Extramedullary hematopoiesis within endothelial papillary hyperplasia (Masson's pseudoangiosarcoma) of the tongue

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ABSTRACT

We report the unique association of Masson's pseudoangiosarcoma (endothelial papillary hyperplasia) and extramedullary hematopoiesis. The lesion was present as a violaceous nodule on the side of the tongue of a 78-year-old man with history of multiple myeloma and long-standing mild anemia. This association between a peculiar form of thrombus organization and extramedullary hematopoiesis has been reported previously only once, in an infant with a cranial hematoma, and raises interesting pathogenetic questions.

Key words: *Extramedullary hematopoiesis, intravascular endothelial papillary hyperplasia, tongue, thrombus organization.*

INTRODUCTION

Endothelial papillary hyperplasia (Masson's pseudoangiosarcoma, vegetant intravascular hemangioendothelioma), regarded nowadays as an unusual form of organizing thrombus (1), occurs usually as dermal or subcutaneous nodules on the head, neck, fingers and trunk. It has also been reported in the oral cavity, with most cases involving the lower lip and the tongue (2-7). Extramedullary hematopoiesis (i.e., the occurrence of hematopoiesis outside the bone marrow) has also been occasionally described in a variety of tumors, as an incidental finding or in the context of haematological disease (8-10).

We report on the unique association of extramedullary hematopoiesis and endothelial papillary hyperplasia of the tongue in a patient with long-standing anemia due to multiple myeloma.

CASE REPORT

A 78-year-old Caucasian male was seen at the Dermatology Clinic of the Hospital General de Elda (Alicante, Spain) in May of 1992 for evaluation of a violaceous nodule on the lateral tongue, which had been present for six months. In 1987 the patient had been diagnosed as having multiple myeloma stage I-A, and invasive high grade transitional cell carcinoma of the bladder, for which he had received 9 cycles of melphalan-prednisone and one cycle of onco thiotepa chemotherapy.

On physical examination, a 1.5 cm rubbery violaceous nodule covered by non-ulcerated mucosa was seen on the right lateral border of the tongue (Figure 1). A punch biopsy was performed, and two fragments of tan rubbery tissue, grossly resembling blood clot and measuring up to 0.5 cm in diameter were obtained. The lesion collapsed after the procedure. Microscopically, a rounded mass of fibrin (with no evidence of a vascular wall at the periphery on elastic tissue staining) showed an excentric irregular lumen bordered by papillary endothelial hyperplasia (Figure 2). Conspicuous foci of extramedullary hematopoiesis were present near the lumen, consisting mostly of red cell precursors, with an admixture of myeloid cells (including rare eosinophilic

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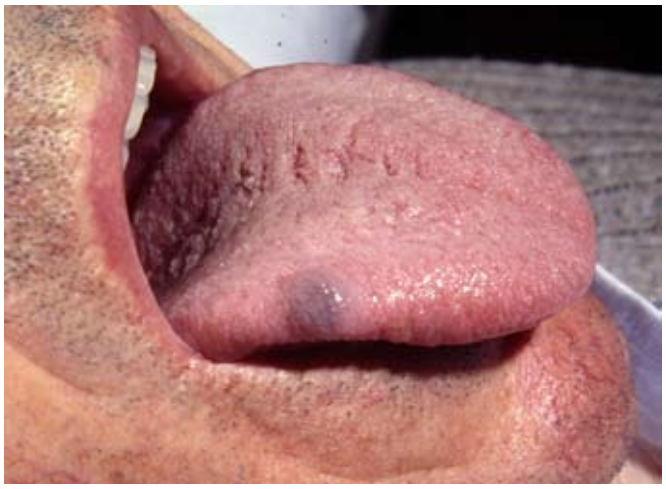

Fig. 1. Clinical photograph of a violaceous nodule on the right side of the tongue.

