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Anatomic and pathological aspects in the pathology of malignant gastric tumors

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Abstract

Efforts in perfecting the methods of early diagnosis, in trying to assess premalignant conditions, and in properly staging malignant tumors are still in trend. The geographic area around Timişoara (Banat Region) is situated on the first place in the country as far as the gastric location of cancer is concerned. The authors aimed to deal with the initial stage in the development of gastric cancer, a stage which has been oncologically termed "precancerous damage", and with the neoplastic invasion of the gastric wall. The present paper is based on the 1995–2005 statistics of the II[nd] Surgical Department of the Timişoara County Hospital, the study group consisting of 802 patients admitted for gastric disorders, 522 of which being later diagnosed with a tumoral pathology. Routine morphological tests were conducted on biopsy pieces dye stained with Hematoxylin–Eosin, standard technique, the van Gieson trichromic staining, the Giemsa staining, the AA–PAS staining and the immunoreaction methods. The age for gastric tumoral pathology ranged between 36–88 years in females, and 31–87 years in males. Most gastric carcinomas are adenocarcinoma, 404 (90%) cases – could be classified as follows: 167 cases of tubular adenocarcinoma; 39 cases of papillary adenocarcinoma; 24 cases of mucinous or colloid adenocarcinoma; 141 "signet ring"-cell carcinoma; 33 cases of undifferentiated carcinoma. Currently there is an increase of the incidence of the "diffuse"-type in women and at younger ages. Attention should be given to precancerous conditions; there was a large number of premalignant or potentially malignant gastric damage: atrophic chronic gastritis (54 cases), intestinal metaplasia (104 cases), and gastric dysplasia (104 cases).

Keywords: gastric tumors, premalignant conditions.

Introduction

Gastric cancer is one of the commonest forms of human neoplasia, constituting a real public health concern. Tumor pathology involves wide and complex research, especially when we consider that in most cases diagnosis is made in advanced stages of loco-regional development and, consequently, the results of therapy are fairly discouraging. Therefore, the early diagnosis of malignant damage is essential for a successful surgical treatment and implicitly for the survival of the patients.

The western part of Romania is a region with a very high incidence of gastric cancer, this type of malignant disorder holding one of the top positions within neoplastic disorders. At the same time, epidemiologic studies have revealed that this geographic area is situated on the first place in the country as far as the gastric location of cancer is concerned. All the above point to the late diagnosis, which involves the general practitioner, the specialist in internal medicine, the oncologist, the endoscopist and the surgeon. These considerations may well justify the authors' efforts in perfecting the methods of early diagnosis, in trying to assess premalignant conditions, and in properly staging malignant tumors. These are the arguments that determined the authors to deal with the initial stage in the development of gastric cancer, a stage which has been oncologically termed "precancerous damage", and with the neoplastic invasion of the gastric wall.

Material and methods

Based on the 1995–2005 statistics of the II[nd] Surgical Department of the Timişoara County Hospital, the present study aims at assessing the significance of precancerous and cancerous damage, relying on the cooperation between the specialist in internal medicine, endoscopist, surgeon and anatomo-pathologist, starting from the premises that this disorder cannot be diagnosed, treated and monitored by a single specialist.

The study group consisted of 802 patients admitted for gastric disorders, 522 of which being later diagnosed with a tumoral pathology. The gender distribution was the following: 329 (63%) men and 193 (37%) women, with a male/female ratio of 1.7. The tumoral pathology was in its turn grouped as follows:

- Benign tumoral pathology – 73 (14%) cases, out of which 43 (58.9%) cases were women and the rest, 30 (42.1%) cases were men, with a male/female ratio of 0.7;
- Malignant tumoral pathology – 449 (86%) cases, out of which 150 (33.4%) women and 299 (66.6%) were men, with a male/female ratio of 1.9.

