CASE 3

A 64-year-old woman with shortness of breath and ill-fitting shoes

CASE AND MCQS

Clinical history and presentation

A 64-year-old woman was brought to the emergency room because of increasing shortness of breath and weakness. Her current problems started a few days ago when she noticed difficulty in fitting on her shoes and shortness of breath on minimal exertion. She has a history of ischemic heart disease for which she has been medically treated, and of multiple episodes of transient ischemic attacks. She denied smoking and drinking alcohol. Her family history is positive for carcinoma of the lung (mother) and carcinoma of the colon (father). Physical examination revealed a lethargic and pale woman, with a blood pressure of 165/90 mmHg, a pulse of 98/min and regular, and a respiratory rate of 22/min. Her temperature was 99.8°F (37.7°C.) The jugular veins were distended; femoral and radial pulses were full and equal bilaterally; the heart apical impulse was displaced laterally. There were diffuse crackling rales at the lung bases. The abdomen was distended and there was shifting dullness to percussion. The liver was palpable about 5 cm below the right costal margin. Examination of the lower extremities showed pitting edema of both legs. The rest of the physical examination was unremarkable except for a guaiac-positive stool on rectal exam.

Admission data

Table 3.1 Hematology

			SI Units	
WBC	6.3	(3.3–11.0 thou/μL)	6.3	(3.3–11.0 × 10^9/L)
Neut	53	(44–88%)	53	(44–88%)
Lymph	42	(12–43%)	42	(12–43%)
Mono	3	(2–11%)	3	(2–11%)
Eos	1	(0–5%)	1	(0–5%)
Baso	1	(0–2%)	1	(0–2%)
RBC	3.8 L	(3.9–5.0 mill/μL)	3.8 L	(3.9–5.0 × 10^{12}/L)
HGB	8.5 L	(11.6–15.6 g/dL)	85 L	(116–156 g/L)
HCT	28.2 L	(37.0–47.0%)	0.282 L	(0.37–0.47)
MCV	72.3 L	(79.0–99.0 fL)	72.3 L	(79.0–99.0 fL)
MCH	22.3 L	(26.0–32.6 pg)	22.3 L	(26.0–32.6 pg)
MCHC	30.1 L	(31.0–36.0 g/dL)	301 L	(310–360 g/L)
Plts	85 L	(130–400 thou/μL)	85 L	(130–400 × 10^9/L)
Retic	0.8	(0.1–2.0%)	0.8	(0.1–2.0%)

Table 3.2 Chemistry

			SI Units	
Glucose	87	(65–110 mg/dL)	4.8	(3.6–6.11 mmol/L)
Creatinine	2.0 H	(0.7–1.4 mg/dL)	176 H	(61.9–123.7 μmol/L)
BUN	68 H	(7–24 mg/dL)	24.3 H	(2.50–8.57 mmol/L)
Uric acid	8.3	(3.0–8.5 mg/dL)	0.49	(0.18–0.51 mmol/L)
Cholesterol	175	(150–200 mg/dL)	4.52	(3.88–5.17 mmol/L)
Calcium	8.6	(8.5–10.5 mg/dL)	2.15	(2.13–2.65 mmol/L)
Protein	6.2	(6–8 g/dL)	62	(60–80 g/L)
Albumin	3.3 L	(3.7–5.0 g/dL)	33 L	(37–50 g/L)
LDH	220	(100–250 U/L)	220	(100–250 U/L)
Alk Phos	54	(0–120 U/L)	54	(0–120 U/L)
AST	24	(0–55 U/L)	24	(0–55 U/L)
GGTP	12	(0–50 U/L)	12	(0–50 U/L)
Bilirubin	1.0	(0.0–1.5 mg/dL)	17.1	(0–25.7 μmol/L)
Bilirubin-direct	0.10	(0.02–0.18 mg/dL)	1.7	(0.34–3.08 μmol/L)
B-type natriuretic peptide (BNP)	950 H	(<100 pg/mL)	950 H	(<100 ng/L)

Table 3.3 Electrolytes

			SI Units	
Na	135	(134–143 mEq/L)	135	(134–143 mmol/L)
K	4.4	(3.5–4.9 mEq/L)	4.4	(3.5–4.9 mmol/L)
Cl	97	(95–108 mEq/L)	97	(95–108 mmol/L)
CO_2	27	(21–32 mEq/L)	27	(21–32 mmol/L)

