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Original Research Paper

General Surgery

HEMORRHAGIC ULCERATED STOMACH CANCER IN A PATIENT WITH PERNICIOUS ANEMIA. A CASE REPORTS.

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ABSTRACT Stomach cancer is one of the most common tumors, often detected in later stages as patients remain asymptomatic until later stages with black stools, accompanied by bodily weakness.
Pernicious anemia. a known cause of vitamin B12 deficiency, is a classic risk factor for stomach cancer.
Patients with PA usually present with megaloblastic anemia and peripheral neuropathy; however, they may also present with nonspecific symptoms, such gastrointestinal hemorrhage with hemodynamic changes. A 73-year-old man presents in the emergency room of the hospital in Lushnja, Albania, with abdominal pain, black stools, accompanied by bodily weakness.
Complaints have started for several weeks, where the pain is constantly aggravated, until it forced him to appear in the emergency department of Lushnja Hospital.
The patient complains of burning sensation in the chest, decreased appetite, physical weakness, and has lost weight 14 kg in the last 3 months, accompanied by nervous disorders.
Up to the moment of hospitalization did not refer for nausea, vomiting, dysphagia, without a history of gastrointestinal disease.
Initial laboratory work revealed severe B12 deficiency, pancytopenia, by the endoscope that revealed a mass of gastric fundus important for adenocarcinoma on biopsy.

KEYWORDS : Pernicious anemia, melena, total gastrectomy, pulmonary embolism

INTRODUCTION:

In 2012, with 1 million new cases of stomach cancer, it was estimated (6.8% of the total) as the fifth most common malignant pathology in the world, after lung, breast, colorectal and prostate cancer [1], and the age group with expressed is age 50-70 years [2], and very rarely under the age of 30 years; grows rapidly and steadily and progressively with age, reaching a peak in the older age groups [3].

The important risk factors of the causes of gastric cancer are *H. pylori*, obesity, smoking, red meat, alcohol, and low socioeconomic status [4].

Pernicious *anemia* is a classic *risk factor* for the development of *primary gastric cancer*, but is uncommonly seen in clinical practice. [5].

Although not common, pernicious anemia has been identified as a risk factor for gastric cancer. Pernicious anemia is defined as a condition characterized by the destruction of intrinsic factor of an autoimmune nature or the destruction of cells in the body of the stomach, where the parietal cells of the fundus that produce intrinsic factor. Consequently, intrinsic factor which plays a key role in the absorption and transport of vitamin B12, where it is already known, its deficiency leads to megaloblastic anemia [6].

Some studies show that patients with pernicious anemia are at high risk or probability of developing stomach cancer [7].

Atrophy and chronic inflammation of the gastric mucosa are thought to significantly increase the chance of developing neoplastic gastric lesions.

In addition to these megaloblastic anemia and low levels of vitamin B12, these patients may present with abdominal complaints, weight loss, pernicious anemia and its association with gastric cancer.

Case presentation: A 73-year-old man presents in the emergency room of the hospital in Lushnja, Albania, with abdominal pain, black stools, accompanied by bodily weakness.

Complaints have started for several weeks, where the pain is constantly aggravated, until it forced him to appear in the emergency department of Lushnja Hospital.

The patient complains of burning sensation in the chest, decreased appetite, physical weakness, and has lost weight 14 kg in the last 3 months, accompanied by nervous disorders.

Up to the moment of hospitalization did not refer for nausea, vomiting, dysphagia, without a history of gastrointestinal disease.

The patient has been a smoker for 40 years, and a regular user of alcohol, sometimes in excess and unaccompanied by quality food, also the patient for 45 years has worked hard physical work with extended hours (tractor driver).

The patient is a resident of a known endemic area of thalassemia, but he and his family had no obvious signs of diseases.

On physical examination the patient appears normal, with vulnerable hemodynamics with moderate hypotension (SBP - 95 mmHg; FC -110 beats per minute).

