

Left Main Total Chronic Occlusion In A Patient With Colorectal Cancer: A Case Report Of A Rare And Severe Localization Of Coronary Artery Disease

ABSTRACT

The aim of this case report is to draw attention at the potential severity of presentation of these associated pathologies. Prevention through early screening of colorectal cancer in patients with coronary artery disease and vice versa is the guarantee of a better management of the two pathologies. Cardiovascular disease and cancer are the two leading causes of death worldwide. Emerging evidence suggests associations between cardiovascular disease and several cancers, including colorectal cancer. Many cases have reported severe coronary artery disease (CAD) in association with colorectal cancer including triple vessel disease. To the best of our knowledge this is the first case reporting a total occlusion of the left main coronary artery in such patients.

We report the case of a 52 years old woman presented to our cath lab for severe angina (Class III of the Canadian classification) and impairment of left ventricle function. Six months before the patient was diagnosed with a metastatic colorectal cancer. Coronary angiography showed absence of anterograde opacification of the left coronary system. Selective right coronary artery angiography showed a retrograde filling of the left coronary system by collaterals issued from proximal and distal dominant right coronary artery.

Several studies have reported the association between colorectal neoplasm and CAD but Isolated left main coronary artery disease is extremely uncommon. Patients with left main coronary artery disease have always a grim prognosis and without prompt revascularization 60% will die after 5 years while survivors live with severe angina; heart failure or both.

Keywords: Coronary disease, colorectal cancer, total chronic occlusion

1. INTRODUCTION:

“Cardiovascular disease and cancer are the two leading causes of death worldwide. Although commonly thought of as two separate disease entities, emerging evidence suggests associations between cardiovascular disease and several cancers, including colorectal cancer. The relationship is thought to arise from common risk factors including obesity, diabetes, hypertension, smoking, unhealthy diet, and physical inactivity” (1). “The total occlusion of the left main coronary artery is always a surprising discovery in a cardiac catheterization laboratory with a very low incidence ranging from 0.04 to 0.43%” (2). “This incidence is surely underestimated because of its highly lethal potential and many patients dies before arriving to the hospital. Occlusion of the left main coronary artery jeopardizes a large territory of the left ventricle; if occlusion is sudden, it should be expected to produce a massive infarction of these structures resulting in death. Only progressive occlusion with development of an extensive collateral circulation from a dominant right coronary artery can keep the patient alive. Many cases have reported severe coronary artery disease (CAD) in association with colorectal

cancer including triple vessel disease" (3). To the best of our knowledge this is the first case reporting a total occlusion of the left main coronary artery in such patients.

2. CASE REPORT:

A 52 years old woman presented to our cath lab for severe angina (Class III of the Canadian classification) and impairment of left ventricle function. Six months before the patient was diagnosed with a metastatic colorectal cancer (Figure 1) and treated with palliative chemotherapy made of 5-fluorouracil/leucovorin.

