Ischemia and Hypoxia as Primary Cause of Cancer

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ABSTRACT

There is no doubt that cancer is caused by progressive ischemia and hypoxia of long time. Both because of atherosclerosis and associated to anatomical variants of the arteries in the affected zone. In this way these hypoxic regions the cellular metabolism is altered; where the final electrons acceptor is not oxygen but a generally inorganic molecule. In contrast, vascular recanalization through aspirin can increase blood flow (greater nutrient intake, oxygen and exogenous anti-oxidants) in ischemic areas and thus, prevent the development of cancerous cells. For these reasons, we must fight against the development of atherosclerosis and avoid exposure to environmental pollutants.

INTRODUCTION

At present, based on clinical and neurosurgical experiences, my colleagues and I believe that neurological diseases such as aging, type 2 diabetes mellitus, DM (early stage), neurogenic hypertension (main representative of essential arterial hypertension, EAH), Huntington's disease, Alzheimer's disease, Pick's disease, neuromyelitis optica, Parkinson's disease, olivopontocerebellar atrophy, and amyotrophic lateral sclerosis; all of them are diseases of ischemic origin in specific areas of the brain [1-11]. In other words, caused by progressive ischemia in the intraparenchymal territory of the perforating and thin collateral arteries in the diencephalon and brainstem [2,6,7,12,13] secondary to atherosclerosis and associated to anatomical variants of the arteries of the carotid and vertebrobasilar systems. The neurons in these structures suffer from progressive ischemia and little hypoxia (y), because they are followed rapidly of oxidative stress and atrophy [6,7-9,14].

Moreover, under normal conditions, the cells of the body produce ATP to cover their needs through two coupled catabolic mechanisms: 1) Glycolysis (Embden-Meyerhof-Parnas pathway), in which glucose degrades to pyruvate, and 2) The Krebs cycle, which a greater energy supply is obtained during the oxidation of glucose in presence of oxygen within the mitochondria. Thus, about 90% of the energy required for normal cell functioning is obtained through these two metabolic pathways of the glucose. In contrast, since 1927, Warburg and colleagues [15,16] have argued that cancer is caused by hypoxia, which creates an acid state in the human body, i.e., cancer cells live in anaerobic media and cannot survive in presence of high levels of oxygen. For these reasons, based on the etiological similarity between the onset of "neurodegenerative" diseases [2,6-9] and cancer [15-17]; we will analyze the effect of this oxygen deficiency and its relation in the pathogenesis of cancer in some abdominal organs.

ATHEROSCLEROSIS IN THE AORTA AND ITS BRANCHES

Atherosclerosis, is a chronic inflammatory disease in the inner wall of the arteries, which is the result of primary and secondary factors [12,18,19]. The first, is related with the mechanical stress generated by hemodynamic factors that provoke a reactive biological

response in the intima of the arteries, i.e., atherogenesis is a histopathological response of the intima to repair the inner wall caused by changes in the blood flow and circulating blood quality. While the second, they are all agents that increase even more, the damage in the inner wall of the arteries and can directly damage the body cells, especially the cells in process of constant formation as the bone marrow, testicles and ovaries, among others [12,14]. These secondary factors are a multitude of substances of the body itself, as well as environmental pollutants, including high temperatures and trauma on tissues and organs, X–rays, gamma rays, and nuclear and solar radiation. The last external agents not only damage the arterioles and capillaries, but also the cells of the skin and of internal organs as the bone marrow, adrenal medulla, islets of Langerhans, ovaries, testicles and prostate, among others.

