Primary adenocancroid of the stomach

By

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Herxheimer (1907) was the first to use the term adenocancroid to name a tumour consisting of both a columnar epithelium with glandular formations and a squamous epithelium showing keratinization. Other names were proposed, such as adenoacanthoma (Pasternack), polymorphous epithelioma (Oberling and Wolf) and adeno-squamous carcinoma (Rabson). Judging from the number of cases published, these tumours are very rare.

Wood (1934) found ten cases in the literature on the subject, and added two more studied by himself.

After a thorough search of the world literature, we found fourteen cases to which we add the present one, observed in the Department of Morbid Anatomy of the Instituto Oswaldo Cruz, from an autopsy done at the Hospital São Francisco de Assis.

The first case of adenocancroid, seems to have been described by Rolleston and Trevors (1905) under the title “A case of columnar-celled carcinoma of the stomach showing squamous celled metaplasia». These authors describe the case of a woman 35 years old. Autopsy showed a tumour with a diameter of approximately 7.5 cm, localized on the pylorus, which developed ulceration, causing perforation of the organ. Microscopical examination of material from the anterior wall of the stomach showed an adenocarcinoma in which the cells tended to a spheroidal form. At the posterior wall, however, according to the author “a remarúable feature was present, namely a further change of the cells of the growth from the spheroidal to the squamous type». At certain points there were typical epithelial pearls. The rest of the stomach (fundus and cardia) did not show tumorous formations.

Lubarsch (1906), examining Lymph nodal metastases of an adenocarcinoma of the stomach, observed clumps of squamous epithelium. Re-examining
primary tumour, localized on the pylorus, he found areas of typical Malpighian epithelium, with spicular cells and keratinization.

Herxheimer (1907) describes the case of a patient who died eight days after an operation. In Khich a tumour the size of a fist was found in the pyloric region, showing on histological examination both glandular and epidermoid elements.

Oberling and Wolf (1927) published the case of a woman who died a few minutes after an exploratory laparotomy. At autopsy, the abdominal organs were entirely covered by viscous reddish masses. «Ces masses aglo-merées, occupent tout le paquet des anses intestinales, elles infiltrent l'épiploon au point d'en former un enorme bloc gelatineux hémorragique du poids de 11kg.» The whole of the pylorus was affected by the growth. Microscopically, glandular formations were seen, either as alveoli or as ducts, limited by columnar cells arranged in one or more layers and «subitement au beau milieu de ces éléments glandulaires nous voyons apparaitre des formations inattendues et totalement differentes de tout le reste. Ce sont des larges boyaux constitutués par des cellules malpighiennes tout a fait tipiques et centrées par des globes épidermiques enormes.» The growth invaded the peritoneum, where it showed an intense mucoid degeneration which characterized the masses mentioned above. It was impossible to find any evidence of transition from the columnar to the epidermoid cells. In the metastases, only the mucoid form of the growth was found. The authors named this growth polymorph epithelioma.

Boedecker (1927) mentions two cases of adenocarcinoid of the stomach. The first case was that of a woman 35 years old who showed an ulcerated tumour situated immediately above the pylorus. Microscopical examination showed formations of squamous epithelium, predominatingly of adenocarcinomatous appearance. This case was the same as that described by Bormann in Henke-Lubarsch's treatise. The second case was a tumour on the lesser curvature of the stomach, in a woman 65 years old, in which both glandular and epidermoid formations were present.

Pasternack (1935) describes the case of a man who was submitted to a gastrectomy and survived four months. The tumour was limited to the pylorus, the rest of the stomach and the oesophagus being normal. Histologically it was predominatingly an epidermoid carcinoma rather than an adenocarcinoma, and whereas in some parts one could see a gradual transition from columnar to squamous epithelium, in other parts the change was sudden and without a clear relation. The tumour measured 9 x 6 x 4 cm. Metastases
on the greater omentum, lymph nodes and pancreas, showed only adeno-
carcinomatous appearance.

Martin and Polosson (1936) described the case of an operation on a
man, in which an ulcerated tumour was removed from the lesser curvature
of the stomach. Microscopical examination showed glandular and epidermoid
formations, the former predominating. There was no evidence of gradual
transition from one to the other.

