Iron Deficiency Anemia as the Warning Sign of Carcinoma of Colon

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Abstract: The common cause of microcytic anemia is iron deficiency and its most frequent cause of deficiency is the occult iron loss from the lesions in the gastrointestinal tract especially in men and menopausal women. Herein we report a case of 74-year old German man who presents with progressive fatigue for a few weeks. The physical examination reveals only pallor. The blood tests show Hb 8.4 g%, MCV 67.1 fL, MCH 20.5 pg, RDW 16.0 %, ferritin 12.8 ng/mL, serum iron 21 ug/dL, TIBC 362 ug/dL, transferrin saturation 6 %, CEA 18.68 ng/mL. He is definitely diagnosed as iron deficiency anemia (IDA) and treated with oral iron tablets. Six weeks later, he complains of abdominal pain and palpates the mass at the left upper quadrant while the anemia becomes more obvious, Hb 6.0 g%, ferritin 62.8 ng/mL, CEA 297.39 ng/mL. The left half colectomy and the adjacent lymph nodes resection are performed and the microscopic pathology of the colon is the poorly differentiated adenocarcinoma with the lymph nodes metastasis. This patient still encourages that when the case of IDA is encountered, the meticulous gastrointestinal tract study cannot be ignored or delayed even though such patient does not complains of any gastrointestinal symptom or the serum CEA is just slightly elevated. Otherwise, the serious cause of iron loss such as cancer of the gastrointestinal tract may be overlooked.

Key words: Iron Deficiency Anemia, Colon Carcinoma

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บทคัดย่อ: **โลหิตจางจากการขาดเหล็กในฐานะสัญญาณเตือนถึงมะเร็งลำไส้ใหญ่**

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**กลุ่มงานอายุรกรรม โรงพยาบาลมหาราชนครราชสีมา จ.นครราชสีมา 30000
เวชสารโรงพยาบาลมหาราชนครราชสีมา 2559; 38: 47-51.

สาเหตุที่พบบ่อยของภาวะโลหิตจางประเภทเม็ดเลือดแดงขนาดเล็ก คือ โรคโลหิตจางจากการขาดธาตุเหล็ก และสาเหตุของการขาดเหล็กที่สำคัญ คือ การค่อยสูญเสียเหล็กออกไปเรื่อย ๆ จากรอยโรคในทางเดินอาหาร โดยเฉพาะในผู้ป่วยชาย และหญิงวัยทอง เช่น ในรายงานนี้ ซึ่งเป็นผู้ป่วยชายชาวเยอรมัน อายุ 74 ปี มาตรวจด้วยอาการอ่อนเพลีย 2-3 สัปดาห์ ตรวจร่างกายพบเพียงซีดเท่านั้น ผลการตรวจเลือด Hb 8.4 g%, MCV 67.1 fL, MCH 20.5 pg, RDW 16.0 %, ferritin 12.8 ng/mL, serum iron 21 ug/dL, TIBC 362 ug/dL, transferrin saturation 6 %, CEA 18.68 ng/mL จึงให้การวินิจฉัยได้อย่างแน่ชัดว่าเป็นโรคโลหิตจางจากการขาดธาตุเหล็ก และให้การรักษาด้วยยาเม็ดเข้าธาตุเหล็ก ในเวลา 6 สัปดาห์ถัดมา ผู้ป่วยมีอาการปวดท้อง และคลำได้ก้อนในท้อง บริเวณช่วงซ้ายบน ส่วนอาการโลหิตจางก็ยิ่งปรากฏชัดกว่าเดิมตรวจเลือดพบ Hb 6.0 g%, ferritin 62.8 ng/mL, CEA 297.39 ng/mL ผู้ป่วยเข้ารับการผ่าตัด left half colectomy ร่วมกับการตัดต่อมน้ำเหลืองรอบ ๆ ก้อนเนื้องอก ผลการตรวจทางจุลพยาธิวิทยา พบว่าลำไส้ใหญ่เป็น poorly differentiated adenocarcinoma และมะเร็งกระจายไป ที่ต่อมน้ำเหลืองหลายกลุ่ม ผู้ป่วยรายนี้ได้ย้ำให้เห็นว่า เมื่อวินิจฉัยโรคโลหิตจางจากการขาดธาตุเหล็กได้แล้วนั้น การตรวจละเอียดหารอยโรคในทางเดินอาหารนั้นเป็นสิ่งที่ไม่สามารถละเลย หรือเลื่อนออกไปได้ต่อให้ผู้ป่วยรายนั้นไม่มีอาการในทางเดินอาหาร หรือระดับ CEA ในเลือดจะขึ้นเพียงเล็กน้อยก็ตาม เพราะมิฉะนั้นแล้ว สาเหตุที่รุนแรงของโรคโลหิตจางจากการขาดธาตุเหล็ก เช่น มะเร็ง ก็อาจจะถูกมองข้ามไปได้
คำสำคัญ: โรคโลหิตจางจากการขาดธาตุเหล็ก, มะเร็งลำไส้ใหญ่

Introduction

The common causes of microcytic hypochromic anemia are mainly due the decreased production of the heme in iron deficiency anemia (IDA), the decreased production of the globin chains in thalassemia, the restricted iron delivery to the heme group of hemoglobin in anemia of inflammation, and defects in the synthesis of the heme group or sideroblastic anemias[1]. To differentiate these entities, it needs the iron study including the serum ferritin, the serum iron and the total iron binding capacity (TIBC) and other appropriate tests. In a case of typical IDA, the combination of the low serum ferritin, low serum iron and high TIBC levels are expected.