In the thoracic and abdominal aorta, the atheromas are progressively accumulated in its dorsal wall and with the progress of the age [18,20], these atheromas are deposited in the lateral and anterior wall, especially after 40 years of age [11,13,21,22] causing varying degrees of stenosis (mild, moderate or severe) [12] at the mouths of the coronaries, intercostal, celiac trunk, renal and mesenteric, and testicular (or ovarian) arteries. Therefore, the appearance of atheromatous plaques on the anterior surface of the upper half of the abdominal aorta can affect the function of the stomach, liver, gallbladder, duodenum, pancreas, kidneys, intestines and reproductive organs. These atheromas at the mouths of the celiac trunk and/or at the origin of nearby arteries [23-25] can cause ischemia and hypoxia in their intraparenchymal territories, especially in people over 40 years. Ischemia and hypoxia manifested with dysfunction of the affected organs (poor digestion of foods, type 2 DM, kidney stones, constipation and climacteric, among others) [7,11-13], and in late stages with cancer. Because in cells with anaerobic respiration, there is an electron transport chain analagous to the cells with aerobic respiration but the final electron acceptor is not oxygen but a molecule usually inorganic. For these reasons the intra-abdominal tissues and organs can continue to function (even with alterations) for many years, but the cells are already suffering from progressive ischemia and hypoxia. In other words, the cells are living with anaerobic respiration, in which cells can only use glycolysis in the cytosol, but not in the mitochondria. Therefore pyruvate is degraded in lactic acid and alcohol+$C0_2$. For these reasons, we agree with Warburg and coworkers [15,16] that cancer is caused by a lack of oxygen in the cells.

At the point of bifurcation of the abdominal aorta and the first centimeters of the medial surface of the primitive iliac arteries (length average 6 cm); the same atherosclerotic process occurs and thus, affects to the internal and external iliac arteries [18,20,24,26]. The internal iliac arteries vascularizes most of the pelvic viscera, perine, clitoris and penis, and also, through its extrapelvic branches nourishes to the obturator muscles, adductors and gluteus muscles. However, similar to other arteries of the body, these internal iliac arteries present anatomical variants in relation to the number of branches, caliber and distribution of the same. For example, in most cases the cecum, vermiform appendix and right ureter receives some thin branches from the right external iliac artery while the lower part of the sigmoid colon receives some thin arteries from left external iliac artery. Likewise, at the point of bifurcation or first centimeters of the primitive iliac arteries, the atheromatous plaque can cause stenosis or occlusion at the mouth of the middle sacral artery and to provoke degenerative changes in the low lumbar spine [21,22]. Consequently, with the progression of age, many pelvic viscera and extrapelvic muscles suffer deterioration, due to the same process of progressive ischemia and hypoxia. The extrapelvic muscles suffer atrophy expressed in a decreasing reduction of the volume of muscular masses in buttocks and thighs. The venous drainage of most of the pelvic organs (bladder, uterus and rectum, among others) is through the internal iliaca veins; however the rectal venous plexus can also drain through the inferior mesenteric vein.

CANCER IN PANCREAS AND GALLBLADDER

In addition to atherosclerosis at the mouth of the celiac trunk and its branches (hepatic, splenic and left gastric arteries), the pancreas and gallbladder(consisting of three layers:mucosa,muscular and serous) can be affecteds more frequently in patients with anatomical variants from their origin of the arterial branches that vascularize to the pancreatic parenchyma and gallbladder [23-25], as well as by its morphological and histological state [11,13]; all of them capable of producing dysfunction in the gallbladder, as well as in the exocrine (represents 90% of the pancreas) and endocrine pancreas. Usually the anatomical variations of the celiac trunk and its branches occur in about 30% of people [23-25]. Head of the pancreas, is the most susceptible of suffering ischemia and hypoxia, because it is vascularized by terminal arteries(arterioles) of collateral branches such as the superior prancreaticoduodenal artery (branch of gastroduodenal artery and this in turn, branch of the common hepatic artery) and by the inferior pancreaticoduodenal artery (branch of superior mesenteric artery, SMA) [24,27]. The arterioles and capillaries of both arteries are anastomosed in the parenchyma of the pancreatic head and therefore, this pancreatic zone is the less vascularized than those of the rest of the pancreas [23,25,27]. The gallbladder is another fragile structure in its vascularization, more even when there are anatomical variants from its origin of the common hepatic artery; but almost always the gallbladder receive irrigation through the cystic artery (branch of the right hepatic artery). Then, the cells in both structures (gallbladder and head of the pancreas) are prone to progressive ischemia and hypoxia in adults, and consequently suffering from cancer. The adenocarcinoma (originating from the epithelium of the pancreatic ducts) and the carcinoma of the gallbladder are the most common malignant tumors, especially in people over 60 years [28-30]. Because cancer cells usually developed in areas with low levels of oxygenation, which creates an acid state [15-17]. That is, cancer is caused by a lack of aerobic respiration and in contrast, they are developed in anaerobic media [16,17,31]. We report two clinical case of this region.

