, Y. Matsuzawa, Y. Kanakura, Y. Shimomura, Y. Kitamura, Gain-of-function mutations of c-kit in human gastrointestinal stromal tumors, Science 279 (1998) 577–580, http://dx.doi.org/10.1126/science.279.5350.577.
[8] M. Gharibo, L. Patrick-Miller, L. Zheng, L. Guensch, P. Juvidian, E. Poplin, A phase II trial of imatinib mesylate in patients with metastatic pancreatic cancer, Pancreas 36 (2008) 341–345, http://dx.doi.org/10.1097/MPA.0b013e31815d50f9.
[9] M.R. Ambrosio, B.J. Rocca, M.G. Mastroguglio, A. Pesci, A. De Martino, M.A. Mazzei, L. Volterrani, F. Accurti, M. Cincinario, S.A. Trippodi, Cystic gastrointestinal stromal tumors of the pancreas simulating cystoadenocarcinoma. Report of three cases and short review of the literature, Histol. Histopathol. 29 (2014) 1583–1591, http://dx.doi.org/10.14630/HJH.29.2014.29484.
[10] B. Zhou, M. Zhang, S. Yan, S. Zheng, Primary gastrointestinal stromal tumor of the liver: report of a case, Surg. Today 44 (2014) 1142–1146, http://dx.doi.org/10.1007/s00595-013-0521-9.
[11] S. Liu, C. Tian, S. Liu, G. Xu, M. Gu, X. Lian, D. Fan, H. Zhang, F. Feng, Clinicopathological feature and prognosis of primary hepatic gastrointestinal stromal tumor, Cancer Med. 5 (2016) 2268–2275, http://dx.doi.org/10.1002/ 1828.3082.
[12] C. Ballarini, M. Intra, A.P. Cerretti, F. Prestipino, F.M. Bianchi, F. Sparacino, E. Berti, S. Peronne, F. Silva, Gastrointestinal stromal tumors: a “benign” tumor with hepatic metastasis after 11 years, Tumori 84 (1998) 78–81, http://dx.doi.org/10.1177/039031349808400117.
[13] K. Furukawa, H. Nakaba, A. Moriguchi, H. Kikkawa, R. Arima, Liver metastasis occurring 11 years after gastrectomy for gastric gist-a case report, Nihon Rinsho Geka Gakkai Zasshi Jpn. Surg. Assoc. 71 (2010) 1764–1767, http://dx.doi.org/10.3918/jjsg.71.1764.
[14] H. Suito, S. Yoshimura, M. Ozaki, I. Oshimma, Y. Kakuta, H. Matsubara, A case of recurrence of duodenal gastrointestinal stromal tumor in the liver 11 years after surgery, Nihon Rinsho Geka Gakkai Zasshi Jpn. Surg. Assoc. 76 (2015) 768–773, http://dx.doi.org/10.3918/jjsg.76.768.
[15] Y. Kishi, S. Takata, T. Fukuhara, N. Mori, H. Okanoubo, K. Tsuji, T. Maeda, M. Fujiwara, K. Nagai, Y. Furukawa, A case of liver metastasis 11 years after resection of a gastrointestinal stromal tumor of the duodenum, Nihon Shokakibyo Gakkai Zasshi 116 (2010) 1030–1038, http://dx.doi.org/10.1140/ nisshosi.116.1030.
[16] H. Masuoka, N. Kawagishi, T. Inoue, N. Ohkohachi, K. Fujimori, N. Koyama, S. Sekiguchi, S. Tsukamoto, S. Satomi, Giant hepatic metastasis from gastrointestinal stromal tumor of the rectum 12 years after surgery, Hepatogastroenterology 50 (2003) 1454–1456.
[17] H. Yonezawa, S. Kanno, H. Satoh, A case of liver metastasis 12 years after operation of the gastrointestinal stromal tumor (GIST) of stomach, Med. J. Jwate Prefect. Hosp. 44 (2004) 77–84, http://export.jamanetwork.com/Dl/ php7278fa75a12a23d30d3d9ff88a8a82547347d757b1929f32a 1e590ccf3c6d7, bitbres.bib (Accessed 25 May 2020).
[18] J. Ueda, H. Yoshida, Y. Mamada, N. Tanai, M. Yoshioka, Y. Kawano, Y. Mizuguchi, T. Shimizu, K. Takeda, E. Uchida, A case of liver metastasis arising from gastric GIST 12 years after resection of primary GIST, Kanjo 53 (2012) 225–230, http://dx.doi.org/10.2957/kanjo.53.225.
[19] H. Kikuchi, M. Yamamoto, Y. Hiramatsu, M. Baba, M. Ohta, K. Kamyi, T. Tanaka, S. Suzuki, H. Sugimura, H. Konno, Manifestation of liver metastases 13 years
after gastrectomy for gastric GIST, J. Jpn. Soc. Gastroenterol., 103 (2006) 1055–1060, http://dx.doi.org/10.11450/nissoshiki.103.1055.