Laboratory tests shown; significant anemia with RBC 2.8 x10^6 /ml *(normal value 4.7 - 6.1 x10^6/ml)*; Hb - 6.9 g/dL *(normal value 13.3 – 16.2 g/dL);* Hct - 22% *(normal value 38.8 – 46.4%);* WBC 8.7 x10^3/μL *(normal value - 4.8 -10.8 x10^3/μL);* PLT 110 x x10^3/μL *(normal value 165 – 415 x10^3/μL);*

The treatment: after initial and emergent treatment with Blood transfusions (2 + 2 + 2 units), PNF 8 units, human albumin 3 x 200ml, the patient received perfusions with isotonic solutions in moderate amounts accompanied by PPI (pantoprazole 40 mg twice daily).

The general condition of the patient began to stabilize, with

hemodynamic stability and no clinical data of abdominal pain, which gave us time for more in-depth examinations to make the diagnosis.

During laboratory tests we had these findings improvement of blood analysis, and other tests were almost in the norm as follow [RBC 3.6 x10^6/ml *(normal value 4.7 - 6.1 x10^6/ml)*; Hb - 9.9 g/dL *(normal value 13.3 – 16.2 g/dL);* Hct - 29% *(normal value 38.8 – 46.4%);* WBC 10.7 x10^3/μL *(normal value - 4.8 -10.8 x10^3/μL);* PLT 195 x x10^3/μL *(normal value 165 – 415 x10^3 /μL);* Blood Urea Nitrogen (BUN) = Azotemia 21.40 mg/dl *(normal value 0 - 50 mg/dl);* Creatinine 0.86 mg/dl *(normal value 0.57 - 1.11 mg/dl);* Sober glycemia 156.11 mg/dl *(normal value 74 – 110 mg/dl);* Calcium (Ca in the blood).7.83 mg/dl *(normal value 8.4 - 10.2 mg/dl); Total* Bilirubin 1.1 mg/dl *(normal value 0 - 1.2 mg/dl);* ALT (SGPT) 44.00 U/L *(normal value < 55 U/L);* AST (SGOT) - 42.00 U/L *(normal value < 42 U/L),* the value D-dimer is 370 ng/mL *(normal value < 250 ng/mL).*

It is worth noting low values of vitamin B12, 138 pg/mL *(normal value 213 - 816 pg/mL);* the iron deficiency 28 pg/mL *(normal value 60-158 mg / dL),* with ferritinemi 11 pg/mL *(normal value 11-307 ng/mL);* total Protein 5.2 g/dL *(normal value 6.1 – 7.9 g/dL),* for this the patient was administered vitamin B12 i/v and iron, in the following doses: Cyanocobalamin 1000mg / mL x1 dose; Iron gluconate i/v, 250 mg x 2 dose, Calcium gluconate 10%-10ml x 3 i/v.

Symptoms improved and the patient was started with Pantoprazole 40 mg twice daily. She continued to take vitamin B12 iv and iron supplements.

The Abdominal Ct scanner the results were controversial, it shows thickening of nonspecific gastric plaques in the fundus of the stomach, so we performed Esophagogastroduodenoscopy (EGD) for further evaluation. (fig. 1).

The results showed moderate esophagus and red mucosa in the gastro-esophageal junction, a deep ulcer is evident, at the level of in the minor curvature, consequently we received many ulcer biopsies to evaluate for malignancy and biopsy to assess if there is colonization by Helicobacter pylori, Immunohistochemistry results for H. pylori were positive.

Due to the size of the tumor, appearance, ulcerations and erosions with hemorrhage, malignant formation was suspected. (fig. 1)

Microscopically, the antral mucosa shows chronic gastritis, and in histopathology and immunofluorescence confirm the diagnosis of adenocarcinoma.

The Abdominal MRI with i/v contrast, reveals a localized but advanced mass, associated with regional lymphadenopathy. His final diagnosis is Stage III gastric adenocarcinoma, and the treatment may include the following possibility Surgery (total or subtotal gastrectomy) followed by chemoradiation therapy. (fig. 3)

The patient is transferred to the Surgery ward, in these conditions after the patient is proposed intervention, which he accepts, where and in the meantime continues with the preparations for the intervention. The patient was operated on, and was performed a total gastrectomy (involves removing your whole stomach, nearby lymph nodes, and parts of your esophagus and small intestine), esophagojejunostomy (with a Roux-en-Y configuration) creation of end-to-end esophagojejunostomy and side-to-end jejunoduodenostomy.