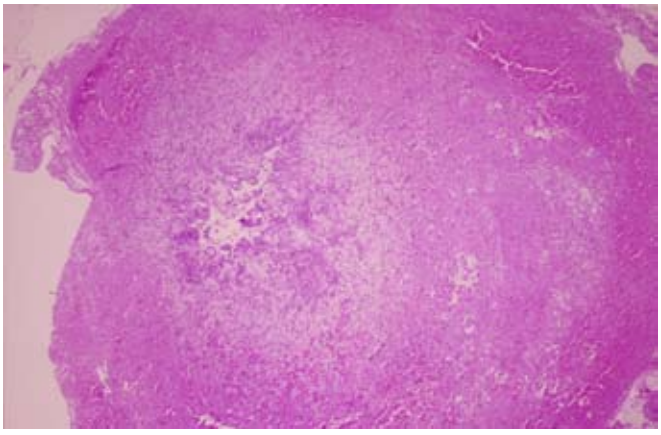

Fig. 2. Microscopic low-power view of the lesion, consisting of blood clot and loose connective tissue surrounding a jagged-contoured lumen.

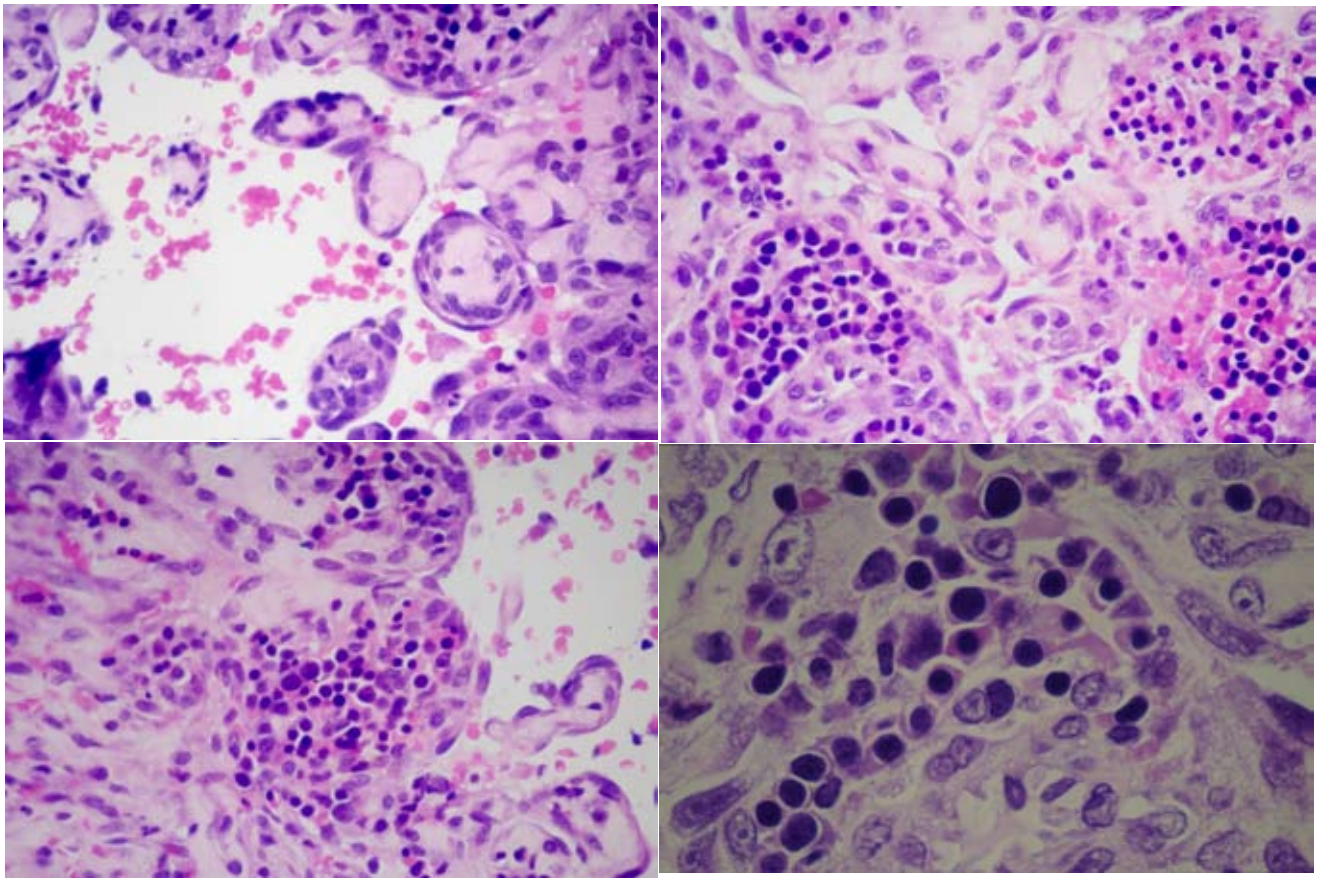

Fig. 3. Coexistence of papillary endothelial hyperplasia and extramedullary hematopoiesis.

cells) (Figure 3). No clear-cut megacaryocytes were identified. No tissue was available for further histochemical or immunohistochemical studies.

