Case Report

Subsequent Development of Desmoid Tumor after a Resected Gastrointestinal Stromal Tumor

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Desmoid tumors (deep fibromatosis) of the mesentery are rare mesenchymal tumors. They are often misdiagnosed, especially with a previous history of resection for gastrointestinal stromal tumor (GIST). Immunohistochemistry can help differentiate between these two tumors. In this article, we present a case we had encountered: a Desmoid tumor developing in a patient with a history of GIST 3 years ago. It is the first case of GIST with subsequent development of Desmoid tumor to be reported in Saudi Arabia. We discuss the two entities of Desmoid tumor and GIST by comparing their definitions, clinical presentations, histological features, immunohistochemistry stains, molecular pathogenesis, prognosis, and treatment. We also discuss the relationship between GIST and the subsequent development of Desmoid tumors and compare our case with case reports in literature.

1. Introduction

Desmoid tumors of the mesentery are the most common primary mesenteric tumors displaying spindle cell morphology although they are very rare. They can occur in any age and can be multiple or solitary. The most encountered risk factor for developing a mesenteric Desmoid tumor is previous abdominal surgery. GIST can also develop in the mesentery and mimic clinical and radiological features of Desmoid tumors. Histologically, both tumors may look alike. We describe here a case of GIST with subsequent development of Desmoid tumor.

2. Case Report

A 46-year-old Saudi male presented to our hospital in 2016 complaining of vomiting and constipation for two days. The patient had previous history of gastrointestinal stromal tumor (GIST) of the small bowel in 2013. He underwent a small bowel resection in an outside hospital and was given Imatinib therapy until 2015 in the United States of America. The previous H&E (Figure 8) and IHC (Figure 9) slides were reviewed in our hospital for confirmation. Computed tomography (CT) of the abdomen showed an oval-shaped soft tissue density lying anterior to the right external iliac vessels measuring 2.9 × 1.7 cm. It had increased in size when compared to a previous CT. The remaining abdominal organs were unremarkable. No lymphadenopathy was identified. The initial clinical impression was recurrence of GIST. The patient underwent a right hemicolectomy with terminal ileum resection. Macroscopic examination of the specimen revealed a small, firm, well-circumscribed mass in the mesentery of the ileum. It measured 3 × 2 × 1.5 cm. The mass was not grossly invading the ileum. Its cut surface was tan and homogenous with some areas of hemorrhage. It was grossly away from the proximal, distal, and mesenteric margins. The remainder of the specimen was unremarkable. Microscopic sections of the mass revealed a poorly circumscribed growth of spindle cells showing amphophilic cytoplasm and open chromatin with distended nuclear membranes (Figures 1 and 2). The cells were in a collagenous background. No atypia was identified. Rare mitotic figures were seen. The growth is infiltrating the mesenteric fat. Differential diagnoses of Desmoid tumor, GIST, leiomyoma, neurofibroma, and inflammatory...
myofibroblastic tumor were considered. A panel of the following immunohistochemistry was performed: B-catenin, smooth muscle actin (SMA), C-kit (CD117), CD34, and Ki67. S100, CKPAN, Vimentin, and ALK were considered at first but were not done, as we believed the case was straightforward. By histology, we excluded neurofibroma and inflammatory myofibroblastic tumor, as there was absence of the characteristic wavy nuclei of neurofibroma and the dense inflammation of inflammatory myofibroblastic tumor. Immunohistochemistry showed that the cells were positive for nuclear B-catenin (Figure 3) and smooth muscle actin (SMA) (Figure 4). The cells were negative for C-kit (CD117) (Figure 5) and CD34 (Figure 6). The Ki67 index was less than 5% (Figure 7). The negativity of C-kit (CD117) excluded GIST. The positivity of smooth muscle actin (SMA) included leiomyoma, but it was quickly excluded with the positivity of B-catenin. The final diagnosis of deep fibromatosis (Desmoid tumor) was made. The patient was put on surveillance and had a CT scan done again in April 2017. The CT scan showed no evidence of recurrence or metastasis. Patient is doing well and has no active complaints as of this current time.

