Anal gland adenocarcinoma

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Abstract

INTRODUCTION

Anal malignancies constitute approximately 1 to 3 % of all large-bowel carcinomas [12] and less than 6 % of all anorectal carcinomas [34] . The latter is either squamous or glandular type. The squamous cell carcinoma is much more common than adenocarcinoma. Anal canal adenocarcinoma is subclassified into adenocarcinoma arising in anal mucosa and extamucosal (perianal) adenocarcinoma. The latter includes adenocarcinoma with anorectal fistula, and adenocarcinoma of anal glands [5] . In this article, we present a case of 49-year-old man with anal mass diagnosed as anal gland adenocarcinoma. We also reviewed the literature of this rare entity.

CASE REPORT

The patient is a 49-year-old man who presented with anal lump associated with mild pain. The lump was diagnosed clinically as anal abscess. He was treated by incision and drainage, but the lesion recurred many times. Then, the lump was ulcerated and the patient had an episode of fresh blood per rectum.

On examination the patient was generally fine with no evidence of cachexia or respiratory distress. His anal exam revealed unhealed ulcer measures 4 x 5 cm with greenish discharge. There was a palpable hard, fixed left inguinal lymph node measured around 3 x 1 cm.

The primary investigation revealed that CBC, blood and urine chemistry were within normal limits. MRI revealed 8 cm-long segment of abnormal soft tissue thickening and enhancement seen at the distal rectum. Anal canal and anal opening was associated with ulceration of the adjacent skin of the gluteal folds. These findings were consistent with anal canal cancer which extended from the distal part of the rectum down to the skin around the anal opening. PET/CT scan revealed intensive FDG uptake in the anal region extending anteriorly to the base of the scrotum. Focal abnormal FDG uptake was noted in left inguinal lymph node most probably metastatic. The mass was not resectable and it was biopsied and colostomy was performed.

Microscopic examination revealed infiltrating well differentiated ductular elements underneath hyperplastic squamous anal epithelium. Some of the ducts were filled with neutrophils and necrotic debris (Fig1). The glands were lined by flattened, cuboidal and columnar cells with high nuclear to cytoplasmic ratio. The nuclei were pleomorphic, hyperchromatic, and showed irregular nuclear membrane. The stroma was infiltrated by neutrophils (Fig2). Peri-neural invasion was demonstrated by synaptophysin immunostaining (Fig.3). Immunohistochemistry showed that the tumor cells were diffusely and strongly positive for cytokeratin 7 (Fig 4-a) , CEA (Fig 4-b), and focally positive for CDX2 (Fig 4-c) and synaptophysin (Fig 4-d). Cytokeratin 20 (Fig 4-e), TTF-1, ER, and PR were negative. In conclusion the clinical, histological and immunohistochemical findings are consistent with adenocarcinoma arising from anal gland.

Figure 1

Figure 1: Shows infiltrating glands filled with neutrophils and necrotic debris. (x 10)

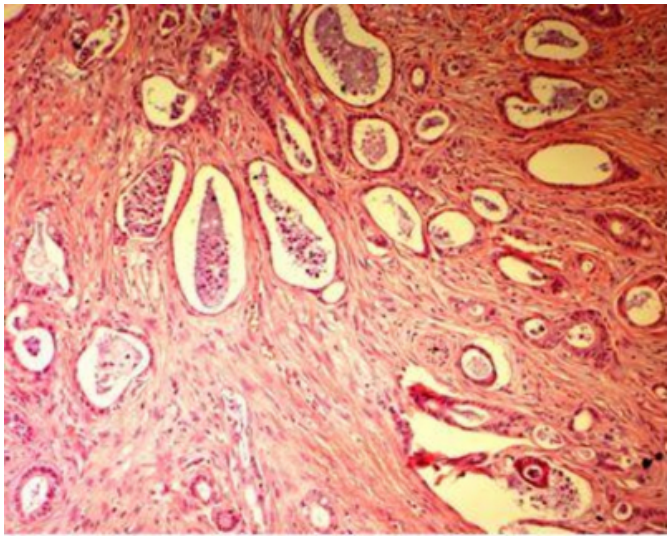


Figure 2

Figure 2: Shows neutrophilic infiltration of the stroma. (x 10)

