Research Article

Clinicopathological study of primary adenocarcinoma of vermiform appendi: Rare entity

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Abstract

Aim: To study pathology of primary adenocarcinoma of appendix and correlate the findings with clinical data and management. **Design:** Eight year retrospective observational study was carried out in our institute. **Result:** All the appendectomies received were studied in detail. Out of 1574 appendectomies, only 6 cases (0.38%) were diagnosed as primary adenocarcinoma of appendix. Most common pre-operative clinical diagnosis was appendicitis (66.6%). Mean age at presentation was 50 years and male predominance (83%) was noted. Majority cases (66.6%) were given radiological diagnosis of appendicitis. Four cases underwent appendectomy alone whereas right hemicolectomy was performed in two. One case underwent right hemicolectomy at a later stage based on histopathological diagnosis of adenocarcinoma appendix. One case presented with metastasis to liver (16.6%) rest all were in early stage at presentation. All the cases are disease free at the end of follow-up of 6 months. **Conclusion:** Adenocarcinoma of appendix is extremely rare neoplasm usually discovered incidentally on the pathological examination of the surgical specimens. The propensity of these neoplasms for presenting as acute appendicitis mandates the clinician to be aware of the appropriate management of this entity and highlights the need of histopathological examination of every surgical removed appendix.
Keywords: primary adenocarcinoma, appendix.

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INTRODUCTION

Primary adenocarcinoma of appendix accounts for 0.4-1% of all gastro-intestinal malignancies and 4-6% of primary appendiceal neoplasms[1]. Primary adenocarcinoma of appendix can mimic appendicitis in its presentation but its identification alters management significantly[2]. To date, only a few hundred cases have been reported in English literature[2]. The purpose of our study is to review the literature and increase awareness of the appendiceal adenocarcinomas.

MATERIALS AND METHODS

A retrospective case analysis was conducted for 8 years period from January 2007 to December 2014 in our institute. All consecutive patients who underwent appendectomy during the study period were included. All patients diagnosed as primary adenocarcinoma of appendix, were analyzed for their demographic details, clinical presentation, radiological investigation, immuno-histochemistry (IHC) findings wherever possible, tumour grade and stage and treatment. Minimal follow-up of 6 months to maximum of 80 months was done for survival and recurrence.

RESULTS

Of the 1574 cases, primary adenocarcinoma of appendix was diagnosed in 6 cases (0.38%). The mean age at presentation was 50 years, the age range being 30-68 years. Male predominance was noted (83%). Most of the patients presented with signs and symptoms consistent with appendicitis (66.6%) followed by intestinal obstruction (33.4%). In majority of patients (66.6%) radiological findings were suggestive of appendicitis. None was suspected clinically to have adenocarcinoma of appendix. Two cases underwent right hemicolectomy as

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the clinical presentation was as subacute intestinal obstruction. In the remaining four, appendectomy was performed; followed in 2 cases by right hemicolectomy at a later stage based on histopathological report of appendectomy specimen as Adenocarcinoma. Three of appendectomy specimens (50%) revealed diffuse thickening of the wall (Figure 1). One revealed glistening white appearance on cut section. Rest 2 showed nodular surface. Caecum and ascending colon were essentially normal in all these cases. Microscopically, majority were colonic type (66%) (Figure 2) followed by mucinous type (17%)(Figure 3) and adenocarcinoid type(17%) (Figure 4). Immunohistochemistry was done in one case which showed posivity for cytokeratin (CK) and cytokeratin 20(CK) and negativity for cytokeratin 7 (CK7) and chromogranin A (CGA) (Figure 5). One case presented with advanced disease and liver metastasis (16.6%) rest all were limited to appendix. Table 1 shows variable clinical presentation with probable clinical diagnosis and surgical procedures performed. Table 2 shows correlation between clinical, radiological, histopathological and IHC diagnosis.

