

## Letters to the Editor

### Myoepithelioma of the submandibular gland occurring after cardiac transplantation

*To the Editor:* Myoepithelioma is a tumor composed entirely or almost exclusively of myoepithelial cells. It is an uncommon neoplasm, accounting for less than 1% of all salivary gland tumors. Immunosuppressed recipients of human donor organ grafts have an increased incidence of neoplasia.<sup>1</sup> This represents an effect of long-term immunosuppressive therapy. In the present report we present a case of myoepithelioma of the submandibular gland occurring in a cardiac-transplanted man. To the best of our knowledge no case of such an association has been reported.

A 61-year-old man underwent a heart transplantation in March 1992. He required it for the treatment of severe left ventricular failure after cardiac valve surgery. The patient has been treated since 1992 with an immunosuppressive regimen consisting of a combination of CSA, prednisone and azathioprine. On June 1995, he was admitted to the hospital for excision of an asymptomatic mass in the right submandibular gland. The mass had been present for 14 months after heart transplantation. Physical examination revealed a firm, non-tender, nonfluctuant and freely movable mass. Excision of the gland was performed.

Gross examination of the submandibular gland showed at the transection a well-circumscribed nodule, 13 cm in diameter, embedded in the gland. The tumor was whitish, firm and it showed a paracentral cyst filled with mucoid fluid. The remains of the gland were normal. Microscopically, a well-delineated tumor mass was separated from the surrounding salivary gland by a thick hyalinized connective tissue capsule. The neoplasm was solidly packed with uniform epithelial cells and a scant, hyalinized stroma (Figure 1). The tumor cells were spindle-shaped, with centrally placed nuclei containing delicately dispersed chromatin and a thin nuclear envelope. The nuclei occupied most of the cell bodies. The cells were bipolar, with slightly eosinophilic cytoplasm which varied from granular to fibrillar. The stroma was characterized by the presence of an amount of amorphous and acellular material in which a few fibroblasts and small collagen fibers were scattered. The tumor contained a few small isolated intercalated ducts; they were lined with a single layer of small cells with round and dense nuclei. The number of ductal structures was 0.4 in every 220x magnification field. The central cyst was lined by a single layer of flattened ductal epithelium. The neoplastic cells were diffusely positive for anti-human alpha-smooth

muscle actin, anti-vimentin, and anti-S-100 protein, and were negative for anti-keratin cocktail CK22. The DNA histogram showed a diploid pattern, GO-GI, S and G2+M phase fractions were 94.5%, 3.4% and 2.1% respectively. Coefficient of variation was 8.9%. With all these findings, the pathological diagnosis was spindle-cell myoepithelioma.

The incidence of the novo neoplasms in patients who have received solid organ transplants is of 3% to 11% within the first year and up to 21% after five years.<sup>2</sup> Lanza et al.<sup>3</sup> reported a 10% incidence of malignant neoplasms in 53 patients who underwent cardiac transplantation. This incidence was approximately 100 times greater than that of the matched general population, and more than double that in recipients of donor kidneys at the same institutions.<sup>3</sup> The higher incidence of malignant tumors in the cardiac transplant recipients was related to a heavier immunosuppressive regimen. The increase of cancer in transplanted patients is very selective. After introducing CSA in immunosuppressive regimens, the most common tumors, in order of frequency, are lymphoma, skin and lip carcinoma, Kaposi's sarcoma, cervix carcinoma, and vulva-perineum carcinoma.<sup>2</sup> The cause of tumors associated with solid organ transplantation is not simply due to immunosuppression interfering with immune surveillance mechanisms. If this were so, one would expect a generalized increase of all tumors rather than the very selective increase that occurs. This selection suggests that there can be other factors responsible.<sup>2</sup> Viral infections are very common in transplant patients, especially Epstein-Barr virus, herpes simplex virus, and cytomegalovirus (CMV). Some of these have been shown to be oncogenic. CMV infection is higher in heart recipients.<sup>2</sup> Oncogenic viruses need a cofactor. In the transplanted patients the main cofactor may be chronic immune stimulation by the

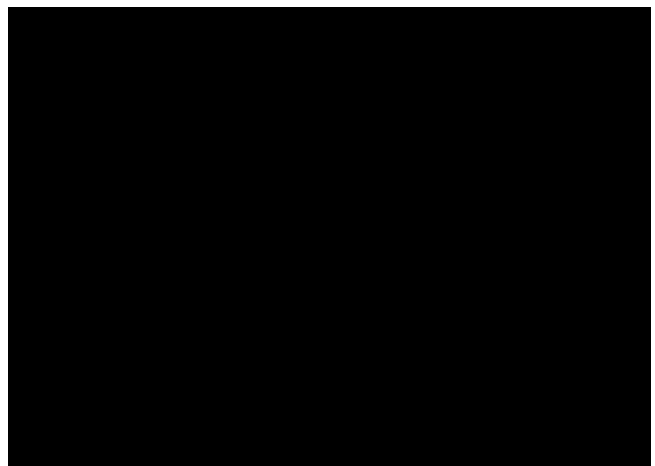


FIGURE 1. Tumor cells are arranged in broad strands and the stroma is of a delicate eosinophilic hyalinized material (hematoxylin and eosin, 10x).