Table 3.4 Arterial blood gases

			SI Units	
pH	7.26 L	(7.35–7.45)	7.26 L	(7.35–7.45)
PCO_2	53 H	(32–46 mmHg)	7.06 H	(4.26–6.13 kPa)
PO_2	52 L	(74–108 mmHg)	6.93 L	(9.86–14.4 kPa)
HCO_3^-	22	(21–29 mEq/L)	22	(21–29 mmol/L)
O_2 saturation	81 L	(92–100%)	81 L	(92–100%)

Table 3.5 Urinalysis

pH	5	(5.0–7.5)
Protein	Neg	(Neg)
Glucose	Neg	(Neg)
Ketone	Neg	(Neg)
Color	Yellow	(Yellow)
Clarity	Clear	(Clear)
Sp. grav.	1.015	(1.010–1.035)
WBC	5	(0–5/HPF)
RBC	2	(0–2/HPF)
Casts	Neg	(Neg)
Bacteria	Neg	(Neg)

Table 3.6 Cardiac enzymes

			SI Units	
CK	106	(0–130 U/L)	106	(0–130 U/L)
CK-MB	4	(0–4%)	0.04	(0–0.04)
Troponin I	0.02	(0–0.5 ng/mL)*	0.02	(0–0.5 µg/L)*
LDH	220	(100–225 U/L)	220	(100–225 U/L)
LDH_1	22	(17–27%)	0.22	(0.17–0.27)
LDH_2	37	(28–38%)	0.37	(0.28–0.38)
LDH_3	20	(18–28%)	0.20	(0.18–0.28)
LDH_4	11	(5–15%)	0.11	(0.05–0.15)
LDH_5	9	(5–15%)	0.09	(0.05–0.15)

*Troponin I: < 0.05 = normal, 0.05–0.5 = possible myocardial injury, ≥ 0.5 = acute MI.

Table 3.7 Electrocardiogram

Sinus tachycardia and non-specific ST-T changes

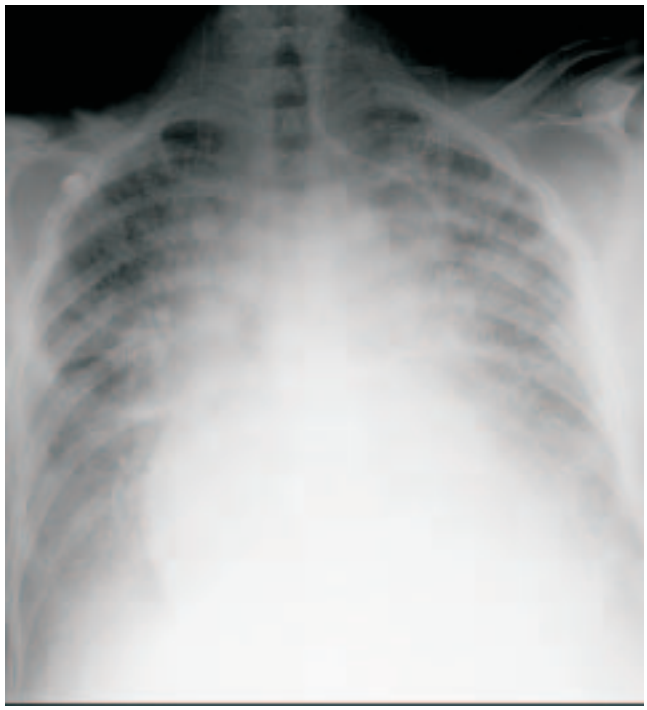

Figure 3.1 Chest X-ray, A-P view (patient).

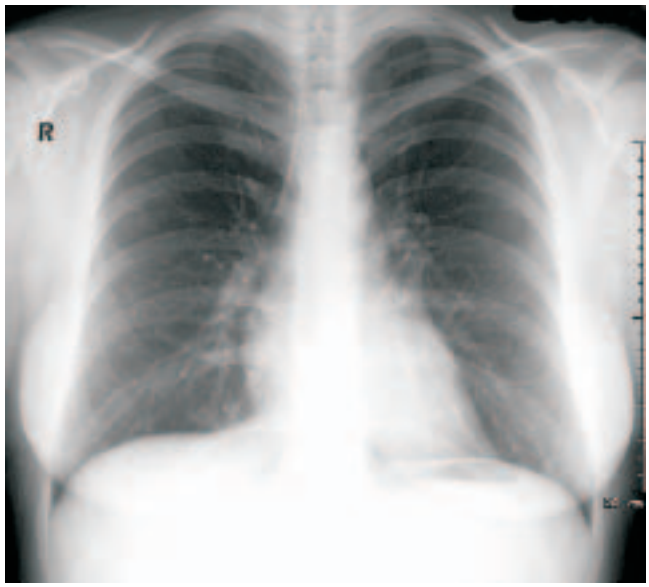

Figure 3.2 Chest X-ray, A-P view (normal).