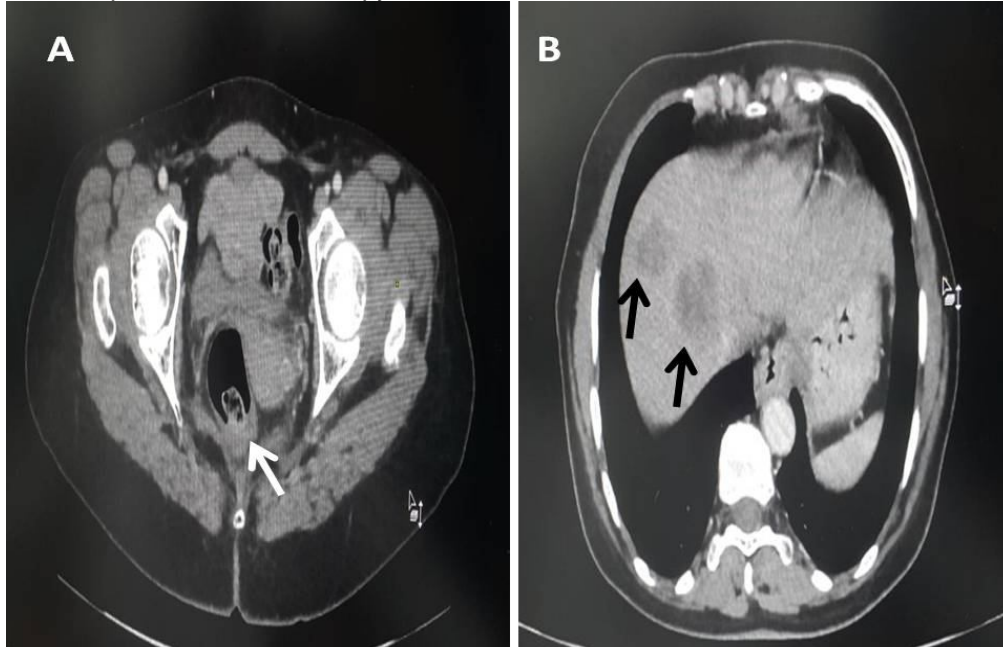


Figure 1: CT scan of abdomen and pelvis revealing rectum wall thickening (Panel A, black arrow) and colorectal liver metastases (Panel B, white arrows)

Her cardiac evaluation before starting the chemotherapy was normal (Normal resting ECG and normal left ejection fraction). The patient never reported chest pain during infusion of 5-fluorouracil. The symptomatology was evolving since 2 months with progressive aggravation and was resistant to medical therapy. The resting electrocardiogram showed regular sinus rhythm with negative T waves (V2-V6) (Figure 2).

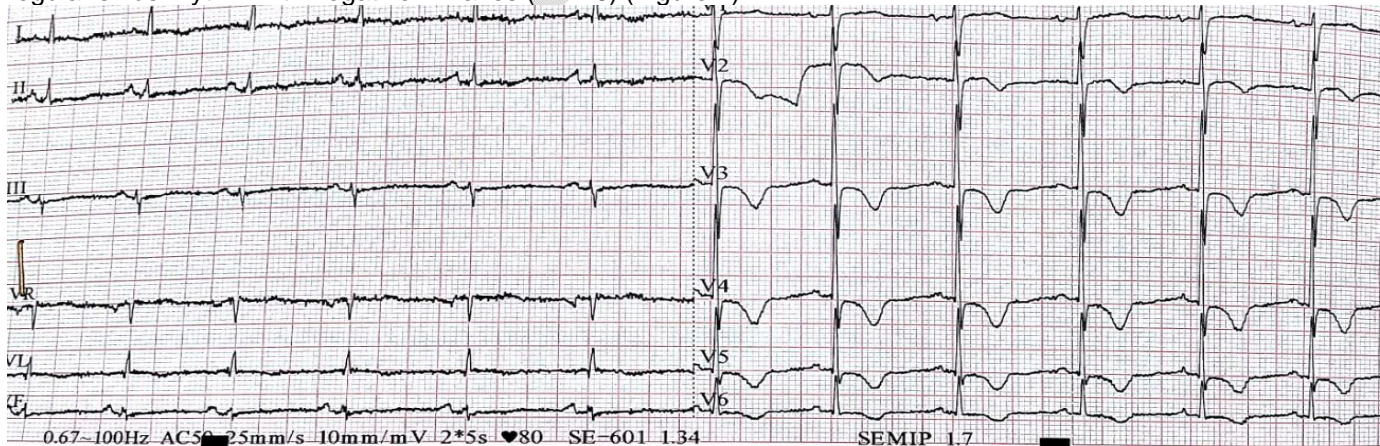


Figure 2: ECG showing a regular sinus rhythm with negative T waves in the territory of the left coronary artery (V2-V6)

Two-dimensional echocardiography showed mild left ventricular dysfunction (Ejection fraction 40%). Coronary angiography showed absence of anterograde opacification of the left coronary system. Selective right coronary artery angiography showed a retrograde filling of the left coronary system by collaterals issued from proximal and distal dominant right coronary artery (Figure 3). We noted also that the other coronary arteries were smooth without any

significant stenosis. Her syphilitic serology was negative. For the treatment, the cardio-oncology team opted for a conservative approach with only medical therapy taking into account her advanced cancer stage.



