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Case Report

Appendiceal neuroendocrine tumors (ANETs)- incidental finding on frozen section of hysterectomy specimen

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Abstract

Appendiceal neuroendocrine tumors (ANETs) occur in less than 1% of surgical resections. Grossly it is difficult to differentiate malignant tumor from benign conditions and clinically patients often present as asymptomatic or with symptoms like lower abdominal pain, nausea, vomiting etc. Present scenerio describes appendiceal neuroendocrine tumor diagnosed as an incidental finding on frozen section of hysterectomy specimen. Appendix was enlarged and edematous appendix, densely adherent to right fallopian tube. Hard lump was noted at tip of appendix and frozen section and histopathological diagnosis favors neuroendocrine tumor of appendix. Immunohistochemistry results showed positivity for synaptophysin and chromogranin with Ki-67 index of 1-2%. Based on the CECT findings after hysterectomy and histopathological report patient was planned for right hemicolectomy (meso-appendiceal spread). The final diagnosis of metastatic lymph node deposits in known case of neuroendocrine tumor (pT3 pN1 M0) was made. Based on the above findings, proper evaluation of appendix should be done during gynaecological surgeries and appendecetomy should be performed if needed. Imparting training of appendectomy to gynaecological surgeons is recommended for early diagnosis and treatment of appendical neuroendocrine tumor.

Keywords: Appendiceal neuroendocrine tumors, Colectomy, Neoplasm grading, Frozen section.

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1. Introduction

Appendiceal neuroendocrine tumors (ANETs) have an incidence of 0.3% to 0.9% and come under the category of gastrointestinal neuroendocrine tumor. Mostly ANET occurs between fourth to fifth decade of life with occurrence more in female as compared to male.[1-3]

The tip of the appendix is involved most commonly accounting for approximately 70% cases, 5-20% cases arise in mid appendix and < 10% cases arise in the base of appendix.[4,5]

Appendiceal neuroendocrine tumor are graded into grade 1, grade 2 and grade 3 neuroendocrine tumor. They are further classified as L - cell tumor, glucagon –like peptide-producing tumor, enterochromaffin –cell carcinoid, serotonin –producing carcinoid, large cell neuroendocrine carcinoma and small cell neuroendocrine carcinoma.[6] Entrochromaffin – cell neuroendomcrine tumor are the most common tumor among NET and the rare subtype is tubular NET. The vast majority of EC cell - NET and L cell –NET are grade 1 or grade 2.

These tumors may have aggressive outcome with its metastasis to mesenteric lymph nodes and liver.[7] Surgery is recommended for better outcomes with a completion right hemicolectomy (CRH) after an initial appendectomy. The

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main purpose of a CRH is to complete the regional lymph node dissection.[2,4,7]

The survival rate is more than >95% compared to all other tumor types located in the appendix, even patients with ilocoregional disease seem to have approximately the same prognosis as those having tumors limited to the appendix.[2]

In only metastatic disease hormone production occurs causing carcinoid syndrome.[4,5]

2. Case Report

A 38-year-old female patient presented to gynecology OPD with chief complaints of heavy menstrual bleeding, pain abdomen mainly on right side. Only ultrasound was done pre operatively and findings revealed fibroid uterus with left ovarian cyst with no visualization of adhesion between cyst and loop of colon. Laboratory investigation results were within normal limits which includes CBC, prolactin, Ca – 125. Patient underwent total hysterectomy with bilateral salpingo-oophorectomy. Intraoperatively the left ovarian cyst was densely adherent to the recto-sigmoid loop of colon. Adhesiolysis and bilateral salpingo-oophorectomy was done. Right ovary was healthy. Appendix was enlarged and edematous appendix, densely adherent to right fallopian tube. Hard lump was noted at tip of appendix and frozen section favored the diagnosis of neuroendocrine tumor of appendix. Histopathological diagnosis was in correlation with frozen section and the final diagnosis was well differentiated neuroendocrine tumor of appendix World Health Organization (WHO) Grade 1 (pT3 pNx pM0). Immunohistochemistry results showed positivity for synaptophysin and chromogranin with Ki- 67 index of 1-2%.

Right ovary and fallopian tube showed endometriosis. Left ovary and fallopian tube was unremarkable. Endometrium showed secretory changes with cervix favoring the diagnosis of cervicitis.

After hysterectomy contrast-enhanced CT (CECT) whole abdomen was done and it showed adhesion bands between the sigmoid colon and vaginal cuff as well as internal iliac vessel. No obvious contrast leakage seen. Based on the CECT findings and histopathological report patient was planned for right hemicolectomy (mesoappendiceal spread).

Histopathological examination of the right hemicolectomy specimen with omentum, ileum, caecum and colon showed no growth, polyp or ulceration. Histopathological report showed both the resection margins free of tumor. In ileum, caecum and colon focal congestion was noted and it was free of tumor. 18 lymph nodes isolated from attached mysentry showed 1 lymph node suggestive of metastatic tumor deposits. The final diagnosis of metastatic lymph node deposits in known case of Neuroendocrine Tumor was made (pT3 pN1 M0).

This patient is on regular follow up in medical oncology department and CECT thorax and whole abdomen shows normal study with post right hemicolectomy status with serum chromogranin – A levels within normal limits.