allograft. It has also been proposed that immunosuppression could have a direct cellular effect, causing chromosome aberrations; and it might also potentiate environmental carcinogens.<sup>2</sup> Nevertheless, any other neoplasm occurring in the general population can occur in the transplant recipients, but with no increased incidence. According to this, tumors such as lung, breast, prostate, and colorectal carcinoma will be found with the standard frequency. The recipient's age will determine the incidence of such neoplasms. Cancer development with time following transplantation reveals progressive logarithmic increase; between 30 and 40 years after transplantation virtually all patients are expected to have some form of cancer.<sup>4</sup> Birkeland cited a case of carcinoma of the parotid gland in a kidney transplanted patient.<sup>1</sup> To the best of our knowledge no case of salivary gland myoepithelioma has been observed in recipients of solid organ transplants. However, this association could be coincidental. Data characterizing cellular DNA content of myoepithelioma have been scarce in the literature. In a study of Carrillo et al.,<sup>5</sup> all the grade I myoepitheliomas (encapsulated tumors without cellular atypia) were diploid, with low proliferative activity (less than 4% of cells in S-phase). None of these tumors recurred. On the contrary, DNA aneuploidy and high proliferative activity correlates with a malignant potential. DNA aneuploidy of the myoepithelial component in pleomorphic adenomas also correlates with an aggressive clinical behavior. Thus, DNA flow cytometry may yield important prognostic information about myoepithelioma.

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#### Melanotic neuroectodermal tumor of infancy in a child

*To the Editor:* Melanotic neuroectodermal tumor of infancy is a rare, well-documented and specific entity of a recognizable neoplasm with a predictable biological behavior.<sup>1</sup>

This benign tumor is seen exclusively in infants less than one year old. It often presents on the maxilla, extramaxillary fontanelle, skull, shoulder, posterior mediastinum and epididymis. Rapid growth, origin from and invasion of bone and the histologic appearances of this tumor often lead to a misdiagnosis of malignancy.<sup>2</sup> The rarity of reports of melanotic neuroectodermal tumor of infancy in the Arab literature prompted us to write this case report.

A six-month-old baby girl was presented to the outpatient clinic of the Dental Specialist Centre in Arar, Saudi Arabia, because of a lesion in the incisor area of the anterior region of the maxilla. The lesion had increased in size over the previous week. Physical examination on 4 August 1993 revealed a firm enlargement of the gum in the anterior part of the maxilla. The mucosa covering was smooth. The swelling measured 2 x 2 cm. There were no palpable cervical lymphonodes. An excisional biopsy was done. Gross examination showed a tissue measuring 1.5 x 1 cm, cut section was nonhomogenous and grayish brown in color. Microscopic examination showed cellular fibrous tissue stroma with epithelial-like cells. The cells were large, polygonal, containing melanin pigment, arranged in sheets and in groups, and gland-like structures were seen (Figure 1). In addition, lymphocyte-like cells with considerable variation were noted. Histological diagnosis of melanotic neuroectodermal tumor of infancy was made. Parts of the specimen, block and slide were sent to King Faisal Specialist Hospital and Research Centre for confirmation and further studies. Follow-up over 2 1/2 years revealed no recurrence and the child is in good health with healthy incisors.

This patient's lesion was alarming at the clinical and histopathologic levels. Clinically it was a firm mass with grossly visible pigmented areas, and measured more than 1.5 cm. The increase in size over a short period was an additional worrisome feature, warranting the differential diagnosis of a nodular melanoma, especially in a Saudi setting, where oral melanomas are proportionally overrepresented; however, the microscopic appearance of the lesion mitigated against this possibility despite the presence of melanin pigmentation and mitosis within the lesion. All other features were diagnostic of melanotic neuroectodermal tumor of infancy.

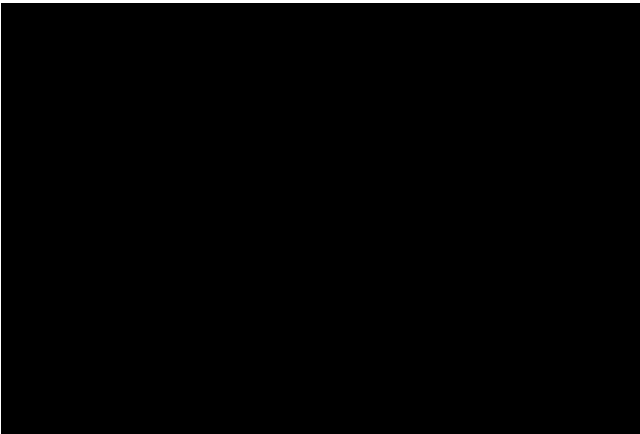


FIGURE 1. Photomicrograph showing cellular fibrous tissue stroma with epithelial-like cells containing melanin pigment, arranged in sheets and in groups, showing glandular pattern (Hematoxylin and eosin, 200x).

Melanotic neuroectodermal tumor of infancy is a benign neoplasm, probably of neural crest origin.<sup>3</sup> The most common site is the anterior maxilla, as in our patient, and it generally presents as an osteolytic, rapidly enlarging swelling. The tumors are firm with pigmented areas. Microscopy commonly reveals tubular or alveolar nests of cells separated by a vascular fibrous stroma. The peripheral cells in the nests are larger, cuboidal or flattened, and some contain melanin. The neuroblastic cells in the centre of the nests are small and round with hyperchromatic nuclei. This tumor has a distinctive immunophenotypic profile.<sup>4,5</sup>

Treatment is conservative excision with a good prognosis,<sup>6</sup> as evident in our patient, but there are occasional recurrences.<sup>7</sup> Melanotic neuroectodermal tumor of infancy may simulate a malignant neoplasm on clinical grounds. A detailed histopathologic examination will exclude this possibility.

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