CASE 1

A 62 year-old man, employee, smoker and chronic alcoholic were attended at the Instituto Mexicano del Seguro Social, IMSS (Mexico city). On November 2016, he started with pain at the epigastrium, initially sporadic and then permanent with increasing intensity. On April 2017, weight loss despite taking all of their foods. Hemoglobin, 15 gr% and glycemia, 100 mg%. One month later, jaundice was added. A computed tomography (CT) scans of the abdomen revealed atherosclerosis at the abdominal aorta and a tumor in the head of the pancreas with metastasis to liver, and stomach. In addition to this, he began to present intolerance to fatty foods. On June, a new CT and magnetic resonance imaging (MRI) scans revealed larger tumor size, and metastasis to lung, pleural effusion and ascitis. He died on July 20, 2017.

CASE 2

A 64-year-old woman, dedicated to housework. Since September 2016, she began with slight loss of appetite and on April 2017, disgust was added to the meat in stews. For this reason, a months later an abdominal ultrasound revealed 1) thickening of the vesicular wall at the fossa for gallbladder, 2) two metastatic foci in the right liver and, 3) lymph node metastasis around the gallbladder. A CT scans revealed atherosclerosis at the abdominal aorta very close to the celiac trunk and confirmed the presence of tumor in the gallbladder as well as metastasis in the liver and surrounding zone. Hemoglobin 12 gr%, glucose 98 mg%, normal bilirubin and carcinoembryonic antigen 28 ng/ml (normal 0 to 5). Through a supraumbilical incision, on May 10, a laparotomy was performed at the Instituto Nacional de Enfermedades Neoplasicas, INEN (Lima, Peru). During surgery was found the hypertrophic gallbladder attached to the liver, with metastatic foci in the right liver and several regional lymph nodes. Biopsy was only taken and the surgical wound was closed by planes. Histopathological study of the biopsy revealed adenocarcinoma of the gallbladder. At present (August 5, 2017), she receives chemotherpy. Moreover, she suffers from moderate loss of appetite, especially to meats and she is thin, walks without assistance and her language is normal.

These two clinical cases demonstrate that the appearance of symptoms in the intraparenchymal territory of the celiac trunk and its branches are very insidious and therefore, would appear to be asymptomatic. For this reason, we believe that our colleagues should be more clinical and not be hopeful in auxiliary studies as CT and MRI scans. These studies should be useful only to confirm the presence of atherosclerosis at the upper half of the abdominal aorta and incipient clinical data. If both findings are positive (or even before symptoms are present), the patients should receive aspirin to reduce the size of atheromatous plaques and thus increase blood flow in the vascular territory of the celiac trunk and their branches [11-13,32]. Reducing in this way the risk of dysfunction and/or cancer in the pancreas and gallbladder, among other organs surrounding. That is use aspirin as a preventive therapy.

Moreover, although the medical literature holds that clinically the dysfunction of the exocrine pancreas is evident when the damage is greater than 85% of the parenchyma; however we believe that we should not wait for such a level of harm, but that we should use aspirin much earlier. Because many people may already experience bad absorption of carbohydrates and fats since the age of 40. Due to an exocrine secretion insufficiency of pancreatic juice especially of bicarbonates and amylolytic, lipolytic and proteolytic enzymes, among other components [11-13].