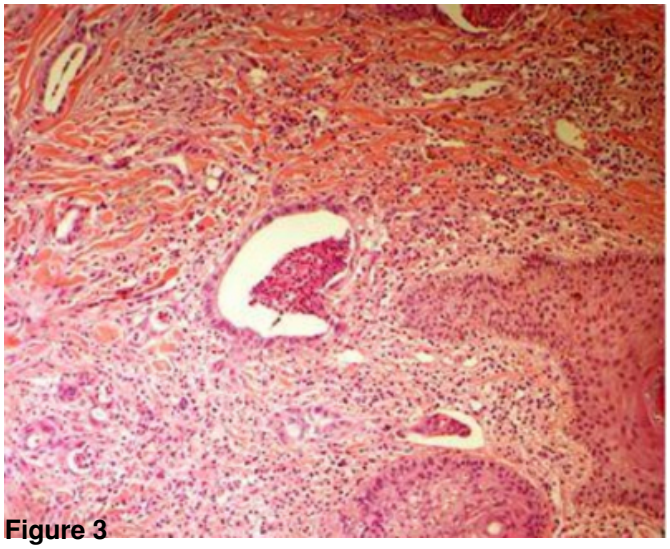


Figure 3

Figure 3: Shows peri-neural invasion demonstrated by synaptophysin staining. (x20)

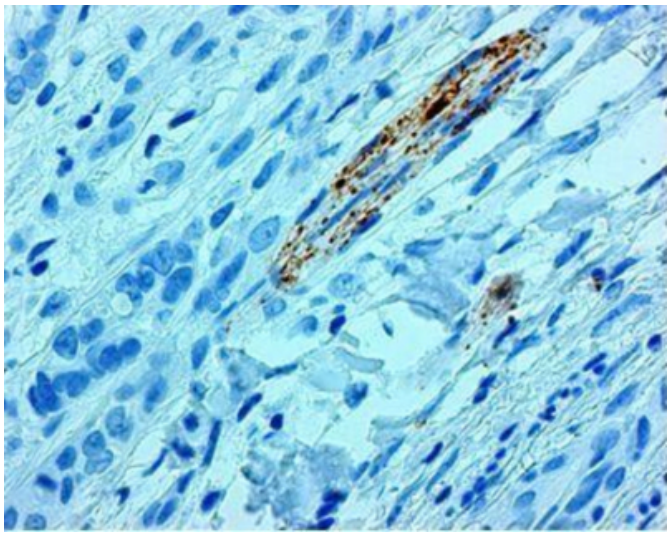
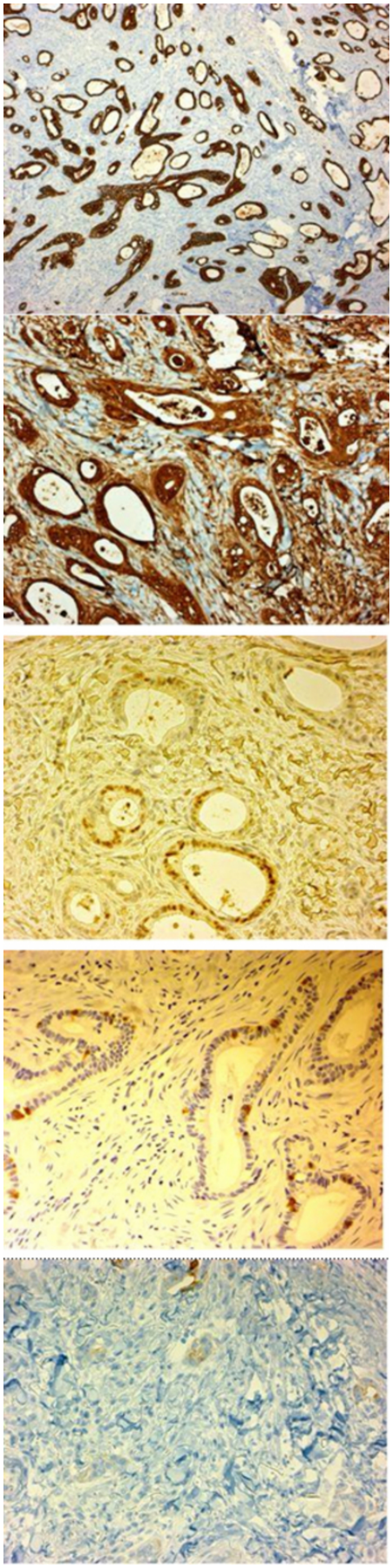


Figure 4

Figure 4: shows the tumor cells were diffusely and strongly positive for cytokeratin 7 (a), CEA (b), and focally positive for CDX2 (c) and synaptophysin (d). Cytokeratin 20 was negative (e).



DISCUSSION

The anal canal is the cylindrical termination of the large bowel, which is approximately 4 to 5 cm in length [1]. Anatomically it is defined to begin at the anal verge and continue to the level of the puborectalis muscle of the anorectal ring or pelvic floor. Histologically the canal had been defined as three zones. The upper part of the canal (colorectal zone) is lined by the same type columnar epithelium as is seen in the distal rectum. The transitional zone, a short segment of mucosa just proximal to the dentate line, is composed of various epithelial elements or "transitional epithelium." Distal to the dentate line is the squamous zone, which is lined by stratified squamous epithelium that continues to the anal verge [12].

