Incidental Finding of a Neuroendocrine Tumor Arising from Meckel Diverticulum During Hernia Repair – A Case Report and Literature Review

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Abstract. Meckel diverticulum is the most common abnormality of the gastrointestinal tract arising from an incomplete obliteration of the vitelline duct during the intrauterine life. Although tumor development in Meckel diverticulum is not a common situation, it can occur due to the persistence of cellular islets with gastric, pancreatic or intestinal origin. The presence of a neuroendocrine tumor arising from Meckel diverticulum is even scarcer. We present the case of a 59-year-old patient in whom a Meckel diverticulum was found during surgery for inguinal hernia; the histopathological and immunohistochemical studies revealed the presence of a well-differentiated neuroendocrine tumor with low mitotic index.

Meckel diverticulum remains the most common abnormality of the gastrointestinal tract development, found in up to 2% of the general population (1, 2). Its development is related to an incomplete obliteration of the vitelline duct during the 8th week of intrauterine life (3), while its prevalence is up to five-times higher in men than in women (4). Meckel diverticulum was first described in the 16th century by Fabricius Hildanus; however, it was named after Johann Meckel in 1809 who also explained its embryologic origin from the omphalomesenteric duct (5). Due to the fact that the omphalomesenteric duct contains pluripotent cells during intrauterine life, Meckel diverticulum may present, at the moment of diagnosis, various types of tissues, including gastric, intestinal or pancreatic cells (6); other histopathological subtypes, such as sarcomas, gastric adenocarcinomas, gastrointestinal stromal tumors or neuroendocrine tumors are rarely seen (3). The estimated lifetime complication rate in patients with Meckel diverticulum reaches approximately 4%, the most frequently encountered complication consisting of gastrointestinal bleeding, which is generally related to a secondary ulcer induced by acid secretion from associated gastric mucosa (7, 8). Complications related to tumoral development in Meckel’s diverticulum are rarely seen, with an estimated incidence of 0.5-3.2% (9, 10). We present the case of a 59-year-old patient in whom Meckel diverticulum was an incidental finding during surgery for hernia repair; moreover, the histopathological findings revealed the presence of a well differentiated neuroendocrine tumor.

Case Report

A 59-year-old patient presented for the apparition of a right inguinal mass associated with pain. The local examination confirmed the presence of an inguinal hernia and, therefore, the patient was submitted to surgery. Intraoperatively, an indirect inguinal hernia was found; when dissecting the inguinal sac, an ileal loop presenting a Meckel diverticulum with an intraluminal mass was found. The diverticulum was widely excised en bloc with the adjacent ileal segment and corresponding mesenteric area, while the intestinal wall was sutured using a monofilament stich. The hernia was treated by performing a Liechtenstein procedure, while the resected...
specimen was sent for histopathological studies. Serial 3-μm sections had been cut from paraffin blocks and stained with hematoxylin and eosin (HE). The sections revealed the presence of a 0.6/0.4 cm well-differentiated neuroendocrine tumor with insular architectural pattern (A type, midgut type), invading the submucosal layer (Figure 1). Immunohistochemistry (IHC) was performed on 3 μm sections from 10% formalin-fixed paraffin-embedded tissues according to the IHC method, an indirect bistadial technique performed with a polymer based detection system (Max Polymer Detection System-Leica Ref: RE 7280-k; by MEDIST Life Science s.r.l., Bucharest, Romania). Tissue sections were spread on poly-L-lysine-coated slides immersed in three changes of xylene and rehydrated using a graded series of alcohol. Antigen retrieval was performed in microwave oven. In each section, endogenous peroxidase was blocked by a 20-min incubation in 3% hydrogen peroxide. The sections were incubated with primary antibody: Chromogranin A (Leica by MEDIST Life Science s.r.l.; 1:100, 5H7), Synaptophysin (Leica by MEDIST Life Science s.r.l.; 1:100, 27G12), SSTR 2 (Thermo by MEDIST Life Science s.r.l; 1:30, Polyclonal), SSTR 5 (Thermo; 1:200, Polyclonal) and Ki67 (DAKO by MEDIST Life Science s.r.l.; 1:100, Mib-1) at room temperature for 1 h. The Max Polymer Detection System was then applied for 30 min. Finally, the sections were incubated in 3’3’-diaminobenzidine for 5 min, counterstained with Meyer’s hematoxylin and mounted. The slides were examined and photographed on a Leica DM750 microscope (address if different from above). Negative controls were obtained by replacing the primary antibody with non-immune serum. As a positive control, a rectal tissue section was used. Immunohistochemically, the tumor cells presented a diffuse strong expression for synaptophysin (Figure 2), somatostatin receptor type 2 (SSTR2) (Figure 3), SSTR5 (Figure 4) and chromogranin (Figure 5); Ki67 was positive in about 2% of the tumor cells (Figure 6).

Postoperatively, the oncological team opined that no adjuvant treatment should be performed due to the fact that the tumor was completely excised, with negative resectional margins, while the histopathological studies revealed a very low proliferation index (Ki67<2%). At one year follow-up, the patient presents no signs of recurrence.