Figure 3: Coronary angiography showing the retrograde filling of left coronary system. Notice the absence of evident atherosclerotic plaques in the other coronary arteries (Panel A). Rich and extensive collaterals issued from the right coronary artery to the left coronary system (Panel B).

3. DISCUSSION

3.1 Association between colorectal cancer and coronary artery disease:

Several studies have reported the association between colorectal neoplasm and CAD, in a large study Chan et al found much higher prevalence of colorectal cancer in coronary arteries diseased patients than in the general population, they also reported a strong association between CAD patients and advanced colorectal lesions (4). This is also remarkable in our patient since she was diagnosed in a metastatic stage of her cancer. Metabolic syndrome and smoking were the two important predictive factors for the association of advanced colonic lesions and CAD in this study. Interestingly our patient didn't have any of these two factors which didn't prevent such association. Both colorectal neoplasm and CAD probably develop through the mechanism of chronic inflammation. Inflammation is now recognized as being a central factor in the pathogenesis of atherosclerosis (5). "Colorectal cancer also progresses through the pathway of inflammation (6). Our patient had unbalanced type 2 diabetes. The direct proliferative/antiapoptotic effects of insulin and related insulin like growth factor 1 on both colorectal neoplasm and CAD has gained support recently" (7).

3.2 Differential diagnosis:

"Complete occlusion of the left main coronary artery has been associated with atheroocclusive disease, Takayasu arteritis, syphilitic coronary ostial occlusion, aortic valve replacement, congenital atresia of the left main coronary ostium, and congenital fusion of the left coronary cusp to the aortic wall. Another diagnosis that can be noted especially on imaging is single coronary artery. Single coronary artery is a rare congenital anomaly, occurring in about 0.024% of the population" (8). Differentiation should be made between isolated complete occlusion of the left main coronary artery and single right coronary artery with the left coronary artery being a posterior continuation of the right coronary artery via the circumflex. Considering the differential diagnosis, syphilitic aortitis usually is limited to the coronary ostia, commonly in association with aortic regurgitation. Our patient had a negative serologic test for syphilis. In Takayasu arteritis, stenosis of the coronary artery characteristically is limited to the ostia and proximal segments of the coronary arteries due to coronary intimal thickening. Symptoms of coronary involvement are rarely the initial presentation. A long history of angina, the presence of diabetes mellitus, the negativity of syphilis serology coupled with the angiographic findings described suggests that our patient had acquired atherosclerotic disease localized to the origin of the left main coronary vessel rather than another etiology.

We discussed also the implication of the chemotherapy regimen in the developing of this severe coronary artery disease. Our patient received 5-fluorouracil three months before the coronarography and her symptomatology was described prior to the chemotherapy first session. Moreover 5-Fluorouracil is a chemotherapeutic agent that has been associated with cardiac toxicities including Prinzmetal's angina, myocardial infarction, arrhythmias, and cardiomyopathy. The mechanisms of these adverse effects are believed to be due to coronary vasospasm and not to atherosclerosis (9). "Changes in protein kinase C and endothelin-1 activity as well as direct vessel injury may all contribute to endothelial dysfunction" (10).

"Finally patients with 5-Fluorouracil related cardiotoxicity typically develop symptoms during infusion, at maximum 3 days after" (11).

3.3 Left main: particular coronary artery disease localization:

"Isolated atherosclerotic left main coronary artery disease is uncommon. Several studies have shown that coronary disease confined solely to the left main stem exists in only approximately 9% of patients with left main coronary artery disease" (12). "In the rest, the coexisting disease in other vessels is typically widespread with approximately 70%- 80% of patients demonstrating multivessel coronary disease. The atherosclerotic disease that is present at other locations in patients with left main coronary artery disease is often complex with a relatively high frequency of chronic total occlusion and extensive calcification" (13).

