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ASSOCIATION OF OVARIAN AND APPENDICEAL MUCINOUS TUMOR: CASE REPORT AND PRACTICAL IMPLICATIONS

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ABSTRACT

The presence of a mucinous tumor suggests a primary appendiceal origin with ovarian metastasis, which is the most common form. However, the presence of synchronous mucinous tumors of the ovary and appendix is infrequent and scarcely described in the literature. The diagnosis is primarily histological. Recent studies have shown the role of immunohistochemical and genetic studies in improving and confirming the diagnosis in cases of doubt. Surgical management is based on the resection of the largest feasible portion of the tumor. An appendectomy is systematically performed even if the appendix appears macroscopically normal. Additional chemotherapy may be proposed as adjuvant treatment. In this study, we present the case of a 58-year-old patient who presented with pelvic pain and abdominal distension. Radiological examination revealed a left ovarian mass with a double component and peritoneal effusion. Exploration revealed a left ovarian mass, gelatinous abdominal effusion, and a normal-looking contralateral ovary and appendix. Pathological examination noted the presence of synchronous mucinous tumors of the appendix and ovary. The patient underwent surgical treatment followed by chemotherapy.

KEYWORDS: ovary – appendix - synchronous mucinous neoplasm- genetic analysis – surgery treatment.

INTRODUCTION

The simultaneous presence of a mucinous tumor in both the ovary and the appendix can be explained in two ways. Firstly, it may result from the presence of a primary mucinous tumor in the appendix with subsequent metastasis to the ovary, typically occurring on the right side

due to its proximity. This scenario is the most commonly encountered. Secondly, the concurrent presence of primary tumors in both the ovary and the appendix at the same time is sporadic but possible.[1]

To address this issue effectively, employing additional and more objective methodologies is essential.

These methodologies may include macroscopic, histological, and immunohistochemical analysis utilizing antibodies that are up to distinguish between ovarian and colonic tumors.

Notably, cytokeratin 7 (CK-7)[2] is a widely used marker, found in all ovarian epithelial tumors and metastatic sites, but generally absent in most colonic tumors. Another relevant approach involves molecular genetic techniques, focusing on the analysis of genetic microsatellites to detect loss of heterozygosity, which indicates chromosomal deletions in tumor suppressor gene regions.[3]

CASE REPORT

Patient history: A 58-year-old patient, with no particular medical history, menopausal for 8 years, has been complaining of chronic pelvic pain for the past month, along with abdominal distension and a sensation of heaviness, evolving in the context of fatigue and unspecified weight loss.

Clinical finding

Clinical examination noted the presence of an abdominopelvic mass reaching the umbilicus, with a dull descent.

Paraclinical examination

Pelvic ultrasound revealed the presence of an abdominopelvic tumor originating from the pelvic region with heterogeneous tissue and cystic echogenicity, measuring 167x18x104 mm, along with a moderate amount of fluid accumulation.

Abdominopelvic CT scan revealed a large left ovarian mass with a double component measuring 202x117x182mm, classified as ORADS5, moderate peritoneal effusion, no intra or retroperitoneal lymphadenopathy, and micronodular infiltration of mesenteric fat, predominantly in the greater omentum.