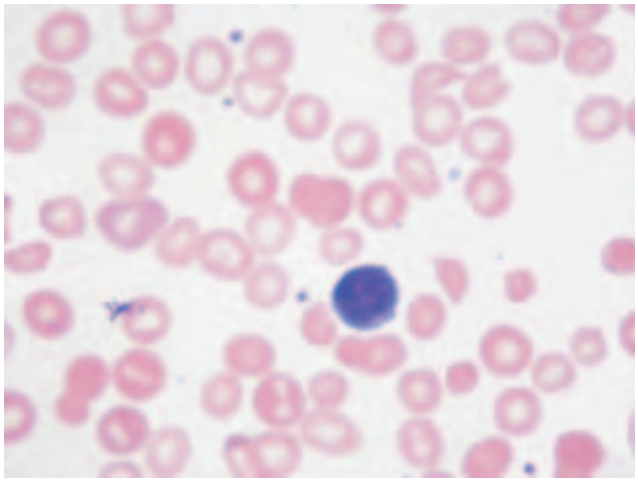

Figure 3.3 Peripheral blood smear (patient). Wright/Giemsa stain.

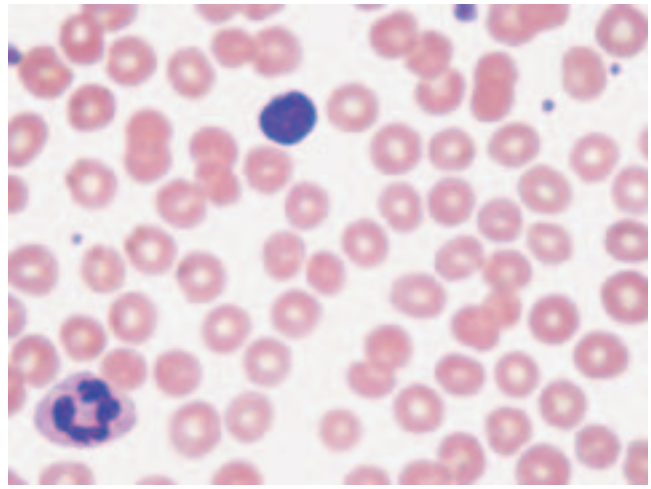

Figure 3.4 Normal peripheral blood smear. Wright/Giemsa stain.

Questions

Based on the above information you can best conclude the following:

BASIC

1. Arterial blood gases in this patient are best interpreted as:

a. metabolic acidosis
b. respiratory acidosis
c. respiratory alkalosis
d. metabolic alkalosis

INTERMEDIATE

2. This patient's abnormal BUN and creatinine levels are most likely due to:

a. decreased renal blood flow
b. laboratory error
c. hepato-renal syndrome
d. none of the above

BASIC

3. The pathogenesis of this patient's pulmonary findings (Fig. 3.1), lower limb edema, and ascites is associated with all of the following EXCEPT:

a. decreased cardiac output
b. increased central venous pressure
c. increased venous hydrostatic pressure
d. decreased production of antidiuretic hormone (ADH)

INTERMEDIATE

4. The patient's peripheral blood smear (Fig. 3.3) and CBC (FBC) are suggestive of:

a. leukemoid reaction
b. megaloblastic anemia
c. iron reutilization defect
d. chronic blood loss
e. none of the above

Clinical course

The patient was admitted to the intensive care unit. After treatment, the patient's dyspnea and edema improved and this was reflected in an improvement of her blood gases (not shown). A colonoscopy was performed and the findings are depicted in Figs 3.5–3.8 (Fig. 3.9 is for comparison). The results were discussed with the patient and she was referred to a specialist for further management.

