Granular cell tumor of the female genital system. Clinical and pathologic characteristics of five cases and literature review

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Summary

The clinical and pathological characteristics of a rare granular cell tumor that developed in the vulva (4 cases) and the breast (1 case) offive women aged 35-52 years are reported. The differential diagnosis from skin carcinomas, melanoma and various soft tissue tumors is emphasized.

Key words: Granular cell tumor; Immunohistochemistry; Vulva; Breast.

Introduction

Granular cell tumor is a rare neoplasm of neurogenic-Schwann cell origin [1, 2], also known as Abrikossoff tumor because it was first described by Abrikossoff in 1926 [3]. It presents as a painless tumor, solitary (90% of the cases), in the soft tissues of the head and neck region (35%) in the skin and subcutis (30%) and in the viscera, mainly the respiratory tract (35% of the cases).

It affects mainly adults and females (male/female ratio is 1/3).

In 7-10% of the cases this rare neoplasm develops in the female genital system, mainly in the skin of the labia majora and the breast [4, 5]. The mean age of patients is 32 years (range 16-68) [4]. The tumor is considered as benign and the rate of recurrence after removal is rare (1-2%) [6].

We present the clinical and pathological characteristics of a series of granular cell tumors studied in Pathology Laboratory during the period 1998-2008, located in the vulva (four cases) and the breast (one case). Additional immunohistochemical investigation was performed at new sections from the paraffin blocks

Case Reports

Four patients, 35-58 years of age presented with solitary painless tumors in the subcutis of the labia majora (left (3/4) and underwent an excisional biopsy.

The pathological examination revealed granular cell tumors measuring from 0.8-1.7 cm which were totally excised. No recurrence or metastasis occurred at a follow-up period of one to three years.

The fifth case, a 42-year-old patient, presented with a painless breast tumor which mammogram ultrasound (US) and breast examination showed to be consistent with a soft tissue lesion. The fine needle biopsy examination was inconclusive. The patient underwent an excisional biopsy after a frozen section biopsy negative for cancer. Pathological examination revealed a granular cell tumor of the breast subcutis. No involvement of the breast tissue was observed.

No recurrence or metastasis was noted in the follow-up period.

Pathological findings

In hematoxylin-eosin stained sections from all our cases the tumors presented similar morphology. Tumor cells were arranged in bundles, fascicles, cords and sheets, which were polygonal or spindle shaped with uniform round nuclei. Most distinctive was the cytoplasm which was abundant, granular and eosinophilic (Figure 1).

No mitotic activity or necrosis was observed. The covering epidermis was intact and showed prominent hyperplasic changes in 4/5 cases. The rete pegs, in 3/5 cases extended up to the tumor cells and deeply in the dermis, presenting a differential diagnostic problem from squamous cell carcinoma (Figure 2).

Immunohistochemical investigation by Ventana Automatic System showed a posititive immunoreaction of the neoplastic cells to S100 (polyclonal Dako Ab) and focal reaction to NSE (polyclonal Dako Ab) and negative to cytokeratins, CK 5/6 (monoclonal, Dako) and 34bE12 (monoclonal, Cell Marque).

Cytoplasmic granules also stained positive to periodic acid Schiff (PAS) cytochemical stain and were resistant to diastase digestion.

Discussion

Granular cell tumor is described by various names such as granular cell myoblastoma, Abrikossoff tumor, granular cell shwannoma, granular neurogenic tumor, newborn epulis and myoblastic myoma.

Granular cell tumor is a typically smaller than 3 cm solitary tumor located in the dermis or subcutis and less commonly in the submucosa or the smooth muscle [7, 8]. It presents a slow growth rate and when superficial no ulceration of the epidermis is reported [7, 8]. The usual presentation is that of a slow growing, nontender nodule in any body site. Approximately, 25% of such lesions

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Fig. 1

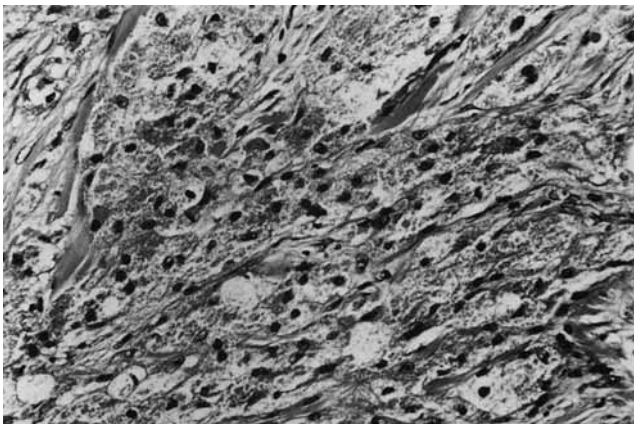

Figure 1. — Histological section of granular cell tumor showing characteristic granular, eosinophilic cytoplasm with uniform nuclei (H&E, x 250).

Fig. 2

Figure 2. — Granular cell tumor with pseudoepitheliomatous hyperplasia of covering epidermis (H&E, x 100).

occur on the tongue, 15% on the skin, 5% in the mammary glands, and 5-16% in the vulva [7-11]. It may develop in the viscera as well, with a predilection to lung tissues.

Among the genital organs, the labia majora of the vulva is the predominant site, and rarely it arises at the clitoris [12].

Grossly it is a pale white-yellowish nodule, usually well-circumscribed a with solid fleshy cut surface.

The pathological examination usually reveals large polyhedral neoplastic cells with eosinophilic granular cytoplasm, small vesicular or hyperchromatic round to oval nuclei separated by fibrous septa and collagen [2, 8, 13]. The granularity of such tumor cells may be the expression of the accumulation of secondary lysosomes in the cytoplasm [2, 8, 13].

The lesions are usually positive for S100, vimentin, CD68 and neural-specific enolase but negative for CD57 and epithelial (EMA), melanocytic (Melan A), smooth muscle, dendritic cell and endothelial markers. The positivity for calretinin, S100 protein and neurospecific enolase excludes a histiocytic or a myoblastic origin and confirms the neural origin of this tumor [2, 8, 13].

Clinicians and pathologists should be aware of such an entity. The differential diagnosis includes schwannomas, basal or squamous cell carcinomas, melanomas and fibrous histiocytomas. In the differential diagnosis verruca simplex, condyloma accuminatum, verruciform xanthoma, vulvar intraepithelial neoplasia, bowenoid papulosis, erythroplasia of Queyrat and verrucous carcinoma should be considered [10, 14].

The treatment of choice is conservative excision in all such tumors followed by a strict follow-up [1, 10]. All the tumors in our patients were completely excised with clear margins. Radiation and chemotherapy are not necessary for further treatment. Recurrence rates could reach 2-8%, however no recurrence or malignancy was observed in our patients.

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