The study material consisted of anatomical pieces resulting from gastric surgery and biopsy material obtained by endoscopy. Routine morphological tests were conducted on biopsy pieces dye stained with hematoxylin-eosin, standard technique, the van Gieson trichromic staining, the Giemsa staining, the AA–PAS

staining and the immunoreaction methods. The quality of the biopsy material and its proper processing are the decisive premises in the histopathological diagnosis of gastric disorders.

Results

Most gastric carcinomas are adenocarcinomas, but a comprehensive classification should also include rare forms, such as adenosquamous or epidermoid carcinomas (Figures 1 and 2).

Particular forms of gastric carcinoma were represented by three colloid and five anaplastic-cell carcinoma (Figures 3 and 4).

"Intestinal"-type carcinoma is present and characterized in Figures 5 and 6. "Signet ring" cell gastric carcinoma is shown in the Figures 7–9.

Eight cases comprise an "unclassifiable" carcinoma, with intermediate aspect (Figure 10).

There were 244 cases in our study group with advanced form of gastric cancer (Figure 11).

Discussions

The WHO classification includes four types of carcinoma: papillary, tubular, mucinous and with "signet ring" cells (Figures 1 and 2).

Lauren's classification of 1965 was influenced by works published by Joroi on the different histogenesis of the types of carcinoma [1].

This classification is confirmed by the high incidence of gastric tumors developing on the gastric mucosa with intestinal metaplasia and divides gastric carcinoma into two morphologically different types: "intestinal" and "diffuse". In spite of this, 12% of all gastric tumors are unclassifiable, having particular morphological aspects [2].

Lauren's classification that we have used in the present study makes the connection between the histological forms and the different geographical distribution of gastric cancer, accounting for existing variations both worldwide and regionally within the same country. Adenocarcinoma is predominant in areas with a high incidence of gastric cancers, being more common in men and at older ages.

Adenocarcinoma represented 90% of the total number of cases – i.e., 404 cases. These 404 cases were further subdivided as follows: 286 (70.8%) were "intestinal"-type carcinoma; 110 (27.2%) were "diffuse"-type carcinoma; eight (2%) were particular forms of carcinoma – colloid (the association between "intestinal" and "diffuse" types), and anaplastic-cell carcinoma (Figures 3 and 4).

Colloid or mucoid carcinoma is a type rarely found in the stomach. It is characterized by large quantities of extracellular mucins and it is very well outlined. It may be a variant of "intestinal" carcinoma, but with a much better prognosis. The association between the "intestinal" and "diffuse" types was observed in a case of advanced carcinoma.

According to Lauren's classification, the carcinoma presented in the current study belonged to the following types:

- intestinal-type carcinoma – 286 cases;
- diffuse-type carcinoma – 110 cases;
- unclassifiable forms – eight cases.

"Intestinal"-type carcinoma are characterized by the presence of pseudoglandular carcinomatous structures made up of potentially malignant cells, disposed in one or more layers, with endoluminal papillary projections; tumoral cells are generally well or moderately differentiated, cuboid or columnar.

When mucin secretion is present, it is mainly extracellular, tumoral cells rarely containing inflammatory infiltrate formed of lymphocytes, plasmocytes and eosinophils. In some cases, when tumoral necrosis is important, eosinophilia is also elevated, possibly as an allergic reaction to its presence (Figures 5 and 6).

"Diffuse"-type carcinoma consists of rather small round or oval cells containing acid or neutral mucins; small amounts of mucin can also be present in the interstice. The nuclei are as a rule pushed to the periphery of the cell. Mitosis is much lower than in "intestinal"-type carcinoma, which are apparently better differentiated.

Characteristically, at the level of the mucosa, these cells do not distort glandular structures, but infiltrate the lamina propria, pushing them aside. The tumoral stroma is more intensely collagenized and inflammatory infiltrate is less apparent than in "intestinal"-type carcinoma. In some cases, "signet ring" cells were noted in small cavities, floating in a mass of mucus, or in other cases associated with markedly anaplastic cells without any secretory character (Figures 7–9).