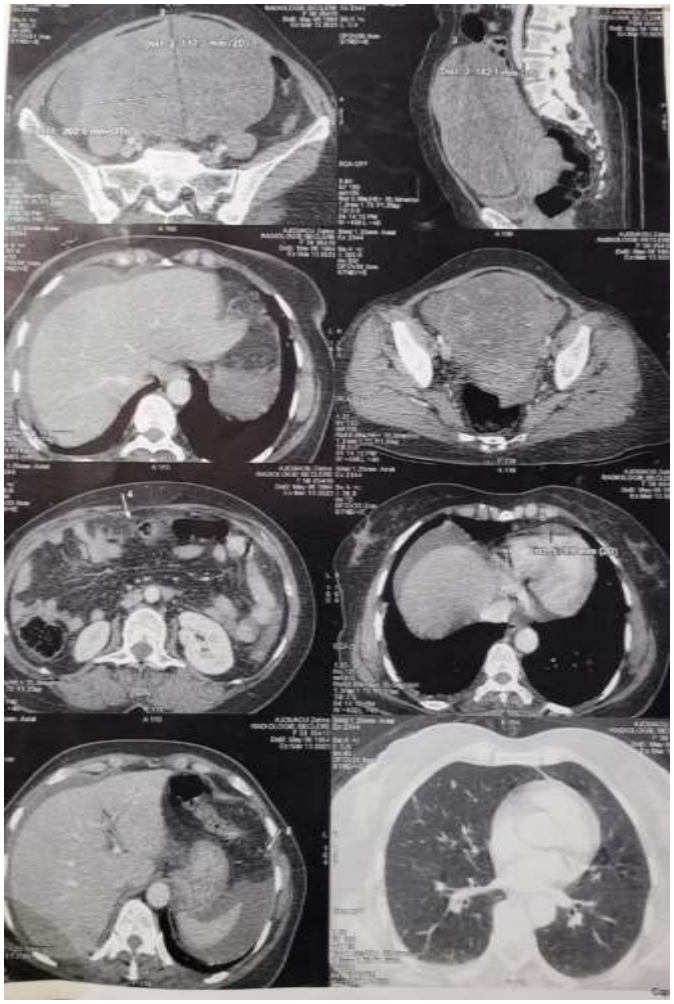

Figure 1: Scan image showing an left ovarian mass with peritoneal ascites."

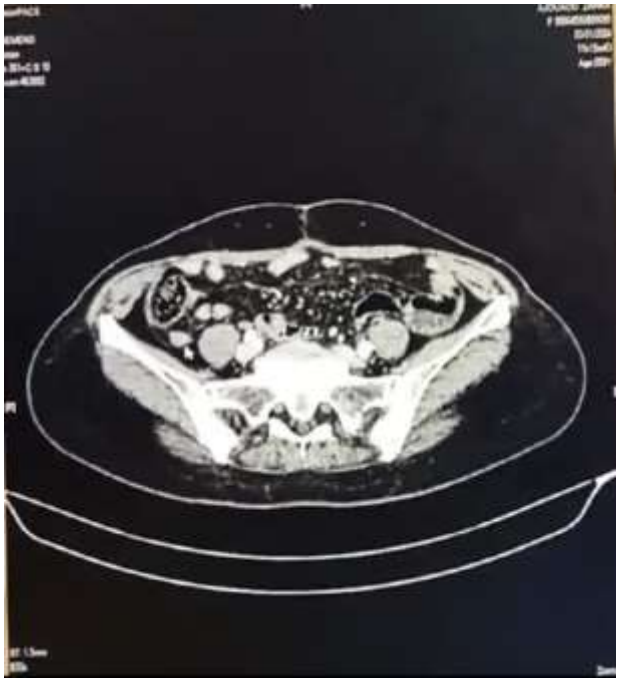

Figure 2: Scanning image objectifying an inflamed appendix.

The serum level of the tumor antigen CA125 was markedly elevated at 12,555.2 U/mL, with the normal value being less than 35 U/mL.

The patient underwent exploration via a midline laparotomy due to the large size of the ovarian mass, which contraindicated the laparoscopic approach because of the risk of perforation.

Therapeutic intervention

During the exploratory laparotomy, we identified a large mass on the left ovary consisting of two components measuring 25cm. The right ovary appeared normal. Moderate gelatinous ascites and peritoneal carcinomatosis were also noted, with a peritoneal carcinomatosis index of 5/39. Surgical interventions included left salpingo-oophorectomy, omentectomy, appendectomy, peritoneal biopsy, and sampling of ascitic fluid. Histopathological examination revealed mucinous adenocarcinoma of the left ovary with capsular rupture, low-grade mucinous neoplasia affecting the appendix, greater omentum, and peritoneum. Mucin deposits were found in the peritoneal fluid without tumor cells present. The patient subsequently underwent chemotherapy.

DISCUSSION

The association of a mucinous ovarian tumor with an appendicular mucinous tumor was first reported in the English literature by Eden in 1912.[4] Eden believed that appendiceal and ovarian tumors were independent primary neoplasms. Over the next decade, this association was further documented by Novak[5] and Ries.[6] The relationship between appendiceal and ovarian tumors in these cases sparked considerable discussion. While the terminology used in many of these reports varied, the histological characteristics of the ovarian, appendicular, and peritoneal lesions appeared to be similar.[1]

Three possible scenarios can be proposed in the presence of synchronous ovarian and appendicular mucinous tumors:

The first scenario involves appendicular tumors being secondary to ovarian tumors, where most mucinous ovarian tumors in these cases are either benign or borderline. However, it is highly unlikely that the appendix would be the sole site of metastasis from an ovarian tumor of these types, and even more extraordinary that the appendiceal mucosa would be lined with neoplastic mucinous cells in each instance. While the spread of ovarian cancer to the

appendix is relatively common[7], it typically remains confined to the serosa and outer muscular layer. Mucosal invasion, when it occurs, particularly in advanced stages, results from progression from the outer layers. Additionally, in cases where mucinous borderline tumors (likely primary in the ovary) are associated with pseudomyxoma peritonei, invasion of abdominal viscera is exceptionally rare.[8.9]

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The second scenario involves the appendicular and ovarian tumors being independent primary tumors, illustrating the synchronous transformation of epithelium from different embryonic origins (endodermal and mesodermal) into cytologically similar neoplastic cells. While it is possible for a patient with a mucinous borderline ovarian tumor to also have a primary tumor of a similar type in the appendix, such an occurrence would be extremely rare due to the low frequency of each neoplasm. Furthermore, the extent of disease in cases of combined ovarian and appendicular tumors suggests that they are unlikely to be independent primary tumors.