In the same way and with greater evidence, progressive ischemia in the endocrine pancreas causes degenerative changes in the islets of Langerhans, being more susceptible in those people with the number of islets within the low normal limits [7,11,13]. In other words, in addition to atherosclerosis at the mouth of the celiac trunk, and its histological constitution of the pancreas; the overweight and obesity is the main cause of type 2 DM in adults (moderate to severe stages). Because there is a vascular deterioration in the pancreas (body and tail) and conversely,a greater need for insulin. The beta cells are unable respond to this requirement of hyperglycemia. Consequently, the treatment should be directed in vascular recanalization to the pancreas through aspirin or non-steroidal anti-inflammatory drugs (NSAIDs) [12,32-34] and not increase the function of the beta cells through the use of oral hypoglycemic agents. Because by means of the a vascular recanalization with aspirin, the ischemic parenchyma (intraparenchymal territory of the celiac trunk) receives an increase in blood flow [12,32] and therefore, a greater intake of nutrients and oxygen to restore aerobic respiration and synthesis of endogenous antioxidants such as superoxide dismutase, catalase and glutathione peroxidase [12]. This is avoided the oxidative stress in the islets [6,7,14] and moreover, through increase in blood flow, the ischemic parenchyma would receive external anti-oxidants such as Vit A, Vit C, Vit E, and resveretrol among others [12]. Therefore, pancreatic ischemia due to atherosclerosis at the mouth of the celiac trunk or at the splenic artery and inferior pancreatic artery (branch of SMA), is cause of loss of the islets of Langerhans and therefore, a progressive reduction in insulin synthesis. In other words, this ischemic damage to the islets is another primary cause of type 2 DM in adults [11,13]. Because ischemia in the anterior hypothalamus is the initial cause of this disease (early stage) and years later, progressive ischemia is added in the islets of Langerhans [1,4,7,11] as well as insulin resistance [13]. That is type 2 DM is initiated in the anterior hypothalamus and years later the same ischemic process affects the islets [3,4,11]. Aspirin can recanalize the territory of the anterior perforating arteries and thus, improve the function of both ischemic areas (anterior hypothalamus and pancreas) as well as insulin resistance [1,2,7,11-13,33].

CANCER IN COLON AND RECTUM

Similar to ischemia and hypoxia in the intraparenchymal territory of the celiac trunk due to atherosclerosis; the same deterioration in blood flow is presented in the intraparenchyma territory of the mesenteric arteries. Normally at its origin ,the caliber of the SMA oscillates between 6 to 12 mm (average caliber, 7.5 mm) and after a long journey, the terminal portion ends as straight vessels in the wall of the jejunum, ilium and right colon; while the inferior mesenteric artery (IMA) of smaller caliber (average caliber, 4 m) than the SMA, they also long-distance and their distal ends vascularize to the transverse colon, descending colon, sigmoid colon and the upper part of the rectum [24,25,35-37]. Thus, the left colon is the most affected structure, since its wall is the least perfused; even more if the IMA is originated as a branch of the SMA. The origin of these two arteries (SMA and IMA) can be demonstrated by means of CT angiography examination [24,25]. Moreover, the rectum receives terminal arteries from the upper rectal artery (branch of IMA), and terminal branches from the medial rectal, internal pudendal and lower rectal arteries (branches of the internal iliac arteries). Usually forming a highly vascular network in the rectum. In other words, normally the rectum is much vascularized. On the contrary, the presence of atheroma plaques in the mouths of the IMA and hypogastric arteries, the rectum undergoes progressive hypoxia for years and therefore prone to cáncer [16,17]. In the same way as the celiac trunk [23,25], both mesenteric arteries present anatomical variants from their origins [24,35,36] and also, both arteries present anastomoses between them, as well as with branches of the celiac trunk such as 1) the gastroduodenal artery (branch of the common hepatic artery), 2) the pancreaticoduodenal artery, 3) the inferior pancreatic artery (branch of SMA), 4) the marginal artery of Drummond, and 5) the sigmoidal–rectum anastomosis between the upper rectal artery (branch of IMA) with the medial and inferior rectal arteries. The blood flow it's diminished in these anastomoses in presence of atheromatous plaques at the mouths of the celiac trunk, SMA and IMA, as well as in the iliac arteries and its branches. In conclusión, the arterial vascularization of the left colon as well as of the rectum, both structures are very susceptibles to ischemia and hypoxia and even more, after 40 years of age, due to a reduction in blood flow by atherosclerosis at the mouths of origin of the IMA and internal iliac arteries [18,20,24,35,36,38,39]. Consequently, progressive ischemia in the left colon and rectum causes histological degeneration of its wall (mucosa, submucosa, muscular and serous). For example, the colon can undergo muscular hypotrophy in its wall and cause constipation, even more in absence or little fiber intake with diet. Moreover can appear pathological changes in its mucosa and submucosa as the formation of colorectal polyps (sessile and pedicled polyps), among other pathological changes [40-42]. In Mexico [40] several authors report that serrated sessile polyps are more frequent than pedicled polyps and even more, that serrated polyps predomínate in the right colon. The presence of gases (CH_4, NH_3 and CO_2, among others) in the lumen of the colon does not seem to influence the development of cancer [43].