The third type of the above classification is represented by "unclassifiable" carcinoma which is intermediate aspects of the previous two types or a mixture of them (Figure 10).

Fragments of non-tumoral mucosa were also examined. Thus, within the various types of carcinoma, infection with *Helicobacter pylori* was more common in the "diffuse"-type carcinoma – 76 cases out of the 110 cases (69%), versus the "intestinal"-type carcinoma – 96 cases out of the 286 cases (33%).

As for the morphological aspects of the mucosa where the two types of carcinoma mentioned by Lauren develop, the aspects found were totally different. Thus, "intestinal"-type adenocarcinoma was associated with atrophic gastritis, with intestinal metaplasia and dysplasia, while "diffuse"-type carcinoma was associated with non-atrophic gastritis, without metaplastic damage.

More than half of the patients of the study group had one or the other of these premalignant conditions (54 cases with atrophic gastritis, 104 cases with intestinal metaplasia, and 104 cases with dysplasia).

Another notable difference was represented by the higher incidence of the "intestinal"-type carcinoma in men – 164 cases, ages between 61–71, versus the "diffuse"-type carcinoma more common in women – 76 cases, ages ranging between the years 50–56.

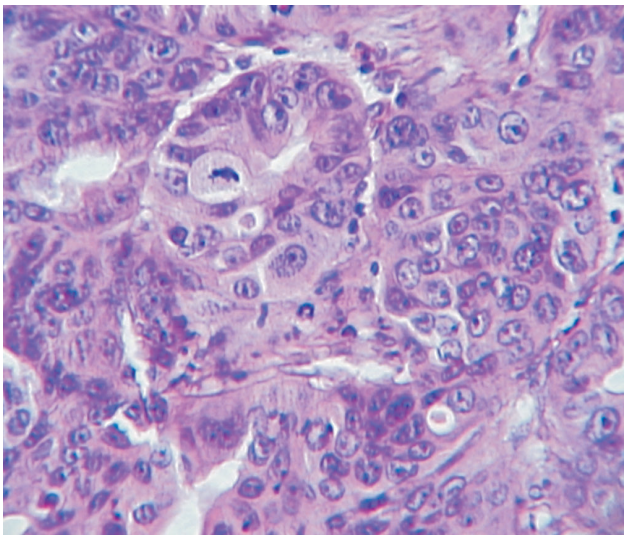

Figure 1 – *Gastric adenocarcinoma*
(HE staining, ×400)

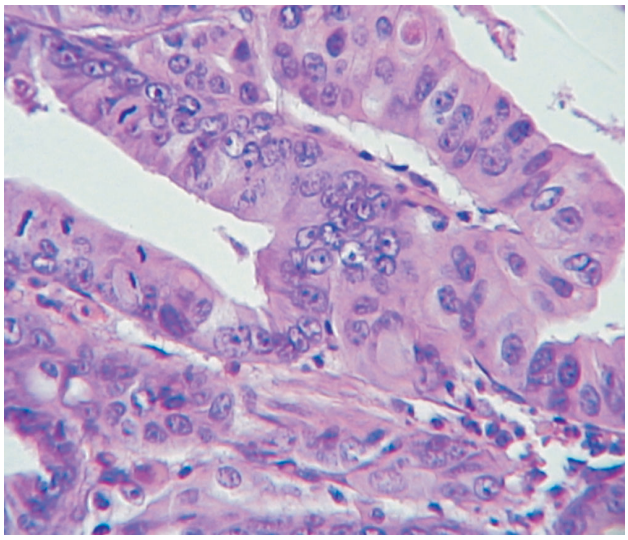

Figure 2 – *Gastric adenocarcinoma*
(HE staining, ×400)

