

*Case report***Sideroblastic anemia as the first presentation of squamous cell tongue carcinoma**K.H. Katsanos, M. Kitsanou, G. Alexandridis, E. Ioakeim¹, V. Daniilidis², K.L. Bourandas, E.V. Tsianos**SUMMARY**

A 60 year-old man was admitted to our department because of progressive weakness and a 10 kilogram weight loss during the previous 2 months. The patient was a tobacco and alcohol abuser and had no previous hospital admissions. Physical examination revealed anemia and hand flapping. Laboratory exams revealed anemia (Ht=24%, Hb=7,9g/dl), decreased reticulocytes (25.000/mm³), elevated serum ferritin (1390ng/ml) and increased transaminase levels. Bone marrow biopsy revealed sideroblasts, maturation abnormalities of the red row and infiltration of malignant cells unknown origin. Further investigation revealed a well differentiated, very small in size, squamous cell carcinoma of the tongue. We discuss the role of alcohol and tobacco abuse in relation to oral cavity malignancies and to sideroblastic anemia. To the best of our knowledge it is the first case of tongue carcinoma presenting with sideroblastic anemia.

Key words: squamous cell tongue carcinoma, sideroblastic anemia, bone marrow infiltration, alcohol, tobacco.

INTRODUCTION

Alcohol abusers may be presented with sideroblastic anemia. Sideroblastic anemia is a descriptive term applied to an heterogeneous group of disorders of unknown cause and characterized by anemia, reticulopenia, ele-

vated serum iron and ferritin levels and ineffective erythropoiesis. Sideroblastic anemia is caused by a diversity of hereditary, congenital or acquired disorders secondary to a variety of agents.^{1,2} Instances of acquired sideroblastic anemia have been described in association with myxedema, hemolytic anemia, thalassemia, infectious mononucleosis, malignant histiocytosis, uremia, celiac disease, systemic lupus erythematosus, allogenic bone marrow transplantation, chemotherapy for HodgkinAs disease, porphyria, chronic lymphocytic leukemia, zinc-induced copper deficiency, lincomycin therapy, D-penicillamine therapy and polyarthritis nodosa. Neoplastic conditions may also be presented with sideroblastic anemia which is sometimes referred to as paraneoplastic sideroblastosis.³

The diagnostic and morphologic hallmark for sideroblastic anemia is ring sideroblast. Another name for this cell is siderocyte containing basophilic granular-appearing inclusions named Pappenheimer bodies.⁴ The sideroblastic anemias display remarkable clinical and hematologic heterogeneity but share common mitochondrial iron loading as evidence of unhinging between intracellular iron metabolism and heme biosynthesis. Molecular defects responsible for this unhinging have now been identified and appear to display matching heterogeneity. Mutations in the erythroid-specific alanine synthase 2 (ALAS2) gene cause microcytic anemia, whereas mitochondrial DNA deletions are responsible for Pearsons syndrome with macrocytic anemia.⁵ A 60 year-old man diagnosed with sideroblastic anemia due to a very small in size squamous cell tongue carcinoma is presented.

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CASE REPORT

A 60 year-old man was admitted to our department because of progressive weakness, dyspnea and a weight loss of approximately 10 kilograms during the previous 2

months. The patient had been a tobacco and alcohol abuser for the last 10 years and had no previous hospital admissions. Physical examination revealed a very thin, neoplastic-looking, person with anemia and with no history and no evidence of upper or lower gastrointestinal bleeding. No lymphnodes were palpable and nothing remarkable was on his abdomen or thorax. Laboratory exams revealed anemia with Ht 24% (Hb 7.9g/dl), normal platelet and white blood cell count. ESR was 60mm/h and C-reactive protein was negative. Biochemical profile showed AST 90 UI/L, ALT 54 UI/L, and γ -GT 167 UI/L. Bilirubin was within normal limits and direct and indirect Coombs were negative. Further investigation of this anemia revealed: reticulocytes 25.000/mm³, iron 98 μ g/dl, ferritin 1390 ng/ml, B12=847pg/ml, and folic acid 4,6ng/ml.

Tumor markers and the hepatoviruses (A,B,C,E) serology proved negative. Elisa tests for cytomegalovirus, Epstein-Barr virus and herpes simplex virus were within normal limits. Chest X-ray and gastrointestinal endoscopy were within normal limits. As clinical suspicion of sideroblastic anemia due to alcohol and tobacco abuse was strongly supported in this case a bone marrow smear was performed and revealed iron excess (ferrum +4), sideroblasts, maturation abnormalities of red row (Figure 1), and infiltration of unknown origin malignant cells (Figure 2). Bone marrow biopsy showed nothing of interest as lymphocytes, myelocytes and megacaryocytes appeared within normal limits.

Further investigation to find this unknown primary malignancy revealed a well differentiated, very small in size, squamous cell tongue carcinoma resulting in a slight

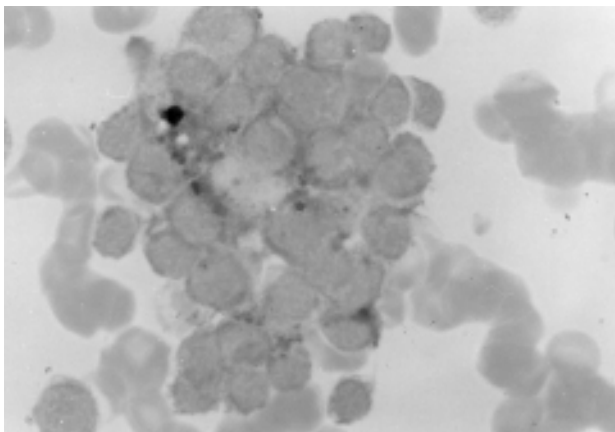


Figure 1: Iron stain in bone marrow biopsy. Findings compatible with sideroblastic anemia (iron excess, sideroblasts, maturation abnormalities of red row).