Table 3.8 Carcinoembryonic antigen (CEA)

			SI Units	
CEA	6.2 H	Non-smoker: 0–3.0 ng/mL Smoker:0–5.0 ng/mL	6.2 H	Non-smoker: 0–3.0 µg/L Smoker:0–5.0 µg/L

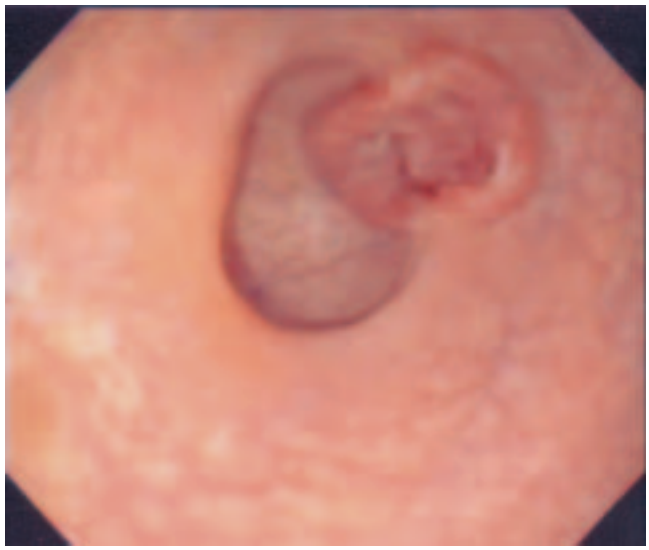

Figure 3.5 Colonoscopy (patient).

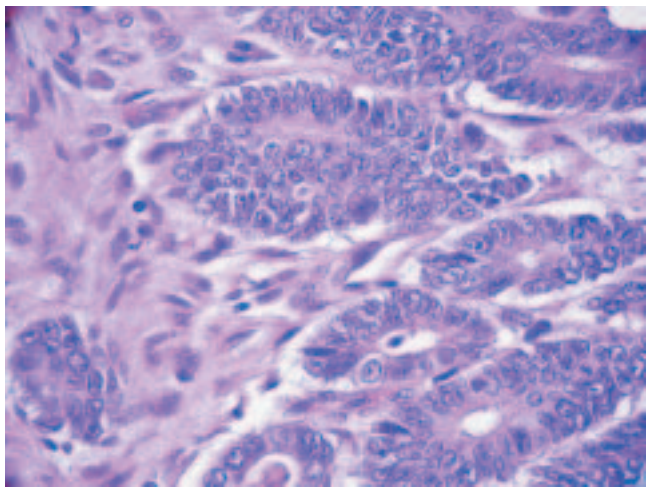

Figure 3.7 Colon biopsy (patient). Hematoxylin & eosin stain.

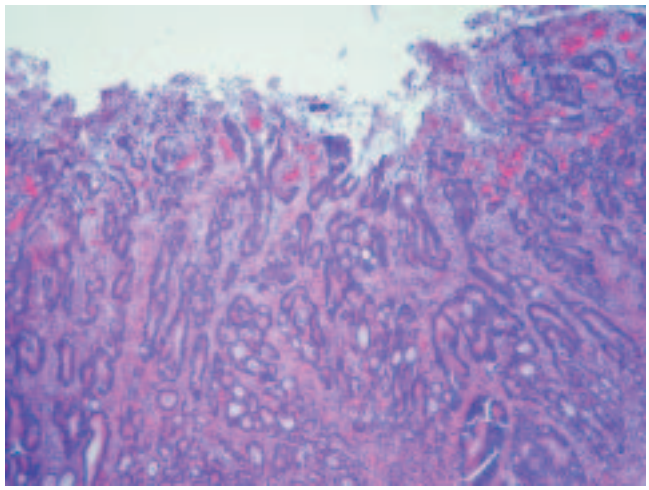

Figure 3.6 Colon biopsy (patient). Hematoxylin & eosin stain.

