TESTING YOUR DIAGNOSTIC SKILLS

The Diagnostic Quiz and Discussion series is offered by Dr. Ron Baughman of AmeriPath/Central Florida, section of oral, head and neck pathology and contributing Florida private practitioners. The series is a self-assessment and review for Florida Dental Association practitioners. Dr. Baughman solicits cases from private offices.

Case No. 1

Dr. Michael Cassatly of Jupiter saw an 81-year-old woman because her tongue was ulcerated, painful and enlarged (Fig. 1). The patient said her tongue had been growing for at least two to three months. She had been hospitalized two months earlier for congestive heart failure and had fluid drained from her shoulder on two recent occasions. A head and neck examination revealed marked firmness and enlargement of submandibular tissue and the tongue was extremely indurated and sensitive to palpation. Which one of the following was the patient's most likely diagnosis, based on the clinical photograph and history provided? Read the discussion for the surprising biopsy proven diagnosis and a better understanding of the offending disorder.

A. Histoplasmosis
B. Squamous cell carcinoma
C. Amyloidosis
D. Tuberculosis
E. Metastatic carcinoma

Figure 1

DIAGNOSTIC DISCUSSION

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Case No. 1 C. Am

The obvious first choice is squamous cell carcinoma, based on the patient's age, clinical lesions and history. However, when Dr. Cassatly sent me a biopsy from the tongue, it did not exhibit cancer. There was normal surface epithelium with an underlying hylanized pink fibrous stroma. The stroma's dense, pink nature was mildly suggestive of amyloid, a nonspecific proteinaceous precipitate. When stained with Congo red and submitted to polarized light, the stroma produced a birefringent apple-green color that is considered diagnostic for amyloid. I called Dr. Cassatly to discuss the findings and explore the patient's history because the presence of amyloid usually signals a very serious and potentially fatal disorder. The patient's physician did a diagnostic work up. As it turned out, the patient had a systemic, multiorgan deposition of amyloid known as amyloidosis.

Amyloidosis can have several origins. Amyloid is a protein precipitate that is fibrillar in nature. Known causes include lymphoid or plasma cell dyscrasias. Multiple myeloma, a plasma cell malignancy, is the most common cause if the patient manifests systemic amyloid distribution. Hemodialysis; long-term infectious processes, such as tuberculosis; histoplasmosis; and sarcoidosis can be causative. There also is a rare heredofamilial form. The disease can be limited to a few organs or have systemic distribution. Organ-limited amyloidosis usually is not serious, but the systemic form generally results in death from heart or kidney failure because those organs become so infiltrated with amyloid that they no longer can function.

So called secondary amyloidosis typically is found in patients who have long-term osteomyelitis, chronic fungal disease, sarcoidosis or tuberculosis. Different types of amyloidosis can contain different microglobulin fractions. Amyloid also is found in the brains of Alzheimer's disease patients. This patient proved to have multiple myeloma (MM), a plasma cell malignancy. Plasma cells evolve in the bone mar- row from B-lymphocytes and function in humoral immunity by producing immunoglobulins. MM patients demonstrate a monoclonal antibody spike when serum immunoelectrophoresis is performed. That occurs because there are millions of malignant plasma cell clones that generate an identical immunoglobulin fraction, which results in a pronounced hyperglobulinemia. The MM-produced immunoglobulins are light chain antibodies. They can become so concentrated in the serum that they precipitate into various organs to produce clinical amyloidosis. Affected patients may develop congestive heart failure from advanced deposition of amyloid in the cardiac muscle. That phenomenon can progress to produce heart failure when the amyloid protein replaces too much muscle. Similar deposits in the kidneys may produce renal failure. When excess proteins spill into the urine, they are known as Bence Jones protein.

The process can progress to involve multiple organs. In such cases, oral involvement is most common in the tongue and gingivae. There is disagreement about which more often is involved, but recent reports indicate it is the tongue. Another commonly involved oral organ is salivary gland tissue, particularly the submandibular glands. That phenomenon, as seen in this case, easily can be confused with metastatic carcinoma because it produces very indurated masses in the floor of the mouth, consistent with tumor-filled nodes. If glandular involvement becomes more extensive, affected patients may develop significant xerostomia because of destruction of the gland's acinar tissue. Some patients develop ecchymotic lesions, which may become hemorrhagic, around the lips and intraorally. Secondary amyloidosis patients also may have hyperglobulemias, but not because of a single globulin fracion. Long-term dialysis patients can develop amyloidosis because certain globulin fractions are not removed from the blood during dialysis. This allows them to build up in the patient's serum to the point of precipitating into the body's tissues.

Clinical diagnosis of amyloidosis can be very difficult in the early stages of the disease. In retrospect, this patient's congestive heart failure and shoulder-fluid accumulations most likely were secondary to the amyloidosis her MM produced.

The key to obtaining a diagnosis for this patient's serious systemic disease was a tongue biopsy, which led to the identification of amyloid and the systemic work up. After several weeks of chemotherapy, the patient's tongue and submandibular gland lesions regressed significantly.

References

1. Van der Waal RFI, va de Scheur MR, et al, Amyloidosis of the tongue as a paraneoplastic marker of plasma cell dyscrasia, Oral Surg Oral Med Oral Pathol Oral Radol Endod, 2002; 94:444-7.
2. Neville BW, Damm DD, Allen CM, Bouquot JE, Oral and maxillofacial pathology, 2nd ed, Philadelphia: 2002; p. 526, 710-12.