Presacral Teratocarcinoma Presenting as Anal Fistula and Rectal Adenocarcinoma: A Unique Case Presentation and Literature Review

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Key Words
Presacral teratoma · Anal fistula · Rectal adenocarcinoma · Somatic malignancy arising from teratoma · Teratoma with malignant transformation

Abstract
Somatic malignancy arising from presacral or retroperitoneal primary teratoma is extremely rare. We report the case of a 37-year-old male patient with adenocarcinoma of respiratory type arising from primary presacral teratoma, but which first presented as anal fistula and rectal adenocarcinoma. The two tumors show the same morphology and immunophenotype (CK7–CK20+CDx2+). Malignant adenocarcinoma transformations from the normal respiratory epithelium are also found. To the best of our knowledge, this is the second case of respiratory type adenocarcinoma arising from primary presacral mature cystic teratoma.

Case Presentation
A 37-year-old male with no significant medical history presented with perianal pain. Anal fistula was initially supposed but the pathology of fistulectomy revealed adenocarcinoma. Digital examination showed a palpable mass. Endoscopic examination revealed an ulcerative mass located 3 cm above the anal verge. After the diagnosis of rectal adenocarcinoma, the patient underwent abdomino-peritoneal resection of the rectum. Pathologic examination of the rectal specimen revealed a low-grade adenocarcinoma, stage I. The patient received regular follow-up after the operation.

Four years later, the patient complained of frequent lower back pain lasting for 2 weeks. An image study was conducted which disclosed a large presacral cyst, measuring 7.8 × 7 × 5.4 cm in its greatest dimension (Fig. 1). An elevated serum carcinoembryonic antigen level of 10.4, was also noted. On suspicion of recurrent rectal cancer, the patient received anterior resection and presacral cyst excision. Microscopic examination of the anterior resection specimen revealed a teratocarcinoma
composed of mature cystic teratoma and adenocarcinoma (fig. 2d, fig. 3a). The teratoma component of the teratocarcinoma consisted of gastrointestinal mucosa (fig. 2a), cartilage (fig. 2b), pseudostratified respiratory epithelium (fig. 2c), and pancreas tissue. The rectum showed extensive ulceration with transmural inflammation and fibrosis. A residual low-grade adenocarcinoma was noted which was localized under the mucosal layer of the rectum. Juxtaposition of the pseudostratified respiratory epithelium of the teratoma and the neoplastic cells of the adenocarcinoma was identified (inset in fig. 3a). By immunohistochemistry, the neoplastic cells of the adenocarcinoma were negative for cytokeratin-7 (CK7) and positive for CK20 (CK7–CK20+) (fig. 3b, c). The adjacent juxtaposed respiratory epithelium had immunophenotype of CK7+CK20– (fig. 3b, c) [1]. The result of the immunohistochemistry stain for caudal related homeodomain transcription 2 (CDX2) was positive in the neoplastic cells of the adenocarcinoma but negative in those of the adjacent respiratory epithelium (fig. 3d).

To clarify whether the original rectal adenocarcinoma was actually the adenocarcinoma component of the teratocarcinoma, the original computerized tomography scan image was reviewed and a 2.7-cm presacral cystic lesion was found. Further studies of the cystic lesion were done. However, all cytology and biopsy specimen of the cyst showed negative findings. After reviewing the HE-stained slides of the original abdomino-peritoneal resection specimen, a benign respiratory epithelium was found in addition to the adenocarcinoma. The presence of the benign respiratory epithelium and presacral cyst strongly supports a diagnosis of teratocarcinoma with rectal invasion in the original diagnosis.

Discussion

Primary teratoma of the presacral area is extremely rare with an incidence of only 6–11% of all presacral tumors [2]. Metastasis from other origin, especially gonadal organ, should be excluded before a diagnosis of primary presacral teratoma is made [3]. Primary presacral or retroperitoneal neoplasm usually presents as a single mass, whereas metastasis from other site, such as testis, usually involves both sites of lymph nodes and peritoneum. In our case, gonadal origin or other primary sites had been excluded by positron emission tomography scans. The incidence of the somatic malignancy arising from presacral teratomas (presacral teratocarcinoma) is extremely rare. Table 1 summarizes our review of the English literature. The type of somatic malignancies reported in presacral teratocarcinoma include adenocarcinoma, squamous cell carcinoma and carcinoid tumor (table 1) [4–16]. Presacral teratocarcinoma presenting as a rectal adenocarcinoma complicated by an anal fistula has not been reported before.

The somatic malignancy arising from teratoma was resistant to chemo- and radiotherapy. A regimen of postoperative chemotherapy of presacral teratocarcinoma has not been established due to its rare incidence [13]. It is unknown whether the prognostic factors of ovarian teratocarcinoma, such as capsular invasion, capsular rupture, dissemination, ascites, adhesions and special differentiation of adenocarcinoma, can be applicable or not on the presacral ones [2]. Our patient received combined chemoradiotherapy and six courses of chemotherapy using folinic acid-fluorouracil-oxaliplatin after surgery. Only a 3 × 2-cm residual presacral cyst was identified on follow-up computerized tomography 9 months after the last surgery. Nine years after the original diagnosis of rectal cancer, the patient is alive with no evidence of recurrence.