Subsequent hematological evaluation yielded the following results: Hemoglobin, 11.5 g/dL , Erythrocyte Count 3.76 x1012/L , Hematocrit 35.2% , MCV 93.7 µm3, MHC 30.7 pg/cell , MCHC 33 % Hb/cell, Platelets 342 x109/L, Leukocytes 6.8 x 106/L (Neutrophils 0.44, Lymphocytes 0.42, Monocytes 0.08, Eosinophils 0.05, Basophils 0.05). No tear-drop shaped erythrocytes or erythroblasts were identified on peripheral blood films, where the percentage of plasma cells was evaluated as 3%.

The patient's clinical course was complicated by paraplegia due to spinal cord compression. He suffered several respiratory infections which required hospital treatment, and died at home in October of 1993, due to bilateral bronchopneumonia.

DISCUSSION

Masson's pseudoangiosarcoma (endothelial papillary hyperplasia), nowadays interpreted as a form of thrombus organization is usually seen as dermal or subcutaneous nodules on the head, neck, fingers and trunk. It has occasionally been reported in the oral cavity2 where -after the lips- the tongue is one of the most frequent sites of oral involvement (3-7).

Although usually arising within vascular spaces (hence the designation intravascular endothelial papillary hyperplasia), some examples arising apparently in extravascular sites have been reported (11-12). In our case a vessel wall was histologically not identified, but there is indirect evidence that the lesion lodged within a vascular space, namely the clinical site (not unusual for lingual thrombosed varices (13), the apparent collapse after biopsy, and the rounded contour of the submitted material with an excentrically placed lumen.

Exramedullary hematopoiesis (EMH) is defined as the occurrence of hematopoiesis outside the bone marrow. It is usually seen in association with haematological disorders, particularly idiopathic myelofibrosis (14) and thalassemia and other causes of anemia. In this setting it most frequently involves the spleen and the liver, but many other organs can be affected, including the mediastinum or paraspinal region, where EMH can form tumor-like masses (15). As an isolated finding in tumors in otherwise healthy subjects, it has been reported in an ever-growing list that includes meningioma (16), pilomatricomas (9), pyogenic granulomas (10), spindle-cell lipoma (17), and mammary fibroadenoma (18).

Extramedullary hematopoiesis has been previously reported only once in association with papillary endothelial hyperplasia (19). In this paper, the case of a 12-day-old infant with a right middle cranial fossa hematoma was described. The resected mass consisted of thrombotic material organizing in a florid papillary pattern, in proximity to reactive fibroblasts, chronic inflammatory cells and foci of extramedullary hematopoiesis (19). The authors hypothesized that the organizing hematoma could have been superimposed on a pre-existent vascular malformation or hemangioma.

The coexistence of an organizing thrombus and EMH raises interesting pathogenetic issues. It has long been know that reorganization of thrombi and emboli is carried out by blood mononuclear cells capable of differentiation into macrophages, endothelial cells and fibroblasts/myofibroblasts (20). These mononuclear cells are primarily derived from the bone marrow and include CD133/VEGFR2 endothelial progenitor cells as well as myeloid cells, and other circulating progenitor cells ("side population") (21). On the other hand, EMH has been explained by a number of theories: the splenic filtration theory (not valid for patients without a history of splenectomy), the theory that EMH is a compensatory phenomenon elicited by bone marrow fibrosis (which does not explain EMH in the absence of fibrosis and anemia), and the myelostimulatory theory (only applicable to organs involved in adult or fetal hematopoiesis). The most recent proposition is the "redirected differentiation theory" (22): cytokines secreted either aberrantly or in response to chronic anemia could induce adult stem cell populations on non-hematopoietic organs to differentiate into cells of the hematopoietic lineage.

In our case, the microenvironment of organizing thrombus seems to have harboured not only cells capable of endothelial differentiation –of whichever origin- but also cells giving rise to hematopoietic elements.

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