In the case of Takagi (1937), a man aged 35 years, showed at autopsy
a tumour in the stomach, extending to the pylorus and cardia, with marked
mucoid degeneration, showing as in the case described by Oberling and
Wolf, great viscous masses covering the upper part of the abdomen, and
invading the greater omentum, spleen and pancreas. The description of the
histological appearance is not clear, the presence of epidermoid elements in
the stomach being doubtful. According to the author there was a slight limited
infiltration of the oesophagus, in the lower portion of which the cells were
some Khat disorganized and with hyperchromatic nuclei. It is noted the
reserve with which the author refers to the oesophagus and Scheffler and
Falk are right when they state that the gastric origin of the tumour is
doubtful whenever the oesophagus is involved. Thus Takagi's case must be
considered with reserve, even though Wood accepts it without restrictions.
In this case the only clear reference to the presence of epidermoid elements
is in the metastases (lymph nodes) and these elements are represented by
spicular cells without keratinization. The paper is not illustrated with
drawings or microphotographs.

Scheffler and Falk (1946) described the case of a man 74 years old
with an ulcerated tumour on the lesser curvature, situated approximately 7 cms.
from the cardia. The predominating appearance was of an epidermoid
carcinoma. In other parts the cells were arranged in alveoli.

Hiraiisi (1941) described the case of a man 45 years old with pyloric
stenosis who had a gastro-enterostomy performed. The tumour was localized
on the lesser curvature, immediately above the pylorus and was the size of a
hen's egg. Histological examination showed a predominantly adenocar-
cinomatous appearance with mucoid degeneration at some points and scattered
cells showing incomplete keratinization. In some parts of the tumour there
were clear signs of intra-cellular connections, the cells possessing a somewhat
basophilic cytoplasm and not showing keratinization. The perigastric lym-
ph nodes showed the same picture of the original tumour.
Wood (1943) describes two cases of adenocancroid of the stomach. One was a man, 51 years old, who died some time after a partial gastrectomy. An autopsy was not done. Apparently there were no liver metastases. The tumour was situated on the lesser curvature and measured approximately 5 x 7 x 1 cms., invading all the layers of the stomach. Microscopically it showed an adenocarcinomatous appearance with epidermoid formations. There that of a man who also had a partial gastrectomy. The tumour was composed was no predominance of one appearance over another. The second case was of an ulcer about 4 cms. in diameter, situated immediately above the pylorus, Kith indurated adges and a thickened base. The histological examination shoKed a mixture of glandular and epidermoid elements, not only in the primary tumour but also in the ganglionic metastases. In neither of the two cases was it possible to show a gradual transition from one histological type to another.

Strassman (1946) published the interesting case of a man 85 years old who died of a respiratory infection, in whom, at autopsy neoplastic formations were found, consisting of numerous nodules situated on the stomach, from the pylorus to the cardia. In Strassman’s words: «The case of adenocanthoma reported in this paper is different from those described in the literature. The tumour had not been suspected during life, although at autopsy it was found that large areas of the gastric wall from the pylorus to the cardia were involved in a neoplastic process preceded or accompanied by chronic hypertrophic gastitis. This was predominantly a more or less anaplastic type of adenocarcinoma, infiltrating all layers of the wall. The adenocarcinomatous cells were of an irregular pale polymorphus type with eccentric nuclei. The part of the tumour which consisted of both adenocarcinomatous and squamous cells was limited to a small circumscribed area of the greater curvature near the cardia, covered by squamous epithelium similar to that normally present in the oesophagus. There was no continuation of the squamous epithelium from this region to the cardia.» The metastases in the liver and lymph nodes showed an appearance of a pure epidermoid carcinoma with numerous epithelial pearls. The cardia and the lower portion of the oesophagus Kere normal.

The case observed by ourselves was as follows:

F.A., 54 years old, Brazilian, male, negro. Unfortunately the clinical history was not obtained.