Good postoperative condition, the patient woke up well, supported anesthesia and surgery well, during the surgery was used Intermittent pneumatic compression (IPC) devices, we had minimal leakage from the drains. He received postoperative therapy as follow (Antibiotic prophylaxis, perfusions, 2 units of blood iso-group iso-rhesus, 4 units of PNF, 3 x 100 ml human albumin, electrolytes, Pantoprazole 2 x40 mg iv, analgesic, Nadroparin 0.4 cc s/c), but on the second postoperative day the condition immediately worsened with severe chest pain with dyspnea and perioral cyanosis with decreased oxygen saturation, rapid and irregular heartbeat, with all urgent resuscitation procedures leading to exitus letalis. Pulmonary thromboembolism resulted in post-mortem assessment at autopsy.

DISCUSSION

The term "pernicious anemia" is an anachronism, that considering from the era when treatment was not yet discovered and the disease was fatal, but remains in use for megaloblastic anemia resulting from vitamin B12 deficiency due to lack of intrinsic factor (IF) [8], which can occur in adults due to autoimmune destruction of parietal cells.

Although vitamin B12 therapy improves the results of anemia, it does not cure atrophic gastritis (which causes anemia), as it can progress to stomach cancer. [9] *Murphy et al.* shown the incidence of gastric adenocarcinoma is 2 to 3 times higher in patients with pernicious anemia than in the general population of the same age.

Currently, periodic gastroscopy and / or barium radiographic studies are not protected in patients with treated pernicious anemia who are asymptomatic, which justifies delays in diagnosis, or presentation of patients in the advanced stage.[10]

Murphy et al. in case-control study using Surveillance, Epidemiology, and Outcome (SEER) -Medical Database, found that older individuals with pernicious anemia were not only at significantly increased risk for non-cardiac gastric adenocarcinoma (odds ratio [OR] 2.18) and carcinoid tumors of the stomach (OR, 11.43), they were also at increased risk for the following [9].

Based on the recommendations of the ASGE *(American Association of Gastrointestinal Endoscopy),* Esophagogastroduodenoscopy (EGD) is suggested if gastrointestinal symptoms are present [11]. If neoplastic process is suspected with endoscopy, biopsy should be taken to establish the diagnosis, the best way is to use immunoreactive markers against carcinomas, because cells can exhibit partial immunoreactivity [12]. As we seen in the in-depth examinations in the analysis, pernicious anemia was found where its treatment requires the administration of drugs by parenteral route. In according the *Andres et al.* the prevalence of pernicious anemia in the general population is 0.1% and approximately 2% of patients are > 60 years of age [13].

As we know the pathology of pernicious anemia, patients with autoimmune diseases are at high risk of developing anti-IF antibodies. *Bizzaro et al.* shown that anti-parietal cell antibodies are found in about 90% of patients with pernicious anemia, but have low specificity. Anti-IF antibodies are found in about 60% of patients with pernicious anemia and are considered more specific for this disease [14].

In their study *Healton et al.* found the relative risk of patients with pernicious anemia developing gastric adenocarcinoma is 6.8% [15], also *Murphy et al.* shown the link between pernicious anemia and gastric cancer becomes more significant 6 years after the diagnosis of pernicious anemia. If pernicious anemia is detected and treated early, cancer is less likely to develop [16].

RBC transfusion is the most common procedure performed in

hospitals, with approximately 12 million RBC units being given to patients in the United States each year. [17]

Based on Adams and Lundy the "10/30 rule" set the standard that the ideal transfusion limits were an Hb of 10 g / dL or a hematocrit of 30%. [18]

There is no doubt that blood transfusions can save lives in the presence of active bleeding or hemorrhagic shock. Prior to the 1990s, clinicians were taught that if the patient needed RBC transfusion, 2 units was the optimal dose for adult patients. [17]

There are several factors that affect the prognosis of cancer. In general, proximal tumors near the gastroesophageal junction and cardia have a worse prognosis [19].