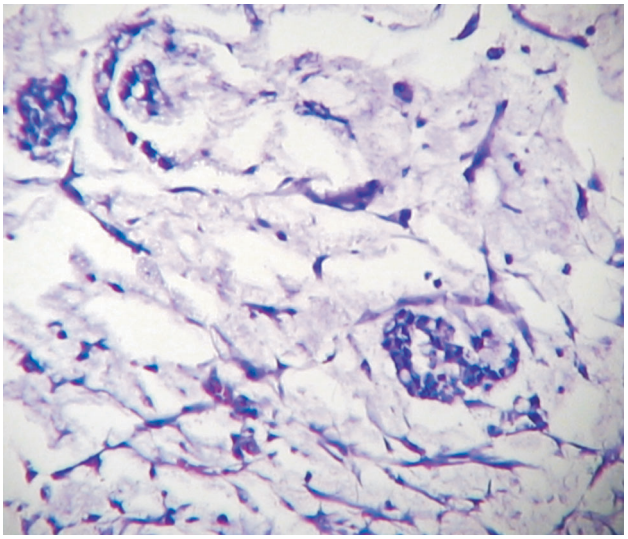

Figure 3 – *Colloid carcinoma*
(HE staining, ×100)

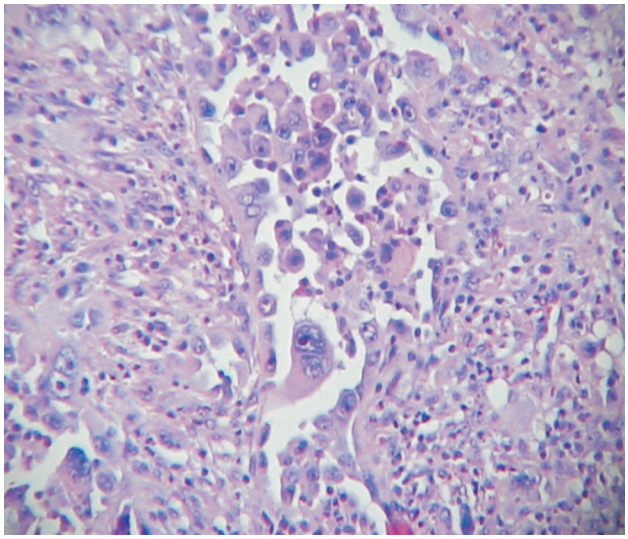

Figure 4 – *Anaplastic gastric carcinoma with pleomorphic giant cells*

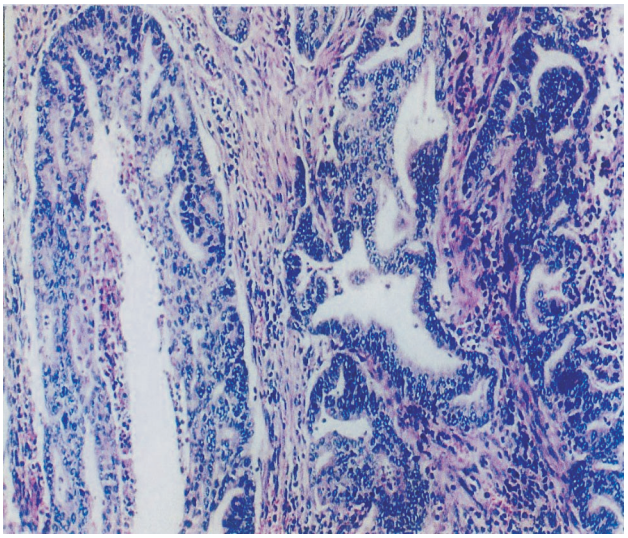

Figure 5 – *Intestinal-type gastric carcinoma*
(HE staining)