[20] H. Miyamoto, K. Kameda, S. Sato, H. Sugiuara, K. Nagamine, Y. Takenaka, A. Kubo, Case of recurrent duodenal gastrointestinal stromal tumor in the liver 13 years after surgery with von Recklinghausen’s disease, Yokohama Med. J. 67 (2016) 23–28, http://export.jamas.or.jp/dl.php?doc=17287a512ca2d306e9d8f88a8a254374d2755f9718293f32ca199fccf3697_bibtex.bib (Accessed 25 May 2020).

[21] Y. Tsuge, F. Suzuki, A case of liver metastasis after resection of the gastrointestinal stromal tumor of stomach (in Japanese), Operation 62 (2008) 243–247, http://export.jamas.or.jp/dl.php?doc=d7f190a228e243556343bdf96a9634cc48446d722a741184ba73b266a56ed_bibtex.bib (Accessed 8 May 2020).

[22] L. Matsuoka, M. Stapfer, R. Mateo, N. Jabbour, W. Naing, R. Selby, S. Gagandeep, Left extended hepatectomy for a metastatic gastrointestinal stromal tumor after a disease-free interval of 17 years: report of a case, Surg. Today 37 (2007) 70–73, http://dx.doi.org/10.1007/s10577-006-3338-y.

[23] T. Uesaka, K. Misawa, T. Oshima, Y. Oshima, K. Saito, A. Sawada, Y. Terasaki, N. Minakawa, K. Okuda, Y. Okawa, Y. Ishii, A liver metastasis 18 years after resection for gastrointestinal stromal tumor of the small intestine, Jpn. J. Gastroenterol. Surg. 50 (2017) 830–837, http://dx.doi.org/10.5833/jjgs.2016.0214.

[24] N. Omura, Y. Fujino, M. Tominaga, K. Kajimoto, Liver metastasis occurring 18 years after gastrectomy for gastric GIST—a case report, Nihon Rinsho Geka Gakkai Zasshi (Jpn. Surg. Assoc.) 78 (2017) 1530–1535, http://dx.doi.org/10.3919/jssa.78.1530.

[25] U. Grossi, F. Ardito, L. Petracca Ciavarella, M. Goglia, F. Giulianeti, Ultra-late recurrence of gastrointestinal stromal tumour: case report and literature review, ANZ J. Surg. 89 (2019) E224–E225, http://dx.doi.org/10.1111/ans.14286.

[26] A. Gini, F. Scaramuzzino, S. Marsili, S. Tripodi, Late hepatic metastasis from a duodenal gastrointestinal stromal tumor (29 years after surgery): report of a case and review of the literature, Int. J. Surg. Pathol. 23 (2015) 317–321, http://dx.doi.org/10.1016/j.ijsupa.2017.106896015573571.

[27] H. Joensuu, Risk stratification of patients diagnosed with gastrointestinal stromal tumor, Hum. Pathol. 39 (2008) 1411–1419, http://dx.doi.org/10.1016/j.humpath.2008.06.025.

[28] T. Nishida, S. Hirota, A. Yanagisawa, Y. Sugino, M. Minami, Y. Yamamura, Y. Otani, Y. Shimada, F. Takahashi, T. Kubota, Clinical practice guidelines for gastrointestinal stromal tumor (GIST) in Japan: English version, Int. J. Clin. Oncol. 13 (2008) 416–430, http://dx.doi.org/10.1007/s10147-008-0798-7.

[29] S. Nunobe, T. Sano, K. Shimada, Y. Sakamoto, T. Kosuge, Surgery including liver resection for metastatic gastrointestinal stromal tumors or gastrointestinal leiomyosarcomas, Jpn. J. Clin. Oncol. 35 (2005) 338–341, http://dx.doi.org/10.1093/jjco/hyo091.