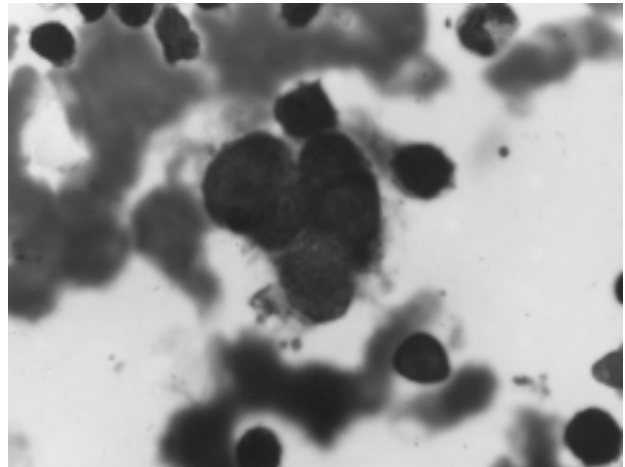


Figure 2: Infiltration of malignant cells in bone marrow biopsy. Their origin was a tongue carcinoma.

asymmetry of the stomatopharynx and altering the shape of the lower left part of the oral cavity (Figure 3). The left sublingual nerve was also slightly affected.

Neck computed tomography reconfirmed the diagnosis and showed absence of regional lymphnodes. Brain CT-scan showed cerebral atrophy while abdominal and thoracic computed tomography were within normal limits. The tumor was surgically removed and the patient followed radiation courses with good results; meanwhile he decided to give up alcohol and smoking. At the 3 month-follow up anemia was more or less corrected and bone marrow smear was within normal limits with no evidence of neoplastic cell infiltration. One year later the patient lives in excellent health.

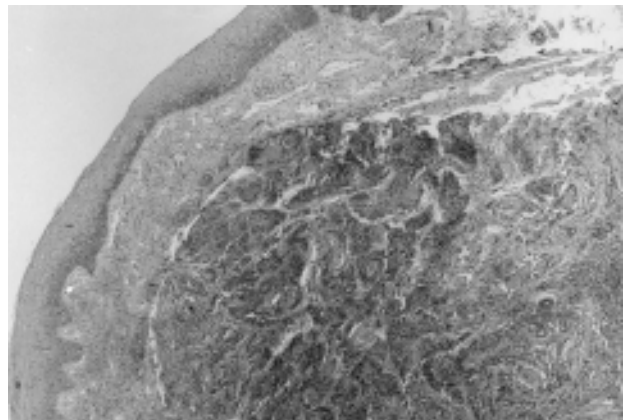


Figure 3: Well differentiated squamous cell tongue carcinoma in an alcohol and tobacco abuser presenting with sideroblastic anemia.

DISCUSSION

Alcoholic patients who present with sideroblastic anemia can pose a diagnostic challenge. Although deficiencies of iron, vitamin B12 and folate commonly result in anemia, bone marrow suppression of red blood cell production related to the direct toxic effects of alcohol can cause a form called sideroblastic anemia.⁶ The abnormal haem biosynthesis in chronic alcoholics results in anemia in which the hematocrit cannot always be predicted. Moreover severe anemia in an alcoholic and smoker should always imply the possibility of a coexistent malignancy because smoking and alcohol consumption are risk factors for leukoplakia and precancerous lesions of the oral cavity; keratosis, dysplasia and lichen tuber planus.⁷ Improvement in nutritional uptake and efficient amounts of vitamin B₆, (pyridoxine) folic acid and magnesium in an alcohol-induced sideroblastic anemia is not always enough. It is essential to exclude this so-called paraneoplastic sideroblastosis apart from the alcoholic sideroblastosis⁸, searching carefully in the bone marrow smear for malignant cells or/and screening target organs that are usually affected by alcohol and smoke: lungs, pharynx, gastrointestinal tract.

Impaired iron uptake by erythropoietic cells in malignancies as well as in myelodysplastic syndromes results in an increased iron flow into the reticuloendothelial iron stores.⁹ The degree of hyperferritinemia parallels very closely the severity of anemia becoming more pronounced with the increasing size of tumor. This parallelism indicates that siderosis is pathophysiologically related to the defect of erythropoiesis observed in malignant disease.³ The distinguishing therapeutic aspect of the sideroblastic anemia due to malignancy is that this so called paraneoplastic sideroblastosis can disappear or ameliorate after removing the malignant tumor¹⁰, which also happened in our case.

Early squamous tongue carcinoma can be effectively treated by surgery and/or radiation therapy offering a

satisfactory enough prognosis, good results and an acceptable quality of life. This approach, however, may not always be translated into longer survival times until effective chemotherapy is available to control distant metastases.⁷ Diagnosis of sideroblastic anemia among ethanol consumers should always be carefully followed up and sometimes further investigated in order to exclude other curable forms of malignancies.

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