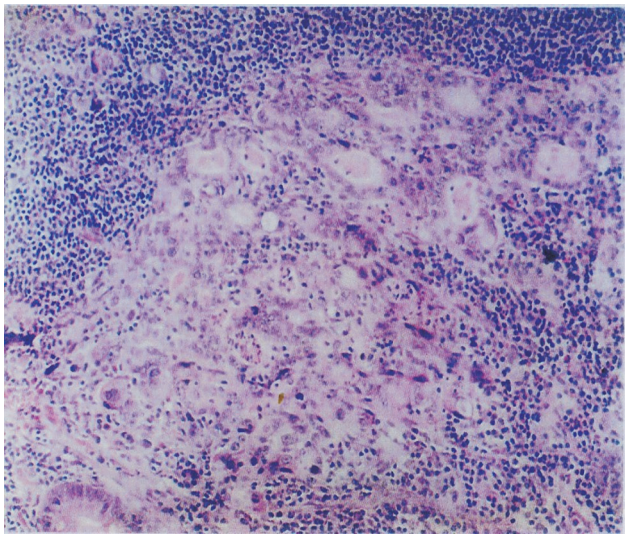

Figure 6 – *Intestinal-type gastric carcinoma*
(lymphoid stroma)

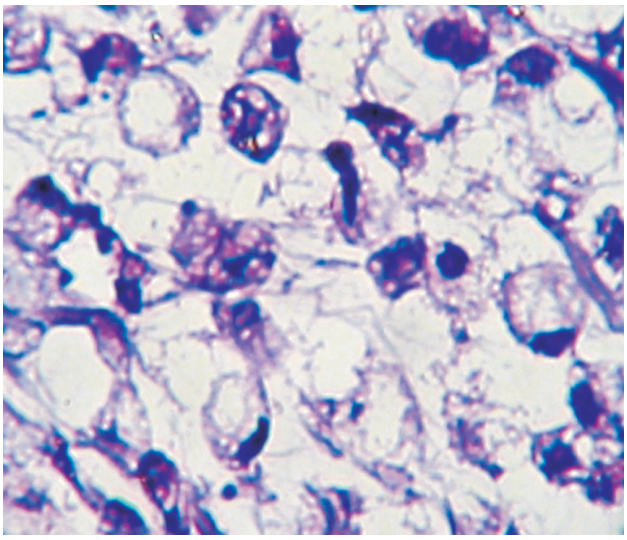

Figure 7 – ***Signet ring cell gastric carcinoma (HE staining)***

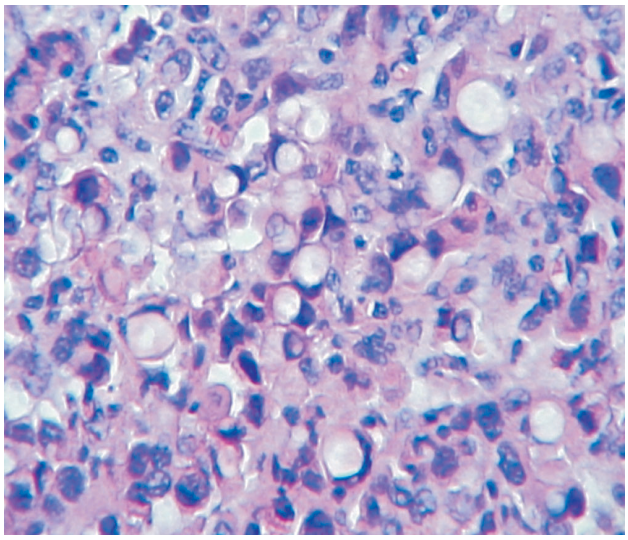

Figure 8 – ***Signet ring cell gastric carcinoma (HE staining)***

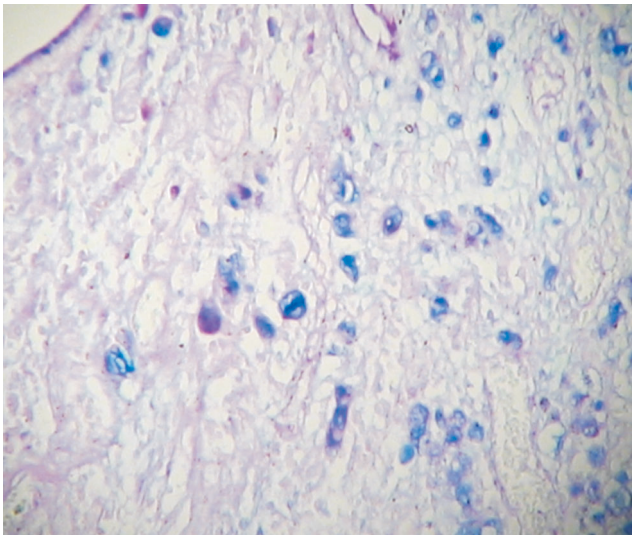

Figure 9 – ***Signet ring cell gastric carcinoma (AA–PAS staining)***

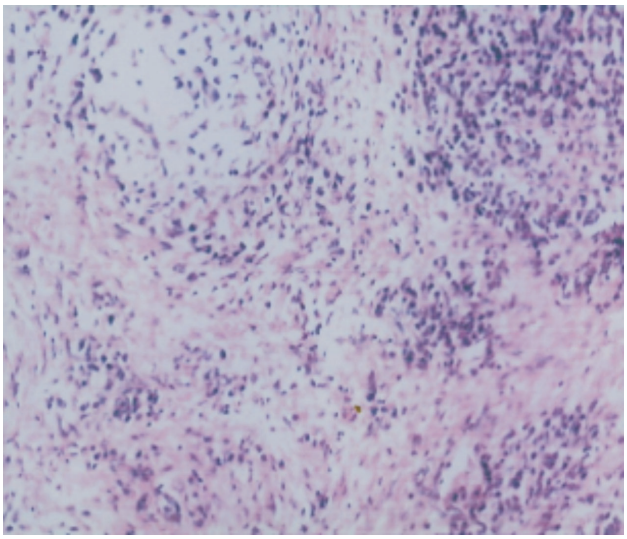

Figure 10 – ***Unclassifiable gastric carcinoma (signet ring cells)***

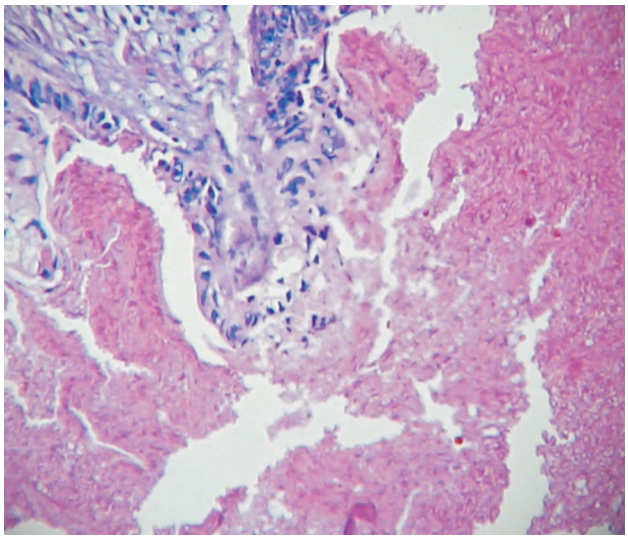

Figure 11 – ***Adenocarcinoma with extensive tumoral necrosis (HE staining)***

The Japanese Society of Gastroenterology classified carcinoma from a prognostic-developing point of view into superficial ("early gastric cancer"), defined as the tumor limited to the gastric mucosa and submucosa, with or without metastasis in the perigastric lymph nodes, and an advanced form of gastric carcinoma [3].

The definition is entirely based on the degree of invasion and not on the size and shape of the tumor. Final diagnosis is established only following histological exam of the resected stomach fragments.

The penetration of the muscular mucosa is a criterion for subdividing the superficial carcinoma into intramucous and submucous carcinoma. While in the majority of countries this diagnosis is quite rare (4–6.2% of carcinoma), in Japan, due to their screening programmes and sophisticated diagnostic methods, the ratio of the patients with superficial carcinoma found in stomach resections raises to 50% [4–9].