Protocol of autopsy: N° 7915.
Time of death: 10 a.m. 21/4/47. Time of autopsy: 11 a.m. 22/4/47. The body is that of an old man, dark skinned, extremely badly nourished, weighing 45 kilos and measuring 1.63 metres. Pupils equally dilated. Pale conjunctivae. Badly kept teeth. Black curly hair. No external anomalies. No jaundice and no oedema. Abdomen somewhat distended with liquid. On section the fatty and muscular layers are very reduced. The peritoneal cavity contains approximately 500 ccs. of a whitish, slightly turbid fluid. The liver does not reach the costal margin. Intestines free from adhesions except in the middle part of the transverse colon which is adherent to the pyloric portion of the stomach.

Thorax — Precordial space of normal area. Lungs showing firm and limited fibrous adhesions to the walls of the thorax and diaphragm. No fluid on the pleural and pericardial cavities. Heart of small size, the apex being formed by the left ventricle. Superficial vessels especially the L. coronary which stands out markedly, show whitish and thickened walls. The epicardial fat is much reduced. On the anterior surface of the L. ventricle there is a whitish round plaque. The heart cavities are diminished in volume. The endocardium is transparent and shiny. The valves are intact and flexible. The heart muscle is reddish brown without increased connective tissue. The inner lining of the aorta shows raised yellow plaques and occasional furrows with tissue retraction. The circumference of the aortic arch is slightly larger than normal. The lungs are covered with a smooth and shining pleura, except in small areas corresponding to fibrous adhesions. The cut surface is light red in the upper lobes and dark red in the lower lobes, a frothy bloody liquid exuding on compression. No nodules or areas of consolidation of the parenchyma are felt.

Abdomen: spleen greatly diminished in size with considerable thickening of the capsule. The cut surface is light brownish red in colour with the lymphoid and connective tissue clearly distinguished. Liver diminished in size, strongly adherent to the diaphragm. On section on the anterior superior surface there is a firm whitish tissue, distinct from the organ and invading it to a depth of 2 cms. On the inferior surface there are two smaller nodules similar to the first. The cut surface is brown in colour, the lobular structure being apparent. The connective tissue is not increased. The gall bladder is contracted containing a small quantity of bile. Stomach diminished in size showing when opened a raised flattened tumour formation, clearly limited, oval in shape situated in the pyloric region and measuring 3 x 2 x 2 cms. The stomach walls in this region are thickened by neoplastic tissue which is whitish and firm like bacon. The central part of the transverse colon is
adherent to the pyloric region of the stomach. The walls of the intestines at this level are thickened by firm and white neoplastic tissue. The mucosa has a normal appearance. Ileo-caecal appendix shortened and twisted with thickened and indurated walls which considerably diminish the lumen of the organ. Pancreas, adrenals and small intestine do not show any macroscopic alterations worthy of note.

Kidneys diminished in size, the R. measuring 8 x 5 x 2.5 cms. and the L. 10 x 3.5 x 2.5 cms. The capsule strips with ease leaving a clean surface. The cut surface is light red in colour and the cortex is of normal thickness.

Prostate, bladder and seminal vesicles do not show any alterations worthy of note.

The cranium was not examined.

Microscopical study.

Stomach: in the pyloric region we found an epithelial type of blastoma which replaced the tissue of the organ and protruded into the interior of the stomach. In this tumour there distinct histological appearances were recognizable:

1) of an adenoma destruens
2) of an adenocarcinoma
3) of an epidermoid carcinoma.