The variety of epithelial cell types of the anal canal leads to a variety of neoplasms with different histological appearances in this region. The most common type is squamous cell carcinoma followed by cloacogenic (basaloid or transitional cell) carcinoma. Adenocarcinoma in this region is very rare and has been subclassified into adenocarcinoma arising in anal mucosa and extra mucosal (perianal) adenocarcinoma. The latter includes adenocarcinoma with anorectal fistula, and adenocarcinoma of anal glands [5].

Normal anal glands are simple tubules or branching ducts ramifying in the submucosa and in more than half of the cases extend into or through the internal anal sphincter. From 6 to 10 anal glands and their ducts lie in a narrow zone of transitional epithelium 6-12 mm long proximal to the anal valves and distal to the dentate line, between rectum and anus. The submucosa is narrow at this point; the ducts open at the dentate line but invariably extend into the internal sphincter and sometimes beyond [6].

Adenocarcinoma of the anal glands is distinctly uncommon. It accounts for about 3-10 % to tumors at this site, as basaloid and squamous carcinomas of the anal canal predominate but these three tumours together only constitute 1% of large bowel neoplasms. Members of the American Society of Colon and Rectal Surgery, in 1994, reported only 52 cases of anal gland adenocarcinoma [1]. Then Christine M et al. in 2001 reported 14 cases [7].

In the largest series, consisting of 52 cases, the male-to-female ration was 1.4: 1 [8]. In the second largest series, consisting of 21 cases, the male-to-female ratio was 8:13 [9]. The average patient's age in the former series was only 54.6 years, whereas in the latter series was 70 years. The symptoms of this tumor are similar to those of benign anal pathologic conditions (bleeding, pain, and discharge), a fact that often contributes to delayed diagnosis. Our case was 49 year-old male who was presented with anal lump associated with mild pain.

Perianal adenocarcinoma can be distinguished from other anal malignancies by its characteristic histological features. These characteristics are prominent ductal structures, often well differentiated, with cytoplasmic mucin droplets and mucinous pools. The overlying anorectal mucosa is nearly always intact. The tumor spreads in an extra luminal fashion around the anal canal and may have widespread submucosal extension into the surrounding perianal soft tissues. The tumor usually spreads along the path of normal anal ducts [10].

Immunohistochemistry of normal anal glands shows the pattern of CK7(+)/CK20(−). Most colorectal mucosal-type adenocarcinomas show the pattern of CK7(−)/CK20(+), whereas most anal gland adenocarcinomas show the pattern of CK7(+)/CK20(−). On the other hand, most mucinous adenocarcinomas arising in the anal canal show the pattern of CK7(+)/CK20(+) [1112]. Recent study showed that the neoplastic cells as well as the normal anal ducts or glands were reactive with MUC5AC, but the normal colorectal-type mucosa and three of four colon adenocarcinomas were negative for MUC5AC [13]. Our case was CK7(+)/CK20(−) which is consistent with anal gland adenocarcinomas. The presented case was different from the previous reported cases in its focal positivity for CDX2 and synaptophysin. MUC5AC was not done as it was not available in our laboratory.

The lack of a large series or a randomized trial of these tumors has led to variability in their treatment. Chemoradiation, local excision, abdominoperineal resection, and combinations of these forms of therapy have been used to treat perianal mucinous adenocarcinoma. Most authors recommend treating adenocarcinoma of the anus with surgery similar to their treatment approach for a very low rectal adenocarcinoma [14]. The National Cancer Data Base Report documents 77.4 per cent of anal carcinoma cases treated surgically with or without adjuvant therapy in 1993. This report cites a major change in the treatment of this disease from 1988 to 1993 as the use of adjuvant chemotherapy and radiation increased. This movement toward the use of adjuvant chemoradiation has been credited to the finding of a distinct survival advantage in patients

with rectal adenocarcinoma.

Anal gland carcinomas, because of their slow growth, are considered by some to have a good prognosis if discovered early [1314] . However, because of their lack of a mucosal component and their intramural insinuating growth pattern, diagnostic delay occurs.

In conclusion we present a rare entity of anal gland adenocarcinoma. This entity should be included in the differential diagnosis of all cases of perianal diseases as the symptoms of this tumor are similar to those of benign anal pathologic conditions (bleeding, pain, and discharge), a fact that often contributes to delayed diagnosis. Most anal gland adenocarcinomas show immunohistochemical pattern of CK7 (+)/CK20 (−) which is different from colorectal mucosal type that shows CK7(−)/CK20(+) immunoprofile. However, CK7 (+)/CK20 (−) pattern is seen also in other adenocarcinoma away from anal canal such as lung, ovary and breast. So, the metastatic adenocarcinoma should be excluded before a definite diagnosis of anal gland adenocarcinoma is made.

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