Table 1

S.N.	Age	Sex	Clinical Features	Clinical Diagnosis	Surgical Procedure
1	50	Male	Chronic abdominal pain	Subacute intestinal obstruction	Rt. Hemicolectomy
2	68	Male	Acute abdominal pain	Acute appendicitis	Appendectomy
3	30	Male	Chronic abdominal pain	Chronic intestinal obstruction	Rt. Hemicolectomy
4	52	Male	Colicky abdominal pain	Acute appendicitis	Appendectomy
5	49	Female	Acute abdominal pain	Acute appendicitis	Appendectomy
6	56	Male	Acute abdominal pain	Acute appendicitis	Appendectomy

Table 2:

S.N.	Clinical Diagnosis	USG	Histopathology	IHC
1	Subacute intestinal obstruction	IC junction obstruction	Adenocarcinoid	Adenocarcinoma
2	Acute appendicitis	Perforation, appendicular lump	Mucinous Adenocarcinoma with perforation, peritonitis	
3	Chronic intestinal obstruction	Appendix-wall thickening. Post-appendectomy USG: Multiple liver mets +,? Omental and peritoneal mets.	Adenocarcinoma infiltrating serosa, pericolic fat. Omental LN and liver mets+	
4	Acute appendicitis	Appendicitis	Adenocarcinoma	
5	Acute appendicitis	Appendicitis	Adenocarcinoma	
6	Acute appendicitis	Appendicitis	Adenocarcinoma	

Figure 1

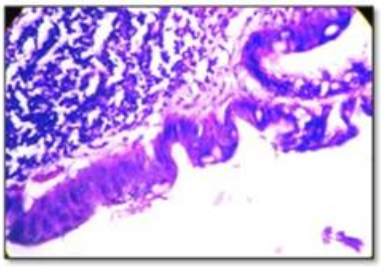

Figure 2

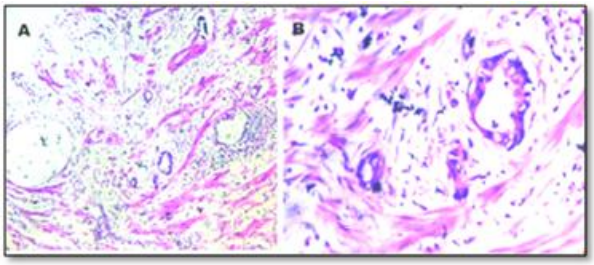

Figure 3(A) Figure 3(B)

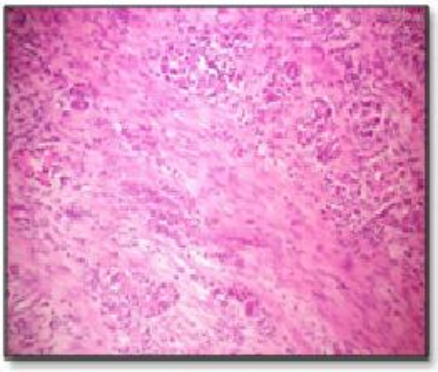

Figure 4

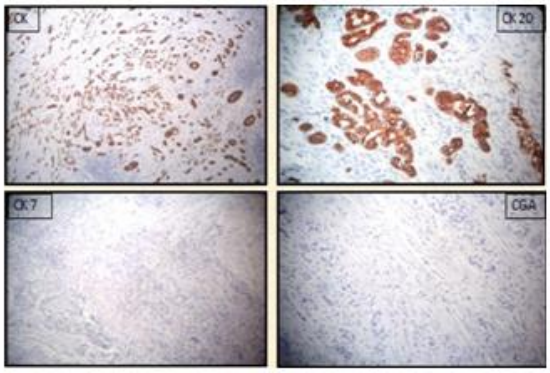

Figure 5

Legend

Figure 1: Gross photograph showing caecum with appendix. On serial C/S, appendix shows g/w mass and narrow lumen

Figure 2: Photomicrograph showing colonic type of adenocarcinoma composed of columnar cells arranged in glandular pattern (HandE,100X)

Figure 3: (A) Photomicrograph showing adenocarcinoma with mucin pools (HandE, 100X); (B) Photomicrograph showing tumour cells invading muscularis propria (HandE, 400X).