The third scenario involves ovarian tumors being secondary to an appendicular tumor. Certain characteristics may support this proposition, such as the presence of a unilateral ovarian tumor on the right side.[10] This can be explained by the proximity of the right ovary to the appendix, increasing the likelihood of involvement through direct or transperitoneal spread. The latter mode of spread is significant in causing ovarian disease in these cases, as evidenced by the frequent presence of mucus, with or without epithelial cells, on the ovarian

surface and varying degrees of penetration into the superficial cortex. "Implantation" on the ovarian surface is a common finding in metastatic ovarian tumors and further supports the secondary nature of these ovarian tumors. Additionally, the presence of appendiceal rupture observed macroscopically or wall penetration seen microscopically may also indicate the secondary nature of the ovarian tumor.

Finally, it is important to note that sometimes during the initial exploration, an appendix may appear "normal" when an ovarian tumor and pseudomyxoma peritonei are discovered. However, this appendix may later develop into a visibly recognizable appendicular tumor. This could be due to an incorrect assessment of the appendix's appearance during the initial surgery or the occasional normal appearance of an appendix already affected by a borderline mucinous cystadenoma.

Given the rarity of the association between appendicular and ovarian mucinous tumors, additional and more objective methods may be necessary to establish this diagnosis. Immunohistochemistry, particularly using cytokeratin 7 (CK-7), can help determine the relationship between mucinous tumors in the appendix and ovary (2). Epithelial tumors of the ovary, whether benign, borderline, or malignant, almost always test positive for CK-7.[12,13,14] Mucinous ovarian tumors also consistently show positive staining for CK-7. In contrast, colonic adenocarcinomas are often negative for CK-7, and since the appendicular mucosa is lined with colonic-type epithelium, appendicular mucinous tumors would be expected to show similar negative results.[2]

Cytogenetic analysis can also be utilized to detect Loss of Heterozygosity (LOH), which indicates a deletion in tumors of a chromosomal region containing a tumor suppressor gene. LOH can be identified by analyzing genetic microsatellites, short repetitive sequences with natural polymorphisms used to distinguish each allele. Microsatellites are also regions of frequent DNA replication instability in tumors, appearing as shifted bands in electrophoretic gels. The authors analyzed microsatellites on chromosome 17q 21.3-22 (nm23) (15. 16), 3p 25-26 (von Hippel-Lindau disease [VHL] gene[17], and 5q 21-22 (D5S346 locus) in 12 synchronous mucinous ovarian and appendicular lesions. LOH at the nm23 locus has been demonstrated in ovarian carcinomas, while genetic alterations at the 3p and 5q loci have been reported in colorectal carcinomas.[2]

The correlation between appendicular and ovarian mucinous tumors carries significant implications for the treatment of patients diagnosed with mucinous ovarian tumors and peritoneal pseudomyxoma. Even if the appendix appears normal during laparotomy in such cases, it is recommended to remove it, if technically feasible, to rule out the presence of an occult tumor. Despite the occasional emphasis on this point in the literature, it is frequently overlooked.[18,19] Moreover, it is advisable to consider removing the ovaries in menopausal or postmenopausal women diagnosed with a borderline mucinous cystadenoma or carcinoma of the appendix to prevent the potential development of mucinous tumors in one or both ovaries. While surgical intervention, involving the resection of as much of the tumor as technically feasible, remains the mainstay of treatment for peritoneal pseudomyxoma, studies by Fernandez[20] and Daly, Cariker, and Dockerty[21] have demonstrated the potential benefit of postoperative abdominal radiotherapy. Chemotherapy for peritoneal pseudomyxoma has generally yielded limited success, with only one reported case showing a potential cure with a three-agent chemotherapy regimen.[22] Attempts to remove intraperitoneal mucus via peritoneal lavage, sometimes using mucolytic agents, have typically been unsuccessful. However, there is one reported case where palliative relief was achieved through peritoneal lavage with 5% dextrose in water.[23]

CONCLUSION

The occurrence of synchronous mucinous ovarian tumors is exceptionally uncommon. In cases where mucinous ovarian tumors coincide with peritoneal pseudomyxoma, meticulous examination and removal of the appendix should be standard practice. Assessing clinical, paraclinical, and histological findings is crucial to consider this diagnosis, and additional immunohistochemical and genetic analyses are necessary to validate this hypothesis.

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