The venous drainage from the intestines, pancreas and other intra-abdominal organs are transported to the liver through the portal vein; which is formed essentially by the splenic vein, and the superior and inferior mesenteric veins. In the rectal wall, the venous network are very developed and therefore, in addition to mild to moderate ischemia in the rectum (height of 15 cm) and left colon, hypoxia is also increased, especially in obese patients or with cirrosis of the liver [38,40]. That is, this hypoxia increases even more, by pathology of portal vein drainage.

Based on the above-mentioned data, we believe that the polyps appear initially in the rectum and then, in the rest of the colon i.e., in opposite direction to its function. Therefore, pedicled polyps of the rectum are more frequent and of greater size than those of the ascending colon, which are generally sessile [40,41]. Likewise, based on the same data of ischemia and hypoxia, we think that the distal end of the polyps (intraluminal portion) is the most affected part; because recent studies have found high levels of prostaglandins and cyclo-oxygenase-2(COX-2) enzyme in adenomas and colorectal tumors compared with normal tissue [44-50].

CASE 3

A 73-year-old man, peruvian and medical surgeon, he was attended at the IMSS (Mexico city). He reported that since July 2016, started with occasional constipation and evident, since December 2016 and January 2017. Symptom that coincided with the summer (Lima-Peru), profesional stress and poor food intake by profesional activity. On February 4, he traveled to Mexico city and during the first 2 weeks continued with constipation. For this reason, a proctological and endoscopic examination of the rectum and colon revealed the presence of sessile polyps in the cecum, ascending colon **(Figure 1)** and transverse colon; all of them of grayish white color and less than one cm in height, which were removed with hot handle gripper. In addition to these, two pedicled polyps (tubular adenoma) [41] were located in descending colon (height, 1 cm) and other large polyp, implanted at 10 cm from the anal ring. This last pedicled polyp was implanted in the rectal mucosa in an area of 3 × 2 cm and projected into the rectal lumen up to 3 cm in length. The proximal third was smooth, white and fibrous, while the distal portion was coliform in appearance, brown and friable (bleeding to the rectal touch) **(Figure 2)**.