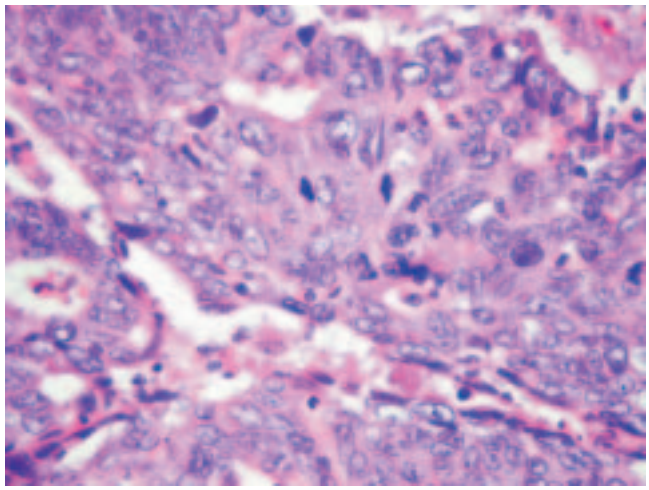

Figure 3.8 Colon biopsy (patient). Hematoxylin & eosin stain.

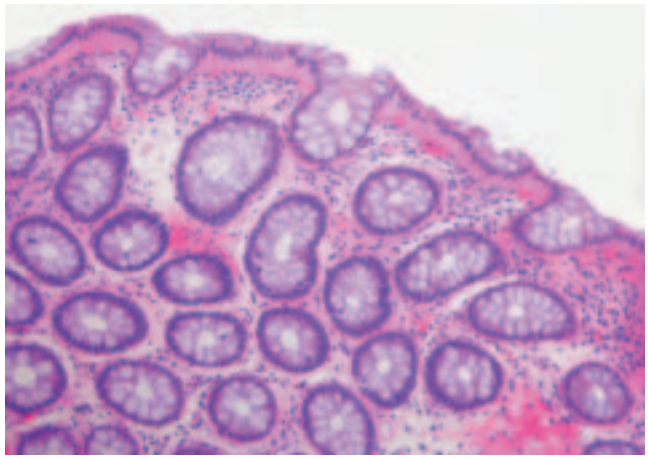

Figure 3.9 Colon biopsy (normal). Hematoxylin & eosin stain.

Questions

INTERMEDIATE

5. The indication(s) for colonoscopy and colon biopsy in this patient is/are:

a. a positive fecal occult blood (guaiac) test
b. a microcytic hypochromic anemia
c. her age
d. her family history
e. all of the above

INTERMEDIATE

6. The colonic biopsy (Figs 3.6–3.8) shows which of the following intestinal problems?

a. diverticulitis
b. a benign colonic polyp
c. a foreign body granuloma
d. an invasive neoplasm
e. a benign ulcer

INTERMEDIATE

7. In general, risk factors for this patient's colonic problem include all of the following EXCEPT:

a. family history
b. high fiber diet
c. inflammatory bowel disease
d. polyposis syndromes
e. physical inactivity

INTERMEDIATE

8. Which of the following statements regarding such a colonic lesion is INCORRECT?

a. its peak incidence is between 60 and 70 years of age
b. it usually starts as an *in situ* lesion
c. dietary habits constitute a predisposing factor
d. it usually presents at multiple sites

INTERMEDIATE

9. Carcinoembryonic antigen level (CEA, shown in Table 3.8):

a. is useful to monitor recurrence of colorectal carcinoma
b. is increased in some benign conditions such as inflammatory bowel disease
c. is increased in pancreatic, gastric, and lung carcinoma
d. all of the above statements are correct

ANSWERS AND FURTHER INFORMATION

Figure descriptions

Figure 3.1 Chest X-ray, A-P view (patient).
Congestive heart failure: This frontal radiograph of the chest shows the presence of diffuse bilateral infiltrates, pulmonary vascular congestion, and cardiomegaly. Increased density at both lung bases is also seen and is consistent with pleural effusions. These findings are characteristic of congestive heart failure.

Figure 3.2 Chest X-ray, A-P view (normal).
A normal frontal radiograph of the chest in a female patient.

Figure 3.3 Peripheral blood smear (patient). Wright/Giemsa stain.
Microcytic hypochromic anemia: The patient's peripheral blood smear shows mild to moderate aniso-poikilocytosis (red blood cells of different size and shape). The red blood cells are microcytic (small in size) as compared with the normal lymphocyte present in the lower half of this photomicrograph. The red blood cells are also hypochromic with a prominent central pallor. This pattern is consistent with a diagnosis of microcytic hypochromic anemia.

Figure 3.4 Normal peripheral blood smear. Wright/Giemsa stain.
The red blood cells are similar in size and shape, and hemoglobinization appears normal. A normal lymphocyte and neutrophil are present, and the platelets are adequate in number and uniform in size.