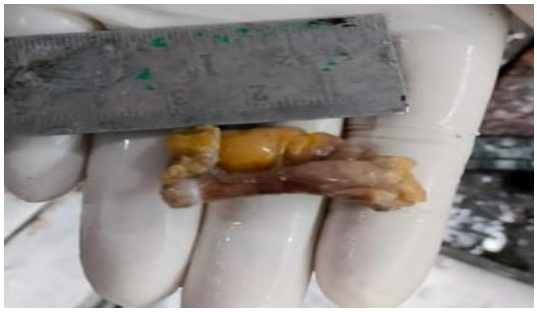

Figure 1: Hard lump at the tip of appendix

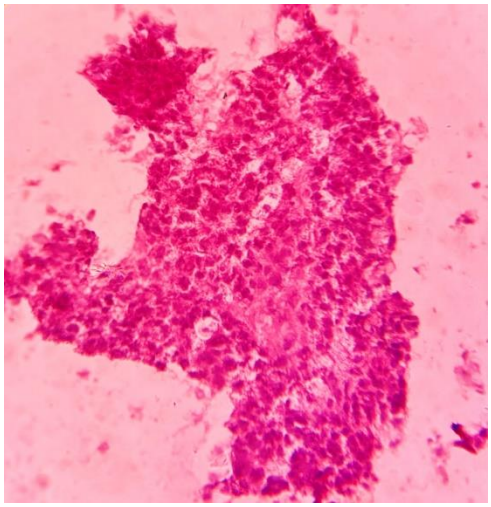

Figure 2: H and E slide, tumoral tissue infiltrating the appendix

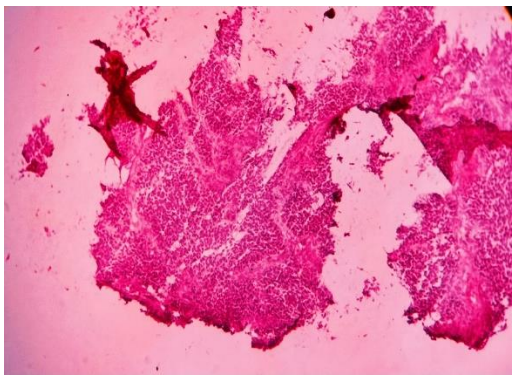

Figure 3: H and E slide – well differentiated aNET

3. Discussion

During gynecologic procedures for the management of heavy menstrual bleeding, lower abdominal pain, appendectomies have become more common. Histopathologic examination and studies have suggested that the appendix may contribute to lower abdominal pain. Coexisting appendiceal neuroendocrine tumors have also been identified during gynecologic surgeries with incidentially detected cases contributing to less than 1%. During laparoscopic

gynecologic surgery, the appendix should be routinely and systematically evaluated. If the appendix appears abnormal, appendectomy should be performed for early diagnosis of appendiceal neuroendocrine tumors.[1]

The neuroendocrine neoplasm of the appendix originates from the chromaffin cells in the lower skin of the appendix mucosa, also known as an argyrophilic tumor.[1,3] It has low incidence rate with high clinical misdiagnosis rate due to a lack of specific clinical manifestations.[3] The diagnosis depends on the intraoperative frozen section, postoperative pathological paraffin and immune histochemical examination.[1-3,8]

The various conditions which mimics like neuroendocrine tumor of appendix includes appendiceal neuroma.[6] On microscopic examination it shows submucosal hyperplasia consists of proliferation of spindle cells, elongated cells arranged in fusiform or nodular pattern. The lesion shows immunoreactivity to S-100 protein and Neuron specific enolase.[3,9] The various other conditions causing neurogenic appendicopathy related to intestinal nerve lesion like Ganglineuromatosis, Schwannoma, Perineuroma, Neurofibromas of von Recklinghausen disease, Mucosal neuroma of MEN 2B syndrome.[6]

In this case patient presented to gynecology OPD with chief complaints of heavy menstrual bleeding and pain abdomen. Patient underwent total hysterectomy with bilateral salpingo-oophorectomy. Intraoperatively the left ovarian cyst was densely adherent to the recto-sigmoid loop of colon. Appendix was enlarged and edematous, densely adherent to right fallopian tube. Tumor was located at tip of appendix and frozen section and histopathological examination favored Well Differentiated Neuroendocrine tumor of appendix (pT3 pNx pM0) which was further confirmed on immunohistochemical examination.

CECT was done and based on CECT findings and histopathological report patient was planned for right hemicolectomy to look for mesoappendiceal spread. Second surgery was done. The final diagnosis of metastatic lymph node deposits in known case of Neuroendocrine Tumor appendix was made (pT3 pN1 M0).

The overall survival rate is better among patients without lymph node metastases compared to those with lymph node involvement, thus indicating patient with lymph node positive status and distant metastasis have poor prognosis.[4]

4. Conclusion

Gynecologic surgeons should receive appendectomy training to aid with incidental detection and early diagnosis of appendiceal neuroendocrine tumors. Training for appendectomies and management of associated complications should become a mandatory component in obstetrics and gynecology programs to prepare gynecologists.

5. Source of Funding

None.

6. Conflict of Interest

None.

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