Adenoacanthoma of Pyloric Antrum of the Stomach

— Report of a Case —

Yoo Bock Lee, and In Joon Choi

Department of Pathology
Yonsei University College of Medicine, Seoul, Korea

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ABSTRACT

In view of rarity and its unsolved histogenesis, a case of adenoacanthoma at the pyloric antrum of the stomach is reported.

The patient was a 43 years old Korean male teacher who had onset of symptoms referable to present illness three months prior to the admission, although he had ulcer symptoms 7 years previously and subsequently free from the symptoms during last 4 years following 3 years' anti-ulcer regimen.

Histopathologic studies of the stomach revealed a large ulcerated lesion at the pyloric antrum, and it was predominantly a well differentiated squamous cell carcinoma occupying the central and superficial part and surrounded by a narrow rim of adenocarcinoma at the periphery. Multiple regional nodes examinations disclosed metastases of only adenocarcinoma in 5 nodes and no metastasis of squamous element was found.

A brief review of the literature and a discussion concerning clinical, histopathologic and especially histogenetic aspects is made. It was interesting to note that all squamous cell nests are surrounded by multi-layers of small indifferrent basal type of cells, and it was thought that this might possibly be a supportive evidence of direct stimulation to basal cells to differentiate into squamous element.

INTRODUCTION

Carcinoma of the stomach containing squamous component is a rare condition. It was first reported by Rolleston and Trevor in 1905. Since then at least 67 cases have been reported in the literature.

When the lesion is a mixture of glandular and squamous elements, it has been called by various names: adenocarcinoid (Herxheimer 1907), adenosquamous carcinoma (Rayson 1986), Malpighian epithelioma (Gauthier-Villars and Leger 1940), polymorphous epithelioma (Oberling and Wolf 1927), and adenoacanthoma (Pasternack 1935).

Most authors state that slow growth and a lesser tendency of distant metastasis is found for this type of tumor in comparison with ordinary adenocarcinoma of the stomach. The academic interest of this entity is concerned with the histogenesis of the squamous element in the lesion, and the theories proposed are direct stimulus to undifferentiated basal cells (Krompecher 1924, Wood 1943, Strassmann 1946, Donald 1967), embryonal rests (Herxheimer 1907), and metaplasia (Lubarsch 1906, Oberling
and Wolf 1927, Boswell and Helwig 1965).

When the squamous element is seen in fundal tumors, most authors are reluctant to consider these primary in the stomach. Consequently the majority of cases reported in the literature were located in the pylorus (McPeak and Warren 1948, Saphir 1959, Boswell and Helwig 1965).

The case reported here is an adenocanthoma of the pyloric antrum of the stomach to be added to the 37 tumors reported already.

REPORT OF A CASE

A 43 years old male school teacher was admitted on October 6, 1966 because of anorexia, postprandial epigastric discomfort, hunger pain and tarry stools for about 3 months duration.

Seven years ago he had suffered from hunger pains for which an anti-acid regimen was given by a private physician. After 3 years of anti-ulcer treatment the symptoms disappeared and he had enjoyed relatively good health during the 4 years prior to the present illness.

About 3 months prior to admission, the above symptoms developed associated with alternate episodes of diarrhea and constipation. He also had marked weight loss during this period. No vomiting was present, however.

Physical examination on admission was not remarkable. The abdomen was soft and there was no palpable mass. Laboratory findings on admission consisted of hemoglobin, 6.2 gm%; white blood cell count, 5,900/cu.mm; with a normal differential count; and the stool gave a negative guaiac test. The fasting gastric juice analysis gave 25 degree of total acidity and a positive test for occult blood. X-ray examinations of the chest revealed no abnormality. However, an upper gastrointestinal study disclosed a large ulcer crater with meniscus sign along lesser curvature of the stomach at antral portion.

Under the clinical diagnosis of malignant ulcer of the stomach, a subtotal gastrectomy and omentectomy was performed on the 16th hospital day, followed by antecolic gastro-jejunostomy. At operation several enlarged lymph nodes were noted along celiac axis, subpyloric, superior gastric, and suprapyloric regions. The liver and the pancreas were essentially normal. The postoperative course was uneventful and he was discharged on the 17th postoperative day.

Seven months later, he was readmitted because of generalized edema associated with oliguria, dyspnea, cough and palpitation.

It was thought to be due to multiple tumor metastases. He was discharged after symptomatic treatment. Since this time the patient has been lost to follow-up.

HISTOPATHOLOGIC FINDINGS

Gross: A subtotal gastrectomy specimen with omental flap attached was submitted with celiac lymph nodes in a separate container.

The stomach measured 14 cm along lesser curvature and 20 cm of greater curvature. About 1.5 cm long duodenal flap was attached to the distal end. Upon the opening of the stomach along greater curvature, a large ulcerated and indurated lesion was found on the anterior wall extending a little toward the posterior wall across the lesser curvature (Fig. 1).