In summary, we presented the first case report of presacral teratocarcinoma presenting as a rectal adenocarcinoma complicated by an anal fistula. What we learned
from our case is that a diagnosis of presacral teratocarcinoma with rectal invasion should also be considered in a patient with rectal carcinoma complicated by an anal fistula. Pathologically, the presence of any benign ectopic tissue, such as respiratory epithelium, in a rectal cancer specimen should raise the suspicion of teratocarcinoma. The presence of a presacral cyst in the image study also indicated this diagnosis.
Table 1. Somatic malignancy arising from presacral or retroperitoneal teratoma [4–16]

| Authors  | Year | Age/sex | Site                  | Somatic malignancy                                           | Transition                  | Local invasion                                    | Recurrence                                      | Postoperative treatment | Prognosis                                      |
|----------|------|---------|-----------------------|-------------------------------------------------------------|----------------------------|--------------------------------------------------|------------------------------------------------|-------------------------|-----------------------------------------------|
| Tezel    | 1995 |         | Retro-peritoneal       | Focal well-differentiated adenocarcinoma                    | Unknown                    | Adjacent to other organs and LAP                 | Local recurrence and metastasis to the rectum | Adjuvant C/T            | Died 10 months after diagnosis               |
| Renato   | 1996 |         | Retro-peritoneal       | Moderately differentiated adenocarcinoma                   | Unknown                    | Invasion to the adrenal gland and adhesion to the aortic wall | C/T and R/T             |                        |                                               |
| Wang     | 2002 40/M |     | Retro-peritoneal       | Mucinous adenocarcinoma, respiratory type                  | Yes                        | Adhesion and intraoperative rupture             | Brain metastasis after 2 months and died 4 months after diagnosis |                        |                                               |
| Wang     | 2002 30/M |     | Retro-peritoneal       | Signet-ring cell type with focal intestinal-type adenocarcinoma | Yes                        | No                                               | No                                             | Neo-adjuvant C/T       | 13 months free of tumor                     |
| Joseph   | 2006 53/F |       | Retro-peritoneal       | Squamous cell carcinoma, well to poorly-differentiated     | Multiple omental seeding   | Unknown                                         | Unknown                                         | Unknown                 |                                               |
| Chu      | 2005 65/F |       | Retro-peritoneal       | Colonic-type adenocarcinoma                                | Yes                        | Adhesion, local invasion and intraoperative rupture | Local recurrence with metastasis               | Postoperative C/T and R/T | Abdominal wall metastasis after 8 and 15 months, died 19 months after surgery. Died 19 months after first diagnosis |
| Wang     | 2008 47/F |       | Retro-peritoneal       | Adenocarcinoma, sinonasal intestinal-type                 | Yes                        | No                                              | No                                             | No                      | 18 months free of tumor                     |
| Kim      | 2009 45/F |       | Retro-peritoneal, presacral | Mucinous adenocarcinoma with elevated CA199               | Unknown                    | Adhesion, local invasion and intraoperative rupture | Local recurrence with metastasis               | Postoperative C/T and R/T | Abdominal wall metastasis after 8 and 15 months, died 19 months after surgery. Died 19 months after first diagnosis |
| Terado   | 2010 27/M |       | Retro-peritoneal       | Small intestinal adenocarcinoma                            | Yes                        | No                                              | Yes                                            | No                      | 18 months free of tumor                     |
| Mc Gawley| 2010 46/F |       | Rectal                | Colonic adenocarcinoma                                     | No                         | No                                              | No                                             | Unknown                 |                                               |
| Present case | 2012 37/M |       | Presacral             | Adenocarcinoma, sinonasal intestinal-type                 | Yes                        | Invasion to the rectum at present               | No                                             | CCRT and C/T            | Residual small cyst and alive after 9 years |

Month of death – 19 months after first diagnosis
**Fig. 1.** Magnetic resonance imaging showing a 7.8-cm cystic lesion of the presacral area.

**Fig. 2.** Presacral lesion showing teratomatous components including gastrointestinal epithelium (a), cartilage (b), and respiratory epithelium (c). Transition between the respiratory epithelium of the teratoma and the dysplastic epithelium of the adjacent adenocarcinoma (d).
Fig. 3. Juxtaposition between the benign ciliated pseudostratified columnar epithelium (R) and the dysplastic epithelium (D) of the adenocarcinoma was identified in both the presacral teratocarcinoma (a) and the original rectal adenocarcinoma (a inset). The respiratory epithelium (R) shows CK7+CK20−CDx2− immunophenotype (b–d), and the dysplastic epithelium (D) of the adenocarcinoma shows CK7+/−CK20+/−CDx2+/− immunophenotype (b–d). The dysplastic epithelium (D) of the original rectal cancer shows more intense CDX2 staining (d inset).

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