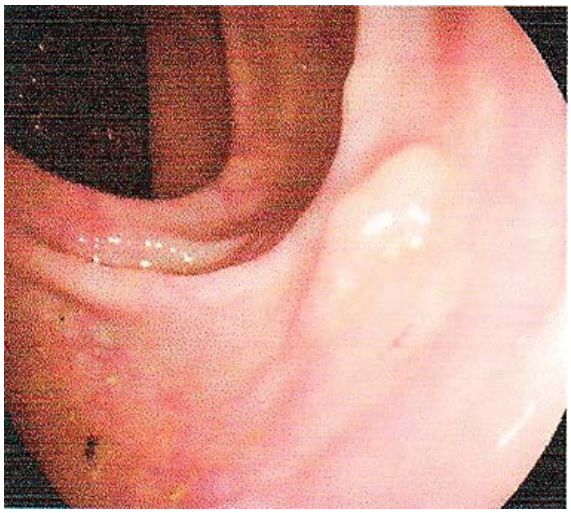

Figure 1. Adenomatous polyp (or sessile polyp) of 4 mm in diameter and 3 mm in height located in the ascending colon. It was completely removed with hot handle gripper and histological study corresponded to low- grade dysplasia.

The histopathological study demonstrated low-grade dysplasia in polyps of the cecum, ascending colon and tranvserve colon; while high-grade dysplasia in the polyp of the descending colon. The rectal adenoma (larger than the previous polyps) showed moderately differentiated adenocarcinoma in the coliform portion and in the poximal portion, revealed doubtful infiltration of cancer cells in the submucosa. A preoperative CT and MRI scans of the peri-rectal zone revealed only thinckning of the rectal wall in the area (3 cm high and 2 cm wide) of implantation. A chest X-ray was normal. Moreover, BMI of 28, hemoglobin 17.5 gr%, creatinine 0.9 mg%, glucose 120 mg%, cholesterol 187 mg%, prostatic antigen 3.1 ng/ml, carcinoembryonic antigen 5.36 ng/ml. By means of a median supra and infraumbilical incision, the left colon and rectum were localized (March 8, 2017). 5 cm below and 20 cm above the implantation area of the adenoma were removed accompanied by its mesentery. An end-to-end anastomosis between the sigmoid and rest of the rectum, as well as a colostomy in the upper right quadrant of the abdomen, were performed. After surgery the patient was transferred to the intensive care unit. Hemoglobin 9.8 gr%. Glycemia, 240 mg%. Once stabilized, the patient happened to his room, where he stayed a week and then, he was discharged from the Hospital de Oncología, Centro Médico Nacional siglo XXI.IMSS. The patient did not receive radiotherpy nor chemotherapy. At his home, he presented clinical improvement slow and progressive.

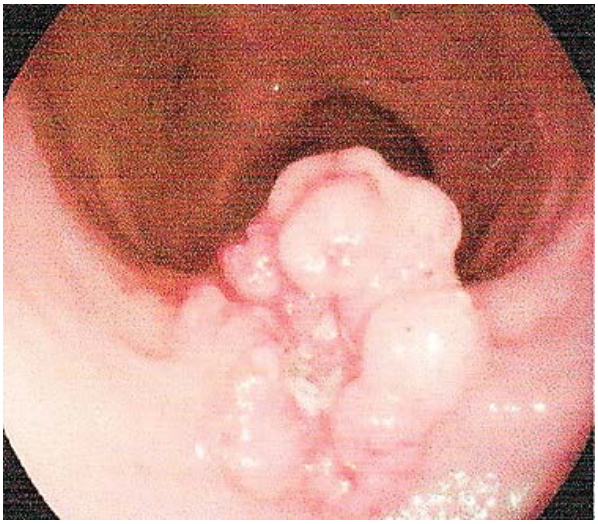

Figure 2. Pedicled polyp showing the multilobular coliform portion. This coliform part corresponded to a moderately differentiated adenocarcinoma. The proximal part was removed from the rectal mucosa with hot handle gripper.