The lesion started at a level 3 cm from the pyloric ring and extended 6.3 cm upward anteriorly along the lesser curvature. The greatest width of the lesion was 9.2 cm. Most of the lesion was ulcerated and surrounded by elevated rolling marginal mucosa. The ulcer base was partly necrotic and dark reddish, and partly grayish white with numerous fine papillae giving a granular appearance. When the lesion was incised,
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it was a faint yellowish white penetrating into the muscular layer. The serosal surface was moderately roughened and coarsely granular. A total of 23 regional lymph nodes were found; 6 at inferior gastric and subpyloric regions, 5 at superior gastric, and 12 at suprapyloric regions measuring up to 1 cm in diameter size.

![Fig. 1. Gross appearance.](image1)

Microscopically, there was an abrupt change from the normal glandular gastric mucosa to neoplastic tissue that became ulcerated toward the center of the lesion. The tumor tissue infiltrated the submucosa, penetrated the muscular layer and extended to the serosa. The majority of the tumor tissue consisted of squamous type epithelial cells arranged in trabecular, alveolar and fascicular patterns (Fig. 2).

At the peripheral portion of the lesion, which was not ulcerated, a narrow rim of well differentiated adenocarcinoma as evidenced by distinct glandular structure was seen. However, there were also areas showing abrupt transition from squamous tissue to the normal glandular gastric mucosa without intervening adenocarcinomatous tissue, especially at the proximal margin of the lesion. The adenocarcinomatous tissue also infiltrated into the submucosa, muscular layer and in some areas it surrounded the deeper border of squamous cell carcinoma. The squamous element showed various degrees of differentiation, some were almost indistinguishable from normal squamous epithelial cells while others showed large bizarre or multiple nuclei with coarse clumping of chromatin (Fig. 3). These cells were large polygonal cells with abundant eosinophilic cytoplasm and distinct cellular borders. Marked desquamation with parakeratotic change and tendency of parakeratotic pearl formation.

![Fig. 2. Well differentiated squamous element.](image2)

![Fig. 3. Squamous element, higher magnification.](image3)
(Fig. 4) were frequently noted, but intercellular bridges were not clearly demonstrable.

These clearly recognizable squamous cell trabeculae or alveoli were always surrounded by several layers of small indifferent type of cells which contained relatively small and rather uniform but hyperchromatic nuclei and a small amount of slightly basophilic cytoplasm (Fig. 5).

These cells morphologically resembled the so-called undifferentiated basal cells. An extensive search through multiple sections failed to demonstrate non-neoplastic squamous cell metaplasia at the periphery of the lesion. The cells in the adenocarcinomatous portion were either tall columnar, cuboidal or pleomorphic and none of them showed evidence of mucus secretion on PAS reaction. Nevertheless all of them were arranged in well formed glandular fashion. Outside the adenocarcinomatous rim at the distal margin of the lesion there were noted marked intestinal metaplasia, which intermingled with neoplastic glands (Fig. 6). The mucosa of the

adenocarcinomatous area was slightly heaped up and thicker than adjacent non-neoplastic mucosa, but no evidence of ulceration over the adenocarcinomatous tissue was noted. The ulceration was large but limited to the squamous part of the tumor and formed a layer of necrotic debris with areas of acute purulent inflammatory
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reaction which extended into the tumor tissue. The stroma showed marked desmoplasia, heavy plasma cell and lymphocytic infiltrations. Both distal and proximal resection margins were free from tumor and consisted of glandular gastric mucosa.

Out of 23 regional lymph nodes examined, five of them showed metastatic tumors: 4 out of 5 superior gastric and suprapyloric nodes and 1 out of 2 celiac nodes. All metastatic tumors were adenocarcinomas with moderate degree of desmoplastic change (Fig. 7), and no metastasis of the squamous element was noted.

DISCUSSION

Heterologous squamous cell carcinoma and adenoacanthomas are not uncommon. They are frequently found at regions where there are contiguous squamous cell and glandular surfaces (bronchus, rectum, uterus, and gastric cardia) and in organs which are the frequent site of squamous metaplasia (bronchus, pancreas, urinary tract, gall bladder, and ducts of many exocrine glands). But it is extremely rare in regions possessing glandular mucosa not contiguous with squamous epithelium and not known to manifest squamous cell metaplasia (pyloric end of the stomach, cecum, and colon). In this group, primary squamous cell containing carcinomas are found at the ileocecal valve, cecum, large intestine, ascending colon, and sigmoid colon, in addition to the pyloric end of the stomach.

Wood in 1943 was the first to collect a substantial number of cases of squamous containing carcinoma of the stomach from the literature, of which 9 cases were pure squamous cell carcinomas and 10 were adenoacanthomas, to which he added two squamous cell carcinomas of his own. Boswell and Helwig in 1965 collected 43 cases of such tumors from the literature up to date and added 23 cases of their own. Of 43 cases collected from the literature 18 were pure squamous cell carcinomas and the remaining 25 were mixed with mucin secreting tumors. Of their own 23 cases 12 were pure squamous cell carcinomas and 11 were adenoacanthomas, making 30 cases of pure squamous cell carcinomas and 36 cases of adenoacanthomas. The latest case in the literature is that of Donald (1967) who reported a case of adenoacanthoma of pyloric antrum with extensive squamous metaplasia, totaling 37 cases of adenoacanthomas of the stomach reported in the literature, and our case is probably the 38th of such tumors to be reported.

