Leuko-Erythroblastic Anemia Due to Bronchogenic Carcinoma

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Standard descriptions of the clinical course and pathology of bronchogenic carcinoma generally are directed toward pulmonary effects and the symptomatology resulting from the more usual visceral metastases. The appearance of a leuko-erythroblastic anemia prior to the above is more unusual. Difficulty is encountered in establishing the etiology of this type of anemia, unless all elements of the differential diagnosis are carefully considered.

Case Report

A 61 year old white male was admitted to the Veterans Administration Hospital, North Little Rock, Arkansas, on March 22, 1949. The complaints were weakness, dyspnea, and pain in the left hip. He had been in fair health until December 1948 at which time the pain developed in the hip. There was a previous history of medical treatment for hypertension and arteriosclerosis. After the onset of the pain in the hip, he fell and struck that side of the pelvis. For this he was treated at another hospital. Laboratory studies showed an anemia and a positive blood serological test for syphilis. Treatment included seven blood transfusions and several injections of some type of antiluetic therapy.

History of primary venereal infection was not obtained and the remainder of the past history was not significant. There were no other complaints.

Physical examination on admission revealed an anemic, seriously ill white male. The skin was pale yellow. Respirations were rapid and shallow. Pulse was 112 per minute and regular. Blood pressure was 110/60. There was mild pharyngitis; elsewhere the mucosae were pale. The pupils were not remarkable. Heart and lungs showed no abnormal changes. There was moderate sclerosis of the peripheral and retinal arteries. The liver was palpated 5 cm. below the right costal margin and the spleen 3.5 cm. below the left costal margin. The lymph nodes were not enlarged. Weakness of the musculature was general and especially prominent in the right lower extremity. The superficial reflexes were diminished on the right; abdominal and cremasterics were absent. Sensory tests were within normal limits.

Laboratory data: On March 23, 1949, there were 2,900,000 erythrocytes per cubic millimeter, 7.5 grams of hemoglobin, hematocrit 28 cc. with mean corpuscular volume 96 and mean corpuscular hemoglobin 25. There

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were 9,800 leukocytes per cubic millimeter with a differential count of six eosinophiles, two basophils, six juveniles, 14 stabs, 54 polymorphonuclear leukocytes, and 18 lymphocytes. There were 14 nucleated red cells per 100 leukocytes counted. The sedimentation rate was 25 millimeters (corrected), bleeding time six minutes, and coagulation time three minutes. There were 31,900 platelets. The urine was acid, dark yellow, specific gravity 1.020, trace of albumin, negative sugar, and many uric acid crystals. The blood Kahn was four plus, with 10 Kahn units. On March 27, 1949, the total blood proteins were 6.20 grams per cent with 3.70 grams per cent of albumin, and an A/G ratio of 1.48:1; the blood uric acid was 2.2 mg. per cent; non protein nitrogen 58 mg. per cent, icteric index 13.5 units; acid phosphatase 0.14 Bodansky units, alkaline phosphatase 11.62 Bodansky units. Subsequent urinalyses were within normal limits, with no Bence-Jones protein found.

Examination of a specimen of sternal marrow on March 25, 1949, showed the cells to be scarce with some increase in younger forms of the myeloid series.

The cerebrospinal fluid on April 5, 1949, contained five cells, and 73 mg. per cent of protein. The Wassermann was positive, and the colloidal gold curve was 5555432000.

Repeated examinations of the peripheral blood showed variation of the erythrocyte count from 1,640,000 to 2,290,000 cells per cubic millimeter. There was between 4.5 and 5.25 grams of hemoglobin. The leukocyte count gradually rose to 17,500 per cubic millimeter with a continued shift to the left. There was a rise in number of nucleated red cells in the peripheral blood to a maximum of 43 per 100 leukocytes counted on April 15, 1949.

On March 23, 1949, a roentgenogram of the chest showed minimal areas of plate-like atelectasis in the right lung base, with evidence of elongation and tortuosity of the aorta. There was advanced deforming spondylosis of the dorsal spine. On April 4, 1949, examination of the skull and long bones was within normal limits with the exception of minimal sclerotic changes of the right ilium in the region of the acetabulum and in the upper end of the shaft of the right femur near the lesser trochanter.

Treatment included transfusions of 1000 cc. each of whole blood on April 8 and 14, 1949. Penicillin and ferrous sulfate were administered. The patient remained weak and showed no response to the above. There were no chest complaints. The pulse continued weak and rapid. On April 13, 1949, the temperature was elevated for the first time to 99.6 degrees Fahrenheit, and remained between 99 and 100 degrees until death on April 16, 1949.

Autopsy findings: The examination was performed on the day of death. Only the pertinent findings are presented. A small bronchogenic carcinoma was found with diffuse granular gray white involvement of the adjacent parenchyma of the left lung. Similar gray streaks were present in the right lung parenchyma. Enlarged lymph nodes involved by neoplasm were seen in the mediastinum, near the bifurcation of the trachea and in a peribronchial location. A neoplastic nodule was discovered in the left adrenal gland. No other metastases were in evidence. The bone marrow of the ribs was scanty and pale gray. In the vertebrae the marrow was dry, pale, red gray, with no obvious trabeculations.