On May 6, hemoglobin 12.7 gr%, leukocytes 5,200/uL, glucose 116 mg% and carcinoembryonic antigen of 2.3 ng/ml. On June 26, hemoglobin 16 gr%, Leukocytes 6,290/uL, glucose 112 mg%, creatinine 0.79 mg% and carcinoembryonic antigen 2.49 ng/ml. For these reasons, on July 21, 2017, the colostomy was closed without complications. This clinical case is a good example which shows that the early diagnosis of this tumor is essential for the surgery and the prognosis. Moreover this clinical case confirm that the coliform portion of the adenoma is the most affected and also is a portion where found high level of prostaglandins and COX-2 enzime [31,49]. Thus, prostaglandins are related with 1) angiogenesis, 2) cell proliferation, 3) inhibition of immune surveillance, and 4) apoptosis [17,42,44,47]. By contrast, aspirin prevents the conversion of free arachidonic acid to prostaglandin, through permanent inactivation of cyclo-oxygenase-1(COX-1) and cyclo-oxygenase-2(COX-2) [12,49,51]. That is, in tissues or organs in

ischemia and hypoxia long-lasting; the cancer cells usually are anaerobic and cannot survive in presence of high levels of oxygen, because your metabolism is already altered [15-17,31]. In these tissues with anaerobic respiraton, the final electron acceptor is not oxygen, but a molecule, usually inorganic like SO_4^{-2}, and NO_3^{-1} and CO_2. For these reasons, aspirin must be indicated since about 40 years of age, in order to reduce the risk of cancer in several organs such as in brain, lung, breast, bladder, prostate, colon and rectum [42,45-47,50,52-62]. First, aspirin can cause vascular recanalization in arteries with stenosis (mild to moderate) and thus, increase the blood flow to ischemic zones (in this case, in the intraparenquimal territory of SMA, IMA and hypogastric arteries) due to its anti-inflammatory, anti-platelet and anti-thrombotic effects [12,34,52,53] and Second because aspirin prevents the conversion of arachidonic acid (polyunsaturated fatty acid) to prostaglandin-H_2, through the COX-2 enzymes [12,34,47,49]. The presence of the COX-2 enzyme in the adenomatous polyps has been related to the size and degree of cellular dysplasia [17,51]. In other words, in small polyps **(Figure 1)** we can already find (in the distal end) high levels of COX-2 enzyme, as well as low degree of cellular dysplasia; whereas in larger polyps (found in rectum), the COX-2 enzyme levels are higher and the degree of dysplasia is high and/or with presence of adenocarcinoma **(Figure 2)**.

So that, we can prevent the appearance of adenomas by recanalizing blood flow in the territories of the SMA and IMA, through the use of aspirin and other NSAIDs [12,34,46,58,60]. Therefore, we have no doubt that the main origin of the cancerous cells in the rectum and colon, is due to ischemia and hypoxia in the intraparenchymal territory of the mesenteric arteries and internal iliac arteries. This risk can also increase by a reduction of the venous return to the liver through the portal vein.

BENIGN HYPERPLASIA AND PROSTATE CANCER

The prostate is a male glandular organ, triangular in shape and weighing 15 to 20 gr, attached to the bladder trigone and surrounding the first portion of the urethra. Laterally receives the eyaculatory ducts. Histologically in the prostate there are 3 zones: Transition zone, represents 5% of the prostate and is attached to the prostatic urethra. Central zone represents 25% of the prostatic glandular-epithelial tissue, and Peripheral zone, which contains 70% of the prostatic glandular tissue. The inferior vesical arteries (branches of the internal iliac arteries) vascularize the prostate through two branches. The urethral branches that vascularize the trígone of the bladder and most of the medial part of the prostate; while the capsular branches do to the most lateral portion. In a lesser degree, the lower portion of the prostate receives some arterial branches from the medial rectal and internal pudendal arteries. Then the prostate is usually very vascularized through the arterioles and capillaries. Therefore a reduction in the blood flow in the hypogastric arteries by atherosclerosis and associated a anatomical variants of their arterial branches [18,24,22,26,39], this can causes muscular hypotrophy in buttocks and degenerative changes in its glandular parenchyma(benign prostatic hypertrophy, BPH) secondary to ischemia and hypoxia; even more, if sexual intercourse are frequent. For this reason, we must use aspirin,before initiating intercourse to increase blood flow in the heart and prostate.