Figure 3.5 Colonoscopy (patient).
Colonic adenocarcinoma: This endoscopic picture demonstrates a polypoid ulcerated mass in the ascending colon, measuring 3.5 cm.

Figure 3.6 Colon biopsy (patient). Hematoxylin & eosin stain.
Colonic adenocarcinoma: This low-power photomicrograph of the colonic biopsy shows an ulcerated, well to moderately differentiated adenocarcinoma of the colon. The tumor is composed of glands of different size and shape exhibiting a cribriform pattern and back-to-back arrangement. The tumor involves the colonic mucosa and submucosa, and the superficial portion of the muscularis propria (not shown).

Figure 3.7 Colon biopsy (patient). Hematoxylin & eosin stain.
Colonic adenocarcinoma: A higher magnification of the colonic adenocarcinoma showing glands lined by cells exhibiting large hyperchromatic nuclei, an increased nuclear/cytoplasmic ratio, and nuclear pleomorphism. Note the back-to-back arrangement of the malignant glands and desmoplastic stroma.

Figure 3.8 Colon biopsy (patient). Hematoxylin & eosin stain.
Colonic adenocarcinoma: This photomicrograph shows malignant glands lined by multiple layers of cells exhibiting hyperchromatic vesicular nuclei. There are numerous mitotic figures noted in this field.

Figure 3.9 Colon biopsy (normal). Hematoxylin & eosin stain.
Normal colon biopsy with a normal crypt architecture, showing colonic glands lined by a single layer of mucus-producing columnar epithelium.

Answers

1. B. This patient's arterial blood gases show reduced pH, pointing to acidosis. The presence of a low pH, elevated arterial PCO_2 and normal HCO_3^- are diagnostic of uncompensated respiratory acidosis resulting from inadequate alveolar ventilation and retention of CO_2. Metabolic acidosis, on the other hand, would show a reduced pH, normal arterial PCO_2, and reduced HCO_3^-.

2. A. The presence of elevated BUN and creatinine with a high BUN/creatinine ratio points to prerenal azotemia (i.e. impaired renal function, due to decreased renal blood flow, in the absence of organic renal disease). The most common causes of prerenal azotemia are heart failure and volume depletion. In both conditions there is sodium and water retention in order to compensate for the decreased effective blood volume. Hepato-renal syndrome is defined as a prerenal azotemia in patients with severe liver disease. Since this patient's liver function tests are within normal limits, a hepato-renal syndrome can be ruled out as the cause of this patient's abnormal renal function.

3. D. This patient presented with signs and symptoms of both left- and right-sided congestive heart failure (CHF). CHF results in the reduction of cardiac output, effective arterial blood volume, renal blood flow, and venous return. Decreased renal blood flow stimulates the production of renin, which leads to secondary hyperaldosteronism and sodium and water retention. In addition, the reduced effective blood volume stimulates the production of antidiuretic hormone (ADH). The fluid retention resulting from these events does not improve renal perfusion, simply because the failing heart is incapable of increasing its output. Moreover, fluid retention leads to worsening of the edema. In congestive heart failure

venous hydrostatic pressure is increased due to fluid retention and reduction of venous return.

4. D. This patient's CBC (FBC) and peripheral blood smear show a microcytic hypochromic anemia, most likely due to chronic blood loss. Her CBC (FBC) and peripheral blood smear do not show any features suggestive of a leukemoid reaction, or of a megaloblastic anemia. A leukemoid reaction is a reactive leukocytosis with accelerated release of immature leukocytes from the bone marrow. Megaloblastic anemia is a macrocytic anemia with asynchronism between the cytoplasmic and nuclear maturation (i.e. there is inadequate DNA synthesis with normal RNA and protein synthesis). Peripheral blood smear examination in megaloblastic anemia would reveal large RBCs (macrocytes), and enlarged hypersegmented neutrophils. Iron reutilization defect (anemia of chronic disease) would show a normocytic normochromic anemia.

5. E. The patient, admitted for the worsening of her congestive heart failure, was found to have a microcytic hypochromic anemia, and a positive guaiac test. She has a positive family history of colon cancer. The patient is 64 years old. The peak incidence of colorectal carcinoma is at 60 to 79 years of age. All the above facts are indications for colonoscopy.

6 D. Figures 3.6–3.8 depict an invasive adenocarcinoma (see figure description). There are no benign polyps, granulomas or diverticula present. Diverticulitis refers to inflammatory changes due to obstruction or perforation of diverticula. None of these are seen in this photomicrograph.