Discussion

Tumoral development in Meckel’s diverticulum is a rare situation, while malignancy-related complications are even scarcer ranging between 0.5-3.2% (9, 10). The most often encountered tumoral transformations of Meckel diverticulum include carcinoids, followed by pancreatic carcinomas, gastrointestinal stromal tumors, leiomyosarcomas and lymphomas (11-15). In the study conducted by Modlin et al., about the sites of development of carcinoid tumors conducted on 13,715 patients identified by the Surveillance, Epidemiology and End Results (SEER) program of the National Cancer Institute between 1950-1999, the incidence of carcinoid tumors located in Meckel diverticulum was 0.74% (16). However, an interesting observation is that, due to its limited dimensions, Meckel’s diverticulum has the highest rate of carcinoid transformation per cm2 of mucosal surface (8).

In order to determine if malignant tumors of Meckel diverticulum are associated with a poorer prognosis when compared to other ileal malignancies, retrospective studies, involving surgically-treated patients presenting ileal and Meckel’s diverticulum carcinomas, were considered. Thus, in a 2011 study, conducted by Thirunavukarasu et al. (9), the results from 163 patients with Meckel’s diverticulum malignant transformation who were submitted to surgery were compared with those obtained from a group of 6,214 surgically-treated patients for non-Meckelian ileal cancer. Among patients with Meckel diverticulum cancer, the mean age at diagnosis was 60.6 years, while the sex ratio revealed a slight predominance in men with a male:female ratio of 1.7:1. Concerning the long-term outcomes of patients diagnosed with Meckel diverticulum carcinomas, the authors reported a median overall survival of 173 months, a value strongly influenced by the histopathological subtype and stage at diagnosis: patients diagnosed with Meckel’s diverticulum carcinoids reported an overall survival of 243 months, significantly higher when compared to those with histopathological diagnosis of gastrointestinal stromal tumors and leiomyosarcomas (62 months) or those diagnosed with adenocarcinomas with a reported overall survival of 13 months. These results were compared with those obtained from patients with non-Meckelian diverticulum malignancies. The authors reported that patients submitted to surgery for non-Meckelian carcinoids demonstrated a poorer outcome when compared to those with Meckel’s diverticulum carcinoids (with a median overall survival of 115 months for non-Meckelian ileal carcinoid tumors and 243 months for Meckel’s diverticulum carcinoid tumors) (9). Finally, the issue about the most appropriate therapeutic strategy in asymptomatic cases, in whom Meckel diverticulum is an intraoperative incidental finding, is still under scrutiny as it remains unclear whether the incidentally discovered Meckel diverticulum is at increased risk of complication or not (6). While Thirunavukarasu et al. widely advocate that Meckel diverticulum should be excised whenever is diagnosed, other authors, such as John Park et al., consider that resection is suitable for cases presenting any of the following four features most commonly associated with symptomatic Meckel diverticulum: patients younger than 50 years, male sex, diverticulum length greater than 2 cm and presence of histologically-abnormal tissue (17). Another important question regarding the surgical approach for Meckel...
Figure 1. Well-differentiated type A neuroendocrine tumor by HE staining (×40).

Figure 2. Synaptophysine-positive diffuse tumor cells by IHC staining (×10).

Figure 3. SSTR2-positive diffuse tumor cells by IHC staining (×10).

Figure 4. SSTR5-positive diffuse tumor cells by IHC staining (×10).

Figure 5. Chromogranine A-positive diffuse tumor cells by IHC staining (×10).

Figure 6. Ki67 was positive in up to 2% of the tumor cells.
diverticulum is related to the extent of resection. Is a simple diverticulectomy enough or a wider resection should be tempted? In the aforementioned study, conducted at Mayo Clinic and involving 1,476 patients intraoperatively diagnosed with Meckel diverticulum, the authors reported that a simple diverticulectomy is not enough in cases presenting palpable ectopic tissues at the base of Meckel diverticulum. Therefore, the authors recommend that if a palpable mass is found at the base of Meckel diverticulum, the diverticulum should be widely resected in order to provide a tumor-free resection margin, while in cases with non-palpable masses a simple diverticulectomy seems to be sufficient (17). Concerning the long-term outcomes, it has been widely demonstrated that the appearance of distant metastases is strongly related to the tumor dimensions: Moertel et al. reported that carcinoids smaller than 1 cm metastasize in 2% of cases, Thompson et al. have shown a metastasis rate of 18% for the same group of tumors (18, 19). Once malignant cells appear in the systemic circulation, they will induce the development of distant metastases, especially in liver, followed by lung and bones (19). Due to the capacity of carcinoid tumors to metastasize, other authors strongly recommend that resection should include the adjacent ileal segment and the corresponding mesentery whenever the tumor ID is larger than 5 mm (9).

**Conclusion**

Although a standard and unanimous agreed therapeutic strategy in asymptomatic Meckel diverticulum has not been established yet, the surgeon should be aware of the risk of malignant transformation, especially in elderly patients. Therefore, a prophylactic excision should be tempted in order to eliminate the risk of further complications that may develop. In our case, the wide resection of the Meckel diverticulum en bloc with the adjacent enteral wall and mesenterial segment provided a good control of the malignancy impeding the development of distant metastases.

**References**


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