Figure 4: Photomicrograph showing innocuous looking relatively uniform tumour cells with bland nuclei arranged in insular pattern (HandE, 100X)

Figure 5: Immunohistochemistry of one case showing positivity for cytokeratin (CK) and cytokeratin 20 (CK20) and negativity for cytokeratin 7 (CK7) and chromogranin A (CGA)

DISCUSSION

Primary adenocarcinoma of the appendix is exceedingly rare usually encountered in 0.08-0.2% of resected appendices and comprise only 4-6% of primary appendiceal neoplasms[1]. Since it was first described by Berger in 1882, cases reported worldwide are less than 500[3,4]. The peak incidence is in 5th and 6th decade[2,4], however youngest case reported was in a 17 year patient[3]. Our study showed mean age at presentation to be at 50years. A slight male predominance is documented in literarture[1,4] while in our study we observed higher male predominance (83%). Seventy-five percent of appendiceal adenocarcinoma present with clinical symptoms whereas 25% are incidental[5]. Most symptomatic appendiceal tumours present as acute appendicitis or mass in right iliac fossa[1]. Our study also revealed acute appendicitis to be most common presentation. Rarer presentations reported in literature include urinary frequency, bladder cancer, hydronephrosis, Crohn's disease, caecal intussusceptions, vaginal bleeding, secondary genitourinary complications, GI bleeding, increased abdominal girth and anemia[1,2,6]. Guarnio and Chitwood defined two criteria necessary for diagnosis of appendicular carcinoma- (i) presence of continuity between the carcinoma and the mucosa of the appendix (ii) presence of mucin containing neoplastic acini within the tumour, tto exclude it from simple mucocele of appendix[3]. Adenocarcinoma of appendix may arise in pre-existing adenomas, with either cystic or colonic growth pattern[1]. Primary adenocarcinoma of appendix can be of 3 subtypes- mucinous (55%), colonic type (34%) and adenocarcinoid (11%)[2]. However, in present study colonic type was more common with incidence of 66.6% (Figure 3). The colonic type adenocarcinoma is highly malignant with tendency to metastasize whereas mucinous has slow growth rate, rarely spread by lymphatics and has good survival rate[4]. Mucinous cystadenocarcinoma tend to rupture and spread through the peritoneal cavity resulting in psuedomyxoma peritonei[1]. Adenocarcinoid tumours have dual origin, sharing histological features of both carcinoid and adenocarcinoma and a predilection for developing ovarian metastases[6]. Primary adenocarcinoma of appendix is the most common perforating carcinoma of gastro-intestinal tract[7]. Only one case in our study presented with perforation. Adenocarcinoma of appendix, spreads by direct extension, local invasion, lymph vessels and bloodstream. The most common metastatic site is peritoneal cavity followed by lymph node, liver, ovaries, abdominal wall and lungs[8]. In our study, one case presented with local infiltration and metastasis to omental lymph node and liver. The preferred surgical treatment is controversial. The simple appendectomy as treatment of choice seems to be sufficient for early, well differentiated, non-invasive carcinoma however according to most of the authors right hemicolectomy is required in cases with (i) liver, lymph node or retroperitoneal metastasis (ii) caecal, mesoappendiceal or peritoneal spread and (iii) histology showing poorly differentiated tumour with high mitotic count[1,2,3]. Hesketh

reported 5-year survival rate was 20% in patients subjected to appendectomy alone and 63% in patients subjected to right hemicolectomy[3]. Right hemicolectomy performed as a secondary procedure results in upstaging of 38% of patients tumour[6]. In present study, appendectomy alone was performed in 50% cases. Adenocarcinoma of appendix often metastasise to ovaries, so bilateral oopherectomy is recommended especially in post-menopausal women[1,6]. Many oncologist recommend 5-fluorouracil based chemotherapy in patients with node positive colonic type adenocarcinoma[2]. One important prognostic factor of primary adenocarcinoma of appendix is histological type of tumour. Park *et al* reported improved survival in patients with mucinous variants. Survival also depends on other factors such as level of invasion, lymph node and distant metastasis, site of perforation and type of operation performed[4,6].

CONCLUSION

Primary adenocarcinoma of appendix is rare, however its propensity for presenting as acute appendicitis mandates the clinician to be aware of the appropriate management of this entity and highlights the need of histopathological examination of every surgically removed appendix.

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