7. B. Risk factors for a colonic problem such as that of this patient (colorectal carcinoma) include: inflammatory bowel disease, polyposis syndrome, family history, and diet, such as a low content of vegetable fiber, high intake of red meat, a high caloric intake relative to requirement and physical inactivity. A high fiber diet, on the contrary, is recommended as a preventive measure.

8. D. Colonic carcinoma affects predominantly older people, with a peak incidence at 60–79 years of age. It starts as an *in situ* lesion but develops different growth patterns in the proximal and the distal colon. The microscopic characteristics of those patterns are, however, similar. Cecum and ascending colon are the most frequent sites of colorectal carcinoma (38%), followed by sigmoid (35%) and descending colon (18%). Only about 1% of tumors are present at multiple sites. Dietary habits constitute a predisposing factor for the development of colorectal carcinoma.

9. D. CEA was the first tumor marker to be used clinically. It is a complex glycoprotein, which is associated with the plasma membrane of tumor cells. An abnormal CEA blood level is not diagnostic for colon cancer or for any malignancy. CEA levels are elevated in a variety of cancers including colonic, pancreatic, gastric, lung, and breast carcinoma. It is also elevated in benign conditions such as hepatic cirrhosis, pancreatitis, and inflammatory bowel disease. CEA level may also be elevated in smokers and in the healthy population. Due to its low positive predictive value, CEA is not recommended as a screening test. On the other hand, CEA is used to monitor recurrence of colorectal cancer and it serves as a prognostic indicator for patients with colorectal carcinoma.

Final diagnosis and synopsis of the case

- Congestive heart failure (CHF)
- Microcytic hypochromic anemia
- Colonic adenocarcinoma

A 64-year-old woman presented with an acute exacerbation of her congestive heart failure (dyspnea, distended jugular veins, ascites, edema, and hepatomegaly). Her chest X-ray revealed pulmonary edema, which was also reflected in her arterial blood gases. The work-up for acute myocardial infarction was negative. The patient's cardiac condition improved considerably with supportive treatment of her heart failure. The rest of her laboratory work-up showed prerenal azotemia, most likely due to her congestive heart failure (reduced cardiac output and renal perfusion), microcytic hypochromic anemia, and a positive fecal occult blood (guaiac) test. Colonoscopy was performed and a colonic adenocarcinoma was diagnosed. The patient was referred to a specialist for further management.

Lab tips

B-type natriuretic peptide (BNP)

B-type natriuretic peptide is a 32-amino acid peptide secreted by the left ventricle in response to increased wall tension. This peptide promotes natriuresis, diuresis, and vasodilatation. The concentration of BNP serves as an indicator of high left ventricular end-diastolic pressure, a chief sign of congestive heart failure.

A low level of BNP will rule out congestive heart failure as an etiology of dyspnea. BNP level correlates with clinical severity of congestive heart failure, and serves as a prognostic indicator of CHF. Because of the short half-life of BNP (18–22 min), it will help to monitor a patient's response to therapy. BNP levels can be also elevated in primary pulmonary hypertension, renal failure, ascitic cirrhosis, and primary hyperaldosteronism.

Fecal occult blood test (guaiac test)

The guaiac test is a non-invasive, low-cost laboratory test that detects the presence of occult blood in stool. The test will be positive in conditions that lead to gastrointestinal bleeding. The guaiac test is one of several chemical indicators that will detect the peroxidase and the pseudoperoxidase activity of erythrocytes. A positive guaiac test indicates the presence of 5–10 mL of blood loss/day (normal gastrointestinal blood loss is approximately 2 mL/day).

False positive results can occur from ingested meats, certain vegetables and fruits, and a number of medications. False negative results have been noted with antioxidant ingestion (vitamin C, etc.).

This test is an important screening procedure for the early detection of colorectal carcinoma.

Test procedure:

1. Patient should have a high fiber diet with no meat, fish, turnips, horseradish, bananas, black grapes, pears, or plums for 2 to 3 days preceding and during the test (these foods have peroxidase activity).
2. Drugs that increase GI bleeding should be withheld (i.e. aspirin, iron compounds, steroids, indomethacin, etc.).
3. Three stool specimens are collected. A small amount of stool is placed on the test paper and mixed with water and reagents. The appearance of dark-blue color within 5 min represents a positive test for occult blood.