There were 37 cases of superficial carcinoma in our study group, with a significant predominance in males versus females (28 *vs.* nine cases). Any malignant tumor that has invaded the muscular layer is considered an advanced form of gastric cancer (Figure 11).

Conclusions

Although gastric carcinoma is more common in men, currently we witness an increase of the incidence of the "diffuse"-type in women and at younger ages.

The total number of adenocarcinoma – 404 (90%) cases – could be classified as follows: 167 cases of tubular adenocarcinoma; 39 cases of papillary adenocarcinoma; 24 cases of mucinous or colloid adenocarcinoma; 141 "signet ring"-cell carcinoma; 33 cases of undifferentiated carcinoma.

Tumors presented variable degrees of differentiation, most of them being well-differentiated (269 cases) or moderately differentiated (135 cases).

The degree of tumoral invasion differed from case to case:

- in 16 cases, tumor proliferation infiltrated strictly the mucosa, without evidence of muscular mucosa invasion;
- in 47 cases, both the mucosa and the submucosa were infiltrated, without muscular invasion (superficial carcinoma);
- in 234 cases, there was a total invasion of the gastric wall;
- in the remaining cases, there were no sufficient elements to assess the degree of invasion.

Well- or moderately-differentiated tubular and papillary adenocarcinoma presented no diagnostic difficulty. There were, however, some diagnostic difficulties in the cases of some slightly differentiated or anaplastic carcinoma. In some of these cases, the scarcity or the absence of certain glandular structures, as well as the aspect of the unrounded tumoral cells, with little cytoplasm, irregular, vesicular nuclei, with obvious nucleolus or gross chromatin posed certain problems of differential diagnosis with lymphomatous infiltrates.

As for the onset age groups, tumoral pathology may occur at any age; it becomes more frequent with age. In our study group, there was an increased incidence in the 61–70 age groups.

Similar to ulcer pathology, which the authors studied in parallel, the number of cases decreased in the last decade. During 1995–2000, gastric tumoral pathology was represented by 203 cases in males and 97 cases in females, while in 2000–2005, the number of cases dropped to 126 cases in males and 96 cases in females.

The age for gastric tumoral pathology ranged between 36–88 years in females, and 31–87 years in males.

As for the distribution of the cases according to the factors of aggression on the gastric mucosa, utmost attention should be given to precancerous conditions. There was a large number of premalignant or potentially malignant gastric damage: atrophic chronic gastritis (54 cases), intestinal metaplasia (104 cases), gastric dysplasia (104 cases).

Analyzing deductively two periods of time (1995–2000 and 2000–2005), it is obvious that a lot of progress has been made concerning both precocious and certainty clinical diagnosis, although gastroendoscopy has been widely used mostly in the second period.

The assessment of the interval between the apparent clinical onset and the first medical check-up shows an average delay of patients going to medical check-ups of 3–17 months. This delay shows the inefficiency of public sanitary measures, also pointing to the degree of interest, culture and concern of the population for their health.

The fact that 81.9% of gastric cancer patients have to be treated surgically is due to diagnosis in stages III or IV, while postoperative success in also heavily influenced by our current possibilities for surgical treatment.

Among the most important incriminating factors that help establish the prognosis for patients suffering from gastric cancer we could mention the following:

- the gastric neoplasm stage, involving an immediate practice concerning the necessity of precocious sidetrack;
- the anatomopathological aspect;
- the ganglionary metastasis.

Gastric cancer will remain a severe illness with fatal prognosis and this is due to its metastasizing character. In our country, the illness is still diagnosed in its advanced stages, in most of the cases the stage being inoperable or impossible subject to curative radical surgery, mainly because of the fact that hospitals are not equipped with a lath for active endoscopic tracing.

This information shows, once again, the necessity for some national programs of gastric cancer screening. Patients incidentally diagnosed with cancer in early stages did not suffer any relapse, prophylaxis remaining the best cure in the cases of premalignant conditions.

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