In these conditions, the first change of BPH is characterized by the appearance of microscopic myxoid lesions constituted by fibroblast and immature hematolynphoid cells in a myxoid fundus [46,56]. However not all hyperplastic nodules end in adenocarcinomas [41,56,62]. It seems that like polyps in the colon,in these hyperplastic nodules,the prostaglandins also have a deleterious effect in the genesis of BPH and adenocarcinomas [12,48,49]. Moreover with the patient´s age, the degree of atherosclerosis in the hypogastric arteries can decrease even more the blood flow and thus cause more ischemia and hypoxia in the bladder, prostate, Cowper glands, uterus and ovaries, among other organs.

CASE 4

A 64-year-old man, truck driver, smoker and chronic alcoholic was attended in IMSS (Mexico). Eight years ago the patient started with desire to urinate frequently, progressively and even at night. He received treatment for urinary tract infection several time. Three years later, he manifested pain in the epigastrium, constipation and loss of muscle mass in buttocks. A CT scans revealed lithiasis in the gallbladder, for this reason was operated. As the pain persisted, the patient consulted with an urologist, who after rectal examination and prostatic antigen of 16 ng/ml, the surgeon operated to the patient. The histopathological study showed adenocarcinoma.

By the above-mentioned data, the patient was admitted in the Hospital de Oncologia del Centro Médico Nacional Siglo XXI,IMSS (Mexico city). Here, a new CT scans and laboratory tests confirmed the diagnosis of prostate cancer with metastasis to bladder, rectum, omentum and liver among other organs. He received chemotherapy and palliative treatment. He died on July 28, 2017. The evolution of the symptoms in this patient suggests that the disease began with BPH and then appeared adenocarcinoma. Moreover, this clinical case suggests also that there was deterioration in blood flow in the intraparenchymal territory of the hypogastric arteries. Thus, this progressive ischemia and hypoxia provoked an anaerobic medium for the development of cancerous cells [16,17,31]. Therefore, aspirin and other NSAIDs can have a preventive benefit to prevent the onset of the symptoms and avoid, prostate cancer [48,52,53,62]. Because aspirin can improve blood flow in the intraparenchyma territory of the internal iliac arteries [12,13,32] and thus reduce prostaglandins synthesis [12,48,49] and the development of cancer.

CONCLUSION

Based on the above-mentioned knowledge and clinical data in our patients, we agree with Warburg that the cancerous cells

are developed in hypoxic zones. However, we must add that prior to hypoxia, different degrees of ischemia occur in any organ of the body. Ischemia that is caused by atherosclerosis, associated to anatomical variants in the arteries of the affected region. Therefore there is a similarity in the beginning of neurodegenerative diseases and of cancer. Both groups of diseases present in late ages and are related with atherosclerosis, which causes different degrees of ischemia and hypoxia. However, unlike neurons in the nervous system, body cells can live longer in anaerobic media, which causes respiratory damage to the cell and induces to dysplasia.

Therefore, we must fight against the genesis of atherosclerosis, reducing in particular the environmental pollutants which injure the intima of the arteries as well as direct damage to the cells (mitochondria, proteins, RNA, DNA, and other intracellular molecules) of the body. So while complying with environmental health programs, we must use aspirin to reduce athermanous plaques at the mouths of the arteries and thus prevent the onset of neurodegenerative diseases and cancer in some organs. In addition to aspirin, we must add quality of food which is important, as well as the use of exogenous anti-oxidants and physical activity. Finally we believe that the increase in incidence of degenerative diseases and cancer is due to an increase in atherosclerosis and parallel to environmental exposure.

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