After the diagnosis of IDA is definitely established in the adult patients, the causes of iron deficiency must be clarified and its major cause in most cases is the iron loss, either overt or occult[2]. All attempt for finding the sources of the iron loss must be performed especially the gastrointestinal (GI)

lesions in men even in the cases of lack of complaint of abdominal symptoms. Herein, we report one case of IDA in a white man in whom the attending physician is satisfied with just only diagnosis and treatment of IDA alone.

Case Report

A 74-year old German man, JK, presented with gradual fatigue, no fever for a few weeks. His underlying disease was well-controlled diabetes. Pallor was the only one sign on the physical examination. The blood tests included: Hb 8.4 g%, WBC 13,980/mm^3, platelet 521,000/mm^3, MCV 67.1 fL, MCH 20.5 pg, MCHC 30.5 g%, RDW 16.0 %, serum ferritin 12.8 ng/mL (normal 15-300), serum iron 21 ug/dL (normal 65-175), TIBC 362 ug/dL (normal 259-388), transferrin saturation 6 % (normal 20-50), FBS 143 mg%, creatinine 0.6 mg%, albumin 3.7g%, globulin 3.4g%, AFP 1.59 ng/mL (normal 1.09-8.04), PSA 1.9 ng/mL (normal <4), CEA 18.68 ng/mL (normal <5). He was definitely diagnosed as IDA and treated with oral iron tablets. One and a half months later, he developed mild colicky abdominal pain and felt a lump at the left upper quadrant for a week while other symptoms included significant weight loss and severe anorexia but no bowel habit change, no melena, no fever. Instead of recovery, the anemia became more obvious. His physical examination revealed moderate pallor and a palpable LUQ mass 4x5 cm, rough surface, tenderness and firm consistency.

Hb 6.0 g%, ferritin 62.8 ng/mL, Hb typing: Hb A2A, Hb A2 2.9 %, osmotic fragility test-positive, CEA 297.39 ng/mL.

Stool-positive occult blood, no RBC, no WBC, no parasite

The ultrasonography and the computerized tomography of the abdomen highly suggested the irregular thickened bowel wall at the distal end of the transverse colon with the pericolic fat infiltration and extension to the greater omentum and anterior abdominal wall, size 13.3x11x8.7 cm, multiple enlarged periaortic lymph nodes (LN), 1.5-2.3 cm, suggesting carcinoma at the transverse colon with extraluminal extension and LN metastasis.

The left half colectomy and the multiple LN excision were performed and the microscopic pathology showed: poorly differentiated adenocarci-noma, invading into the peritoneum and the omentum, and metastatic to pericolic LN. The patient was still alive 4 months after operation when this case report was performed.

Discussion

At the first presentation, the diagnosis of IDA can be definitely concluded because of the combination of hypochromic microcytic anemia, low serum ferritin, low serum iron, low transferrin saturation[3] and the normal Hb typing. And he is appropriately treated with the iron tablets. But the attempt to identify the causes of iron deficiency has not been tried. The main cause of IDA in adults is the chronic blood loss, opposed to the infants and children of that is the poor intake. For adult males and postmenopausal women, GI loss is the only one route[4] whereas in adult females, both GI and genital tracts should be emphasized.

Bleeding lesions in GI tract are identified using gastroscopy and colonoscopy in about 50% of patients with IDA. Although the GI malignancy is not the most frequent lesion, with a prevalence of 10-17%[5], but it

is serious and needs early detection and management particularly in men and postmenopausal women.

For our case, he does not complain about the GI symptoms, even though the CEA is slightly raised, the attending physician does not convince the patient for further meticulous investigations for the silent GI malignancy, one serious cause of IDA. The CEA > 2.5 ng/mL has limited use in detecting the early colorectal cancer because of the low sensitivity of 30 %[6], it is more useful for detecting early recurrence and for pre-operative evaluation of colon cancer. Its high level may be found in other benign conditions: peptic ulcer disease, diverticulitis, liver disease, chronic inflammatory disease[7]. However in case of benign conditions, they rarely give rise the serum value >10 mcg/L, therefore if serum level is highly increased, e.g. >5 times the upper limit of the normal range, it strongly suggests the presence of cancer[8].

The patient is the caucasian with German origin. In Germany, thalassemia is considered the rare entity[9]. When the microcytic hypochromic anemia is encountered, IDA must be in the first order of differential diagnosis[10].

The TIBC is lowered as one of the negative phase reactant proteins in any chronic inflammatory diseasesuch as rheumatoid arthritis, as compared with normal, 45 (25-70) vs. 61 (46-80) micromole/L, therefore the TIBC that should be higher in pure IDA than normal, 74 (54-97) vs. 61 (46-80) micromole/L, will be lowered to be 59 (43-84) in IDA occurring in rheumatoid arthritis[11]. Our patient has TIBC 362 ug/dL that falls within the normal range of 259-388 ug/dL which may be the combination of the effect of chronic inflammation and the IDA. However the transferrin saturation in our case is still low 6 % (normal 20-50) as pure IDA in general.

When the IDA is encountered, the full GI investigations should be considered essential in all patients unless there is a history of significant non-GI blood loss.Upper GI endoscopy can be expected to reveal a cause in between 30 and 50% of patients. And all should be further investigated with lower GI study because dual pathology (lesions in both upper GI and colon) can be found around 10-15 %[12], furthermore the most common pathology in the lower GI tract is cancer. In case of gastroscopy and colonoscopy are both negative, the small bowel study should be considered[13].

Conclusion

A 74-year old German man presents with fatigue due to iron deficiency anemia (IDA) and is later proved to be due to carcinoma of the colon. This is to emphasize that the complete gastrointestinal tract study should not be ignored even in the case of IDA who has no complains of the gastrointestinal symptoms especially in the elderly population.

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