"Patients with total occlusion of the left main coronary artery have various clinical presentations. Symptoms and survival depend on the development of adequate collaterals. In patients with good collaterals, left ventricular function may be preserved and symptoms may not be evident. Occlusion of the left main coronary artery jeopardizes the anterolateral, lateral, apical, septal, and lateral parts of the left ventricle; if occlusion is sudden, it should be expected to produce a massive infarction of these structures resulting in death. Gradual development of complete occlusion may have allowed for functionally adequate collateral circulation to develop. Extensive development of collateral circulation and dominant right coronary artery are the principal determinants of myocardial vascularization" (14). The extensive collateral network from the normal dominant right coronary artery was probably sufficient to prevent severe myocardial damage in our patient; however, it was not large enough to prevent severe angina and the impairment of the left ventricular function. Patients with left main coronary artery disease have always a grim prognosis and without prompt revascularization 60% will die after 5 years while survivors live with severe angina; heart failure or both (15).

3.4 Treatment:

Myocardial revascularization, whether surgical or percutaneous, remains the best treatment of total chronic occlusion of the Left main coronary artery. In A meta-analysis De Rosa et al found no significant difference between Coronary artery bypass surgery (CABG) and Percutaneous coronary intervention (PCI) in the composite endpoint of death, stroke and myocardial infarction (16). "The two strategies generally provided similar results with respect to the composite end point of death, myocardial infarction, stroke, or unplanned ischemia-driven revascularization. Stroke occurred more frequently in the CABG group than in the PCI group, whereas the need for repeat revascularization was greater in the PCI group than in the CABG group" (17). As a consequence, PCI with drug eluting stents is being used with increasing frequency, currently exceeding the frequency of CABG in many centers. However, CABG will be preferred to PCI in patient with a complex anatomical setting judged by a high syntax score, whereas PCI is the method of choice in older age patients and less extensive coronary vascular disease. According to literature, patients with metastatic colorectal cancer have a one-year mortality rate approaching 50 % (18). The heart team decided that the advanced stage of our patient's cancer was not compatible with a revascularization strategy. We put our patient under statins and aspirin. "Statins have been shown to have beneficial effects in both colorectal cancer and CAD, probably through an anti-inflammatory mechanism" (19). Aspirin also has long been proven to be beneficial in both conditions, through different mechanisms.

4. CONCLUSION

Association between colorectal cancer and CAD has already been described in the literature. Shared risk factors and inflammation seem to be the common point of these two severe pathologies. Through this case we aimed to draw attention at the potential severity of presentation of this association. Prevention through early screening of colorectal cancer in patients with CAD and vice versa is the guarantee of a better management of the two pathologies.

CONSENT

All authors declare that written consent for publication was obtained from the patient.