Other interesting gross findings were numerous small, pale red, friable, irregular vegetations averaging less than two millimeters in diameter on
the mitral valve of the heart. Two similar larger vegetations were on the aortic valve. All had smooth glistening surfaces. The chordae tendineae of the mitral valve were shortened and thickened. In the spleen were several wedge shaped infarcts. The brain weighed 1270 grams and showed atrophy of the convolutions with thinning of the cortex most prominent in the frontal lobes.

Microscopic examination of the lung and bronchus sections showed involvement of the bronchial epithelium and submucosa by neoplasm. There was diffuse invasion of the pulmonary parenchyma. Lymphatics and blood vessels adjacent to the bronchi contained groups of neoplastic cells. There was some involvement of the visceral pleura. The neoplastic cells occurred in groups and strands, with some tendency to gland formation. The nuclei were oval or irregular and hyperchromatic. The cytoplasm was moderate in quantity and pale eosinophilic. There was pleomorphism. Occasional mitotic figures were noted. The larger masses of neoplasm showed areas of necrosis.

A large bronchial lymph node was almost completely replaced by neoplasm with invasion of the adjacent connective tissue. Similar changes were observed in other lymph nodes. Some intravascular groups of neoplastic cells were found in a section of the pancreas. The left adrenal gland showed almost complete replacement by neoplastic tissue. There was marked tendency to glandular arrangement. Considerable necrosis was present, and the neoplastic cells occurred in strands along the cortical cords. There was invasion of the periadrenal adipose tissue.

The marrow sections obtained from rib showed partial to complete replacement of the marrow spaces by neoplastic cells and fibrous tissue. Some bony spicules were intact; others showed osteolytic changes. Hematopoietic tissue was not observed in several rib sections. In the vertebrae there was invasion by neoplastic tissue, fibrosis, and considerable necrosis. Small areas of active erythropoiesis were seen.

Sections of the spleen showed the infarcts. Hematopoietic tissue was not observed here nor in the liver. Cerebral cortical changes were consistent with the clinical diagnosis of paresis.

Comment

In the case presented, the bronchogenic carcinoma was obscured by the absence of respiratory tract symptoms. The admission examination suggested an anemia. Investigation of this disclosed a leuko-erythroblastic anemia. Further investigation for possible etiological factors failed to incriminate the lungs or other sites of primary malignancy and the tentative clinical diagnosis was myelofibrosis.

The appearance of an anemia with not only a large number of circulating nucleated red cells in the peripheral blood, but also an increase in immature forms of the myeloid series suggests a space occupying disorder of the bone marrow. Differential diagnoses should include metastatic carcinoma to bone marrow, multiple myeloma, myelosclerosis, Albers-Schonberg disease, and various disorders of the reticulo-endothelial system.

The common factor to these various diseases appears to be some
degree of loss or replacement of marrow from neoplastic invasion, necrosis, fibrosis, or other degenerations. The blood picture resulting from these pathological changes shows features other than those expected alone from destruction of marrow. Some cases show areas of active erythropoiesis adjacent to masses of carcinoma cells or regions of necrosis of marrow. Some degree of marrow stimulation appears to be present in leuko-erythroblastic anemia. There is discussion of the effect of toxicity of the various diseases on the marrow causing both a stimulation as well as destruction; another suggestion has been the loss of essential nutrients to the marrow due to the presence of the neoplastic cells.

Metastatic carcinoma appears to be the most frequent of the etiological factors in production of leuko-erythroblastic anemia. Primary malignancies should be searched for in the various organs, particularly in the prostate, breast, lungs, thyroid, kidneys, adrenals, and gastrointestinal tract. Bone marrow studies often offer aid in establishing the diagnosis.

Bronchogenic carcinoma is notorious for its ability to metastasize widely. Nevertheless, it is unusual to find the blood changes of a leukoerythroblastic anemia before the primary neoplasm or some of the other visceral metastases. In this case, the positions of the primary neoplasm and metastases to organs other than the reticuloendothelial system were not obvious clinically, nor even after studies of the blood and marrow. The absence of any respiratory signs or symptoms was particularly important and failed to provide a lead for further diagnostic studies in this system.

Pathologically this case is of interest in that the tendency to glandular arrangement of the neoplastic cells was more apparent in the metastases than in the lung. No evidence of myeloid metaplasia was found in the liver, spleen, or other organs. Splenomegaly was due to infarcts associated with an endocarditis. The marrow showed degenerative changes due to neoplastic infiltrates, and there was considerable necrosis and fibrosis.

CONCLUSIONS

1) A case of bronchogenic carcinoma is discussed in which leuko-erythroblastic anemia was the most important clinical finding. 2) Differential diagnosis of this type of anemia is discussed.

REFERENCES