The parts of the tumour with the appearances of an adenoma destruens and of an adenocarcinoma were situated in the internal parts of the stomach replacing the mucous and sub-mucous as well the muscular layer. The part with the epidermoid appearance was situated mainly in the external muscular layer and outwards in the serous coat (Fig. 1). The epithelium which constituted both the adenoma destruens and the adeno carcinoma was composed of high columnar cells with a tendency to form more than one layer (Fig. 5). The height of these cells was fairly variable and some of them were cuboid. The nucleus, very rich in chromatin, usually occupied the inferior part of the cell and was in most cases ovoid. Mitotic figures were found but in small numbers. In many parts there was a gradual transition from columnar to squamous cells and the adenocarcinomatous appearance gradually changed to epidermoid (Fig. 5). The squamous epithelium in the tumour was formed by cells showing a marked degree of polymorphism (Fig. 1). They were arranged in groups of many cells, though isolated cells were not uncommon, some of them appearing to possess
spicules (Fig 3). There was occasional keratinization of cells (Fig. 3) and what seemed to be epithelial pearls were observed in some parts (Fig. 1). The nuclei varied in shape and size. Chromation content was considerable and the nucleoli were prominent. In the epidermoid carcinoma part mitotic figures were frequent. The stroma was infiltrated by numerous mononuclear cells. The liver showed extensive metastases and large areas of necrosis. In this organ the adenocarcinomatous appearance was predominant (Fig. 4) epidermoid elements being found, however, in isolated spots. The liver cells adjacent to the tumour were long and atrophied. Lymph nodes at the hilum were infiltrated by blastomatous cells with a predominance of the adenocarcinomatous appearance. The part of the large intestine near the stomach was incised by the growth in the serous and muscular layers. The lungs showed oedema, hyperaemia, anthracosis, broncho-pneumonia, emphysema and atelectasis. No metastases. Heart — arteriosclerosis of the coronary vessels. No metastases. Spleen — atrophied and fibrosed. Hyperaemia Chronic fibrous peri-splenitis. No metastases. Aorta — arteriosclerosis. Kidneys — chronic glomerular nephritis (slight). Diagnosis: adenocarcinoid of the stomach. Metastases in the liver, regional lymph-nodes, appendix, transverse colon, peritoneum and diaphragm. Arteriosclerosis of the coronary vessels and aorta. Glomerular nephritis. Bronchopneumonia. Oedema and hyperaemia of the lungs. Atrophy and fibrosis of the spleen. Chronic fibrous peri-splenitis. Bilateral chronic fibrous pleurisy. Cachexia.

Discussion

Of the fifteen cases reviewed in this paper including the one observed by ourselves, four were females (Rolleston and Trevors, Oberling and Wolf, and Boedecker two.) and ten were males (Pasternack, Martim and Polosson, Wood two, Hiraisi, Takagi, Scheffler and Falk, Strassman and our own). Herxheimer and Lubarsch do not give the sex or age of their cases. The age varied between 35 and 85 years. In ten cases the adenocarcinomatous appearance was predominant in the primary tumour (Rolleston and Trevors, Lubarsch, Herxheimer, Oberling and Wolf, Martim and Polosson, Boedecker, one Hiraisi, Takagi, Strassman and our own); in two cases the epidermoid (Pasternack and Scheffler and Falk); and in three an equal mixture of both. (Boedecker one and Wood two.) The histological picture in the metastases was mixed in seven cases (Lubarsch, Wood
two, Hiraisi, Takagi, Scheffler and Falk and our own). adenocarcinomatous in only (Oberling and Wolf and Pasternack), and epidermoid in only one (Strassman). Metastases were not present in one case (Herxheimer) and in four they were not mentioned by the authors (Rolleston and Trevors, Boedecker two and Martim and Polosson) The commonest localization was the pylorus, occurring in ten cases (Rolleston and Trevors, Lubarsch, Herxheimer, Oberling and Wolf, Boedecker two, Pasternack, Wood two and our own. In three cases the tumour was situated on the lesser curva-ture (Martim and Polosson, Hiraiso and Scheffler and Falk); and in two cases it extended from the pylorus to the cardia. (Takagi and Strassman). In three tumours it was possible to find a gradual transition between the various histological types present.

The presence of stratified squamous epithelium in a primary blastoma of the stomach may be due to heterotopia, although in Strassman’s case normal squamous epithelium was found. This interpretation is more difficult to accept when the tumour is not a pure epidermoid carcinoma but an adenocarcinoid. In Herxheimer’s opinion (1907) the original cells would be embryonic, undifferentiated ones abnormally situated in the gastric mucosa and which, at a certain moment under the action of an undetermined carcinogetic agent, would start to proliferate irregularly, differentiating in both directions (squamous and columnar cells) and giving rise to the tumour.

The old conception of strict cellular specificity according to which the cell during its whole life would always follow the same morpho-physiological pattern is being gradually abandoned.