Gastric cancer is more common in men and has a higher mortality rate in men. In this case the patient must undergo surgery, gastrectomy combined with chemotherapy and radiotherapy is recommended. The patient should be followed according to an individualized plan. The postoperative problem remains the dynamic monitoring of vitamin B12 and iron levels should be monitored along with bone health, especially in women who have had a complete gastrectomy. [19].

Pulmonary thromboembolism (PE) is one of the life-threatening complications of gastric cancer surgery. Because both the cancer per se and surgery are known to be independent risk factors for the development of venous thromboembolism (VTE), routine thromboprophylaxis is recommended in patients undergoing cancer surgery [20]. D-dimer assay is a safe and rapid tool to exclude the presence of deep venous thrombosis (DVT).

Intermittent pneumatic compression (IPC) is usually used during and after surgery to prevent the complication of PE. However it may be ineffective and possibly lead to fatal PE.

The D-dimer assay is a safe and useful tool with a high sensitivity (97–100%) for excluding DVT and a high negative predictive value (96–100%) [21-23].

Although the D-dimer assay has a high negative predictive value (97–100%), which allows exclusion of VTE [21-23], its specificity is only 36–44% [24, 25].

Larsen et al. [26] investigated the incidence of DVT in esophageal and gastric cancer patients, and reported that the incidence of DVT in gastric cancer patients was 37% (10 of 27 patients).

CONCLUSION

Stomach cancer remains one of the most common malignant tumours in the world and usually has a poor prognosis. This is related to the fact that patients are asymptomatic up to advanced stages. Detecting data from physical examination and linking it to laboratory tests may be the first step in early detection of stomach cancer. In advanced cases, as in the above case, it is important to perform imaging examinations and Esophagogastroduodenoscopy (EGD). Unfortunately, therapeutic solutions in some patients are related to the stage of the disease and the time of diagnosis.

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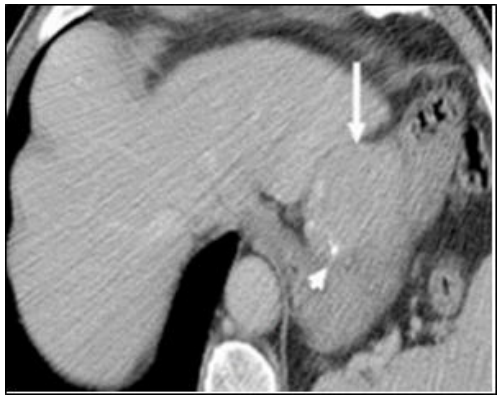

Figure 1. *Axial contrast-enhanced CT*

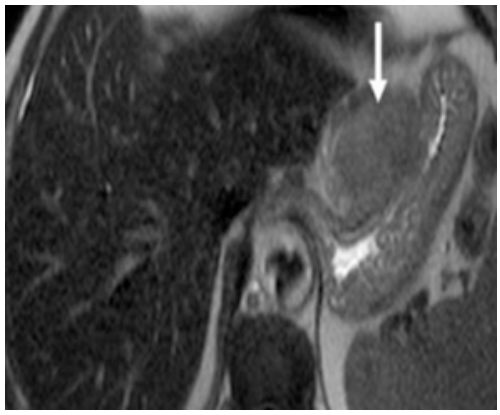

Figure 2. *Contrast-enhanced arterial phase MRI*

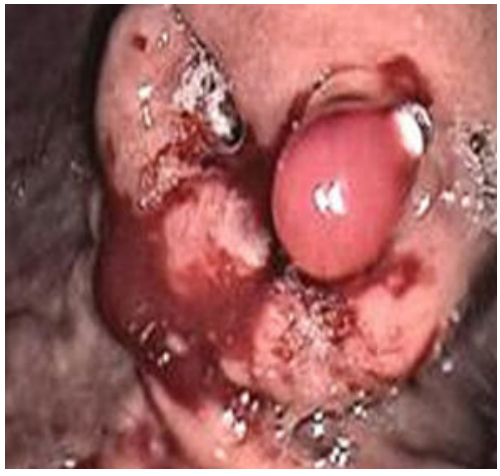

Figure 3. *On gastroscopy there is bleeding ulcer and gastric neoformation.*

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