3. Discussion

Desmoid tumors are a group of proliferative tumors that originate from the musculoaponeurotic stromal elements. They mostly present in adolescence and young adults. The estimated incidence in the general population is two to four per million population per year [1]. Their clinical presentations vary and depend on their location. They may mimic cancer and cause destruction or compression of adjacent organs. Desmoid tumors can arise in any skeletal muscle. They most commonly develop in the anterior abdominal wall and shoulder girdle. They can also develop in the retroperitoneum and mesentery. Risk factors of development include previous history of abdominal surgery, familial adenomatous polyposis (FAP) [2, 3], and Gardner syndrome [4]. Desmoid tumors of the mesentery should raise the suspicion of Gardner syndrome especially after a surgical resection [5]. Estrogen elevation and pregnancy status are also found to be risk factors [6, 7]. On gross examination, these tumors have infiltrative margins and a large, firm, white, and gritty cut surface. Microscopically, they demonstrate poorly circumscribed lesions with infiltrative margins. The neoplastic cells are proliferating fibroblasts and myofibroblasts with reduced amphophilic cytoplasm, open chromatin of the nuclei, well-defined nuclear membrane, and a distinct nucleolus. No atypia is identified. Perivascular lymphocytes at edge of lesion may be seen. Few mitotic figures are identified. The molecular pathogenesis of Desmoid tumors includes mutations in B-catenin or APC [8]. APC is a component of the WNT signaling pathway. A major function of the APC protein is to hold β-catenin activity in place. APC forms a destruction complex with B-catenin and prevents its accumulation in the cytoplasm. Signaling by WNT blocks the formation of the destruction complex, allowing β-catenin to translocate...
from the cytoplasm to the nucleus. Once in the nucleus, β-catenin forms a transcription activation complex to promote the growth of epithelial cells. Mutations of B-catenin are due to mutations in the encoding gene CTNNB1. A study in 2008 [9] revealed that three discrete mutations in two codons of CTNNB1 exon 3 were identified: 41A, 45F, and 45P. Patients with 45F mutations had higher risk of recurrence. By immunohistochemistry, Desmoid tumors usually have nuclear positivity for B-catenin, which indicates a B-catenin mutation. Although B-catenin has a good reputation of being one of the best stains for Desmoid tumors, one must remember that it is sensitive but not specific for this tumor. They are also positive for vimentin and variably positive for smooth muscle actin and muscle specific actin. CD117 (C-kit) is usually negative, but if positive, Desmoid tumors tend to have a membranous staining pattern [10]. CD34, S100, keratins, and ALK are negative. A study showed that some Desmoid tumors stained positive for PR, ER, and Androgen receptors [11]. This further implicates the theory of a hormonal effect in the pathogenesis. Ultrastructural analysis of Desmoid tumors by electron microscopy shows complete myofibroblastic/fibroblastic differentiation [10]. Prognosis-wise, these tumors are locally infiltrative and aggressive but do not metastasize [12]. They have a high recurrence rate and are mainly treated by surgical resection with wide margins. Some studies reported that Desmoid tumors show a partial response to Imatinib therapy [13, 14]. They can also respond to combined chemotherapy [15].

GIST originates from the Cajal cells, a group of cells which control gut motility. It is the most common mesenchymal tumor of the abdomen. These tumors mostly occur in the stomach, but can occur in the esophagus, colon, rectum, small bowel, omentum, and mesentery. The incidence of GIST is between 11 and 20 per million. The peak age is 60 years but can occur in those of 40 years. Risk factors of developing GIST are related to nonhereditary syndromes like Carney triad, familial GIST syndrome, Carney-Stratakis syndrome, and neurofibromatosis type 1. GIST may be discovered incidentally. It may present as a mass with bowel obstruction, abdominal pain, melena, or blood loss with anemia due to mucosal ulceration. On gross examination, this tumor is large, solitary, and well-circumscribed. The cut surface is whorl-like and fleshy with some cystic, hemorrhagic, or necrotic areas. Microscopically, these tumors can be spindle-celled, epithelioid, or mixed pattern. The spindle-celled form shows proliferation of bland spindle cells with pale to eosinophilic fibrillar cytoplasm growing in short fascicles. Nuclear palisading may be identified. Perinuclear vacuoles may be seen. The stroma is extensively hyalinized. Minimal pleomorphism and a mitotic rate of <2 mitotic figures/50 HPFs are identified. In GIST epithelioid form, sheets of epithelioid cells with round small nucleoli are seen. The cytoplasm is eosinophilic and dense. The stroma is hyalinized.
Table 1: Presented case (1) compared to other case reports.

| Case number | Sex | Age | Location of GIST | Location of subsequent Desmoid tumor | Time interval between the two entities (months) | Management |
|------------|-----|-----|------------------|--------------------------------------|-----------------------------------------------|------------|
| (1)        | Male| 46  | Small bowel      | Small bowel                          | 36                                             | Resection and Imatinib                          |
| (2) [16]   | Male| 54  | Jejunum          | Retroperitoneum                       | 36                                             | Resection only                                  |
| (3) [16]   | Male| 45  | Duodenum         | Duodenum                             | 12                                             | Resection and Imatinib                          |
| (4) [17]   | Male| 62  | Antrum           | Infrapyloric, mesentery               | 48                                             | Resection and Imatinib                          |
| (5) [18]   | Male| 37  | Gastric          | Mesentery                            | 11                                             | Resection and Imatinib                          |

In conclusion, Desmoid tumors (deep fibromatosis) and GISTs are both different and rare neoplasms. It is critical to differentiate Desmoid tumors from GIST due to their different biological behavior and treatment methods. Although literature has observed an association between these two entities [16, 18, 23], they have different pathogenesis. Desmoid tumors can be easily mistaken for GIST as both tumors overlap in clinical presentation, morphology, and immunohistochemistry. We recommend further studies to pinpoint why both tumors are associated with each other.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

[1] V. Ravi, P. C. Raut, and F. T. DeLaney, Desmoid tumors: Epidemiology, risk factors, molecular pathogenesis, clinical presentation, diagnosis, and local therapy, Up to Date, 2016.
[2] C. Soravia, T. Berk, R. S. McLeod, and Z. Cohen, “Desmoid disease in patients with familial adenomatous polyposis,” *Diseases of the Colon & Rectum*, vol. 43, no. 3, pp. 363–369, 2000.