As regard to the histogenesis of squamous element, Wood (1943) after reviewing clinical and experimental data suggested that direct stimulation to the undifferentiated basal cells of the gastric mucosa is the essential factor in the histogenesis of squamous cell tumors of the pyloric end of the stomach. To support this theory, he quoted experimental works of Stewart and Lorenz (1942) who produced experimentally adenoacanthoma in mice by injection of methylcholanthrene directly in the wall of the stomach whereas squamous metaplasia and heterotopic squamous cells in the human stomach are extremely rare. Donald (1967) supported this theory based on the observation of his own case in which intimate association of glandular and squamous elements in the tumor and transitions of cell types within a single acinar structure, which he thought to indicate dichotomous differentiation of tumor cells. On extensive examinations he failed to find squamous metaplasia in surrounding stomach tissue away from the tumor. Boswell and Helwig (1965), however, suggested that squamous element could only arise in pre-existing squamous epithelium or by
squamous metaplasia in an adenocarcinoma based on the facts that, 1) heterotopic squamous epithelium in the stomach are found in their own material and by Oberling and Wolf (1927), 2) squamous metaplasia is observed at the margin of benign ulcer in their material and 3) squamous metaplasia can be produced experimentally (Futterer 1904, Hare et al. 1952). They dismissed the idea of squamous metaplasia in pre-existing adenocarcinoma by the reason that over one half of the cases are pure squamous cell carcinomas. However, there is no report of normal squamous epithelium at the margin of neoplastic tissue, which would favor the theory of heterotopic or pre-existing squamous metaplasia.

In our case, neoplastic squamous epithelial trabeculae or nests were surrounded by several layers of small round undifferentiated or indifferent type of cells. These cells neither resembled squamous epithelial cell nor columnar glandular epithelial cell, but were reminiscent of the so-called basal reserve cell. It is true that cells at the periphery of the squamous cell carcinoma frequently show basal cell type of appearance and arrangement, but usually they are single layered and frequently tall cuboidal with perpendicular arrangement. The cuffing by several layers of these indifferent basal reserve type of cells may not conclusively indicate the origin of the squamous element directly from the reserve cells but is strongly suggestive of such histogenesis.

The finding that the squamous element occupied the central and superficial part of the tumor and was surrounded by a narrow rim of adenocarcinoma is very interesting. This pattern was also described by Donald (1967), and Martin and Pollosson (1938). The squamous cell containing tumors of the stomach are known to be invariably ulcerated (Boswell and Helwig 1965), and it is interesting to note that ulceration in our case was large but limited only to the area composed of the squamous element, which may be more vulnerable to gastric digestion than adenocarcinoma at the periphery.

Metastatic lesions from adenoacanthomas of the stomach can be either simple or a mixture of both components. Among 37 cases of adenoacanthomas reported in the literature, only 12 cases were specified for the histologic nature of the metastatic lesions. Of these 7 were mixture of glandular and squamous components, 3 were pure adenocarcinomas (Oberling and Wolf 1927, Pasternack 1935, Donald 1967), and 2 were pure squamous cell carcinomas (Nagel 1956, Strassmann 1946). Our case is the fourth case which showed only adenocarcinoma in the metastatic lesion while the primary tumor was predominantly squamous type. These evidence may suggest that squamous component has less tendency of metastasis than glandular one. The common sites of metastases do not differ from that of ordinary adenocarcinoma of the stomach, and the most frequent sites are the regional lymph nodes, omentum, peritoneum, and the liver. In our case, only regional nodes adjacent to the primary tumor had metastases and the liver appeared free from a metastatic lesion at operation.

The duration of the illness prior to treatment ranged from 2 week to 3 years and survival period after the operation ranged from 2 weeks to 14 months in the series of Boswell and Helwig (1965). Our case had onset of symptoms referable to the present illness at 3 months prior to admission. However, the presence of ulcer symptoms at 7 years prior to admission, although they disappeared during last 4 years, gives some suspicion that the tumor might have started 7 years ago. In the histologic sections,
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there was no evidence of previous penetrating ulcer, namely interruption of muscular layer by fibrous scar tissue.

The age incidence of adenocanthoma is said to be younger than that of ordinary adenocarcinoma of the stomach (Boswell and Helwig 1965), and distributed between the 3rd and 9th decade of life with peak incidence at the 6th to 7th decade. The sex incidence had marked male preponderance.

In spite of some of differences from the ordinary adenocarcinomas of the stomach, the clinical course of the adenocanthomas does not differ from ordinary adenocarcinoma, and the most of the patients will die eventually due to the metastatic disease.

REFERENCES


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