ETHICAL APPROVAL:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

REFERENCES

1. Koene RJ, Prizment AE, Blaes A, Konety SH. Shared risk factors in cardiovascular disease and cancer. *Circulation* 2016;133:1104–14.
2. Ipek G, Omeroglu SN, Ardal H, Mansuroglu D, Kayalar N, Sismanoglu M, Guler M, Daglar B, Yakut C. Surgery for chronic total occlusion of the left main coronary artery – myocardial preservation. *J Card Surg.* 2005;20(1):60–4.
3. Ueda K, Shinji S, Ishii Y, Yamawaki H, Yamada T, Koizumi M, Yokoyama Y, Hotta M, Takahashi G, Iwai T, Takeda K, Hara K, Oota K, Nitta T, Uchida E. [Obstructive Colon Cancer with Triple-Vessel Coronary Artery Disease - A Case Report]. *Gan To Kagaku Ryoho.* 2017 Nov;44(12):1868-1870. Japanese. PMID: 29394803.
4. Chan AO, Jim MH, Lam KF, Morris JS, Siu DC, Tong T, Ng FH, Wong SY, Hui WM, Chan CK, Lai KC, Cheung TK, Chan P, Wong G, Yuen MF, Lau YK, Lee S, Szeto ML, Wong BC, Lam SK. Prevalence of colorectal neoplasm among patients with newly diagnosed coronary artery disease. *JAMA.* 2007 Sep 26;298(12):1412-9. doi: 10.1001/jama.298.12.1412. PMID: 17895457.
5. Tiong AY, Brieger D. Inflammation and coronary artery disease. *Am Heart J.* 2005;150(1):11-18.
6. Clevers H. At the crossroads of inflammation and cancer. *Cell.* 2004;118(6):671-674.
7. Renehan AG, Zwahlen M, Minder C, O'Dwyer ST, Shalet SM, Egger M. Insulin-like growth factor (IGF)-I, IGF binding protein-3, and cancer risk: systematic review and meta-regression analysis. *Lancet.* 2004;363(9418):1346-1353.
8. Lipton MJ, Barry WH, Obrez I, Silverman JF, Wexler L. Isolated single coronary artery: diagnosis, angiographic classification, and clinical significance. *Radiology* 1979;130:39-47.
9. Alter P, Herzum M, Schaefer JR, Maisch B. Coronary artery spasm induced by 5-fluorouracil. *Z Kardiol.* 2005;94:33–7.
10. Becker K, Erckenbrecht JF, Haussinger D, et al: Cardiotoxicity of the antiproliferative compound fluorouracil. *Drugs* 57:475-484, 1999.
11. Jensen SA, Sørensen JB. Risk factors and prevention of cardiotoxicity induced by 5 fluorouracil or capecitabine. *Cancer Chemother Pharmacol.* 2006;58:487–93.

12. Serruys PW, Morice MC, Kappetein P, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med* 2009;360:961-72.
13. Ragosta M, Dee S, Sarembock IJ, Lipson LC, Gimple LW, Powers ER. Prevalence of unfavorable angiographic characteristics for percutaneous intervention in patients with unprotected left main coronary artery disease. *Catheter Cardiovasc Interv* 2006;67: 357-62.
14. Hori T, Kurosawa T, Yoshida M, Yamazoe M, Aizawa Y, Izumi T. Factors predicting mortality in patients after myocardial infarction caused by left main coronary artery occlusion: significance of ST segment elevation in both aVR and aVL leads. *Jpn Heart J*. 2000;41(5):571–81.
15. Bruschke AVG, Proudfit WL, Sones FM Jr. Progress study of 590 consecutive nonsurgical cases of coronary disease followed 5-9 years. II. Ventriculographic and other correlations. *Circulation* 1973;47:1154-63.
16. De Rosa S, Polimeni A, Sabatino J, Indolfi C. Long-term outcomes of coronary artery bypass grafting versus stent-PCI for unprotected left main disease: a meta-analysis. *BMC Cardiovasc Disord*. 2017;17(1):240.
17. Lee PH, Ahn JM, Chang M, et al. Left main coronary artery disease: secular trends in patient characteristics, treatments, and outcomes. *J Am Coll Cardiol* 2016;68:1233-46.
18. Cowling TE, Bellot A, Boyle J, Walker K, Kuryba A, Galbraith S, Aggarwal A, Braun M, Sharples LD, van der Meulen J. One-year mortality of colorectal cancer patients: development and validation of a prediction model using linked national electronic data. *Br J Cancer*. 2020 Nov;123(10):1474-80.
19. Demierre MF, Higgins PD, Gruber SB, et al. Statins and cancer prevention. *Nat Rev Cancer*. 2005; 5(12):930-42.

DEFINITIONS, ACRONYMS, ABBREVIATIONS

Coronary artery bypass surgery: CABG
Percutaneous coronary intervention: PCI
Coronary artery disease: CAD
Electrocardiogram: ECG