[3] C. Penna, E. Tret, R. Parc et al., “Operation and abdominal desmoid tumors in familial adenomatous polyposis,” *Surgery, Gynecology and Obstetrics*, vol. 177, no. 3, pp. 263–268, 1993.

[4] A. P. Burke, L. H. Sobin, and K. M. Shekitka, “Mesenteric fibromatosis: A follow-up study,” *Archives of Pathology & Laboratory Medicine*, vol. 114, no. 8, pp. 832–835, 1990.

[5] L. V. Pinheiro, J. J. Fagundes, C. S. R. Coy et al., “Multiple desmoid tumors in a patient with Gardner's syndrome - Report of a case,” *International Journal of Surgery Case Reports*, vol. 5, no. 7, pp. 370–374, 2014.

[6] A. P. Burke, L. H. Sobin, K. M. Shekitka, B. H. Federspiel, and E. B. Helwig, “Intra-abdominal fibromatosis. A pathologic analysis of 130 tumors with comparison of clinical subgroups,” *The American Journal of Surgical Pathology*, vol. 14, no. 4, pp. 335–341, 1990.

[7] W. A. Robinson, C. McMillan, A. Kendall, and N. Pearlman, “Desmoid tumors in pregnant and postpartum women,” *Cancers*, vol. 4, no. 1, pp. 184–192, 2012.

[8] D. Kotilgiam, A. J. Lazar, R. E. Pollock, and D. Lev, “Desmoid tumor: a disease opportune for molecular insights,” *Histol Histopathol*, vol. 23, pp. 117–126, 2008.

[9] A. J. F. Lazar, D. Tuvin, S. Hajibashiet al., “Specific mutations in the β-Catenin gene (CTNNB1) correlate with local recurrence in sporadic desmoid tumors,” *The American Journal of Pathology*, vol. 173, no. 5, pp. 1518–1527, 2008.

[10] R. K. Yantiss, I. J. Spiro, C. C. Compton, and A. E. Rosenberg, “Gastrointestinal stromal tumor versus intra-abdominal fibromatosis of the bowel wall: A clinically important differential diagnosis,” *The American Journal of Surgical Pathology*, vol. 14, no. 7, pp. 947–957, 2000.

[11] M. Ishizuka, M. Hatori, O. Dohi et al., “Expression profiles of sex steroid receptors in desmoid tumors,” *The Tohoku Journal of Experimental Medicine*, vol. 210, no. 3, pp. 189–198, 2006.

[12] J. Rosai, “GIST: An Update,” *International Journal of Surgical Pathology*, vol. II, no. 3, pp. 177–186, 2016.

[13] F. Folli, G. Galimberti, M. Pastore, A. M. Davalli, and E. Bosi, “Paraneoplastic insulin resistance syndrome in advanced aggressive fibromatosis (desmoid tumor) treated by imatinib mesylate [6],” *Diabetes Care*, vol. 29, no. 9, pp. 2178–2180, 2006.

[14] M. C. Heinrich, G. A. McArthur, G. D. Demetri et al., “Clinical and molecular studies of the effect of imatinib on advanced aggressive fibromatosis (desmoid tumor),” *Journal of Clinical Oncology*, vol. 24, no. 7, pp. 1195–1203, 2006.

[15] S. R. Patel and R. S. Benjamin, “Desmoid tumors respond to chemotherapy: Defying the dogma in oncology,” *Journal of Clinical Oncology*, vol. 24, no. 1, pp. 11-12, 2006.

[16] D. Jiang, D. He, Y. Hou et al., “Subsequent intra-abdominal fibromatosis mimicking recurrent gastrointestinal stromal tumor,” *Diagnostic Pathology*, vol. 8, no. 1, article no. 125, 2013.

[17] C. K. Lee, A. Hadley, K. Desilva, G. Smith, and D. Goldstein, “When is a GIST not a GIST? A case report of synchronous metastatic gastrointestinal stromal tumor and fibromatosis,” *World Journal of Surgical Oncology*, vol. 7, article no. 8, 2009.

[18] M. Khan, G. Bozas, J. Cooke, K. Wedgwood, and A. Maraveyas, “Mesenteric desmoid tumor developing on the site of an excised gastrointestinal stromal tumor,” *Rare Tumors*, vol. 2, no. 2, pp. 91–93, 2017.