The numerous examples such as the epidermoid transformation of bronchial mucosa in cases of chronic inflammation, the ossification of cartilages, the gastric metaplasia of the jejunal mucosa after gastro-enterostomy etc., reduced the force of the old ideas. However, in the stomach of man, until now, it was not possible to observe noncancerous epidermoid metaplasia unless Strassman’s case is considered as such. He admits that it may be the case of a metaplasia in virtue of the patient’s hypertrophic gastritis, but he does not entirely discards the hypothesis of a congenital heterotopia.

Futterer (1904) was the first to prove experimentally, working on rabbits, the possibility of epidermoid metaplasia of the gastric mucosa, resecting a piece of the mucosa of the posterior wall of the stomach and injecting pyrogallic acid to delay cicatrization. He was able to observe typical malpighian formations in the wound. Refuting the hypothesis of a heterotopia he argues that if there were embryonic remains, these would
have been removed at the operation and no stratified squamous epithelium would appear at the site. Futterer believes there is a transformation of the columnar cells of the stomach into squamous cells. Other workers have not been as fortunate as Futterer when trying to produce epidermoid metaplasia in the gastric mucosa, their experiments almost always failing. Stewart and Lorenz (1942) were able, however, to obtain adenocarcinoid in four cases in the pyloric region (glandular) of the stomachs of rats using ethylcholantrene as the carcinogenic agent.

Rolleston and Trevors favour the hypothesis of a metaplasia because according to them the malpighian appearance develops in the growing tumour and not in the gastric mucosa.

Krompecher (1924), also favoured metaplasia, but whereas the majority of the other authors accept a regressive or anaplastic metaplasia in which there would be initially an unordered proliferation of the columnar cells reaching as ontogenetically lower stage, practically embryonic, from which a new differentiation would start which could be towards the original epithelium or to some other type, Khich in this case would be stratified squamous epithelium; he admits that in the case of organs lined by columnar cells one layer of nonembryonic basal cells demonstrable with difficulty and composed of scattered multiplying cells which normally give rise to normal columnar epithelium in which under the action of an undetermined carcinogenic agent could give rise to neoplastic epidermoid formatinos. Momigliano says he found cells in the uteri of mice similar to those described by Krompecher and by the action of irritating agents he brought about the proliferation of these cells and their differentiation either into squamous or columnar epithelium.

Penna de Azevedo e Villela (1936) described a case of pure epidermoid carcinoma of the stomach. To these authors the hypothesis of metaplasia is the more acceptable. According to Delarue (1947) «ainsi le type morphologique d’un cancer, et l’aspect des éléments cellulaires qui le constituent paraissent dependre dans une large mesure, non pas des cellules d’origines, en vertue d’une specificité transmite, mais de l’adaptation de ces elements aux conditions physico-chimiques dans lesquelles ils se trouvent, et aux exigences des metabolismes locaux. Si la morphologie des tumeurs malignes se rapproche parfois de tres prés de celle de leur tissu matriciel, c’est parce que les conditions d’adaptation locale sont semblables à ce qu’elles etaient pour les elements normaux. On peut admettre que, inversement, les structures paradoxales «heteromorphe» par rapport au milieu dans lequel prend
naissance le cancer sont dues à l’apparition en même temps que le processus cancéreux, de conditions «fonctionnelles», nouvelles, différentes de celles du tissu matriciel pour les expliquer, il n’est nullement besoin d’ invoquer une hétérotopie embryonnaire."

To resume, the hypothesis of metaplasia seems to be at present the one which best explains all the factors involved in the phenomenon. Both experimental and theoretical evidence speaks in its favour. It remains to decide whether it is a regressive metaplasia or whether the changes occur according to Krompecher’s interpretation.

SUMMARY

The authors report a case of primary blastoma of the stomach showing side by side, structures of adenoma desruens and adenocarcinoma that of an epidermoid carcinoma. The tumour corresponded to the type described in the literature as an adenocarcinoid and showed metastases in the liver, regional lymph nodes, appendix, transverse colon, peritoneum and diaphragm. They review the literature on the subject and discuss the origin of these tumours.