The Australian & New Zealand journal of obstetrics & gynaecology.

UNIVERSITY OF THE WEST INDIES
DEPARTMENT OF CLINICAL SURGICAL SCIENCE
Bldg 68 Eric Williams Medical Sciences Complex
Trinidad
TRINIDAD & TOBAGO

TITLE: AUSTRALIA AND NEW ZEALAND JOURNAL OF OBSTETRICS AND GYNAECOLOGY
VOLUME/ISSUE/PAGES: Vol 27 No 4 p349-52
DATE: 1987
TITLE OF ARTICLE: GRANULAR CELL TUMORS OF THE VULVA

Aust NZ J Obstet Gynaecol
1987; 27: 349

Granular Cell Tumours of the Vulva

G.C. Raju, MD, MRCPath and V. Naraynsingh, FRCS
Departments of Pathology and Surgery, Port-of-Spain General Hospital Trinidad, West Indies

Summary: Granular cell tumours occur in a variety of sites, including the vulva. Origins from myogenic, histiocytic, fibroblastic and neurogenic elements have been proposed. Female preponderance suggests that oestrogenic hormones are involved.

Seven cases of granular cell tumours of the vulva have been studied. In none was the correct diagnosis made preoperatively. They were solitary lesions and local excision was curative. Paraffin sections of these cases were studied by peroxidase-antiperoxidase method for myoglobin, lysozyme, alpha-1-antitrypsin and S-100 protein localization. Antimyoglobin, antilysozyme and anti-alpha-1-antitrypsin antibodies were not localized in these tumours; however, S-100 protein was localized in all of them. These results agree with previous data that suggest a neurogenic origin for granular cell tumours.

Granular cell tumour (GCT) is a relatively uncommon lesion, and no organ or tissue in the body seems immune from development of this entity. Although the tongue and superficial soft tissues are the common sites (1), the vulva is an infrequent location and GCT should be considered in the differential diagnoses of an obscure nodular lesion of the vulva (2,3). Also benign pseudocarcinomatous hyperplasia, which usually overlies this lesion, must not be misinterpreted as squamous cell carcinoma, which may be possible especially if a very superficial biopsy is submitted for microscopic diagnosis.

The original name coined for GTC was granular cell myoblastoma, because this tumour was considered to be of muscle cell origin (4). Ultrastructural and histochemical studies have not confirmed the myogenic origin, but have suggested Schwann cell (5,6) or undifferentiated mesenchymal cells as the origin of this tumour (7). This paper reports the details of 7 cases of GCT of the vulva including immunoperoxidase study using antibodies to myoglobulin, lysozyme, alpha-1-antitrypsin and S-100 protein, and discusses the histogenesis of this tumour located in the female genital tract.

MATERIALS AND METHODS

Seven cases of GCT of the vulva were identified from the files of Surgical Pathology, Port-of-Spain General Hospital, Trinidad over a 10-year period (1975-1984). Pertinent clinical data of the cases are shown in table 1. All specimens were fixed in 4% buffered formalin and paraffin-embedded. One section from each specimen was stained with haematoxylin and eosin, periodic acid Schiff (PAS) stain with or without prior diastase treatment. In addition, all the cases were stained for S-100 protein, myoglobin, alpha-1-antitrypsin, and lysozome (Dakopatts, Denmark) by peroxidase-antiperoxidase (PAP) technique (8).

Staining procedure: The sections at 4mu were

Table 1. Granular Cell Tumour of the Vulva

Case No.	Race and age (yr)	Site	Size	Presentation	Clinical diagnosis
1.	Indian 33	Left labia	1 cm	3 months mobile painless nodule	Fibroma
2.	Black 52	Left labia	1 cm	14 months itchy skin nodule	Fibroma
3.	Black 30	Left labia	5 cm	24 months cystic lump	Inclusion cyst
4.	Black 28	Left labia	2 cm	16 months mobile painless nodule	Fibroma
5.	Black 36	Right labia	5 cm	12 months mobile tender lump	Inclusion cyst
6.	Black 45	Right labia	2.5 cm	6 months mobile painless nodule	Fibroma
7.	Black 64	Left labia	1.5 cm	9 months mobile painless nodule	Lipoma

Address for correspondence:
Dr. G.C. Raju,
Department of Pathology
National University of Singapore,
National University Hospital,
Lower Kent Ridge Road,
Singapore 0511.

Table 2. Details of 32 Granular Cell Tumours

Site	Number of cases	Race		Age	Sex		Size
		Negro	Indian	Range (yrs)	F	M	Range (cm)
Vulva	7	6	1	28-64	7	0	1-5
Lower extremity	7	6	1	21-65	7	0	2-12
Breast	6	6	0	19-73	5	1	1-3
Upper extremity	5	5	0	9-27	3	2	2-4
Trunk	5	5	0	25-29	4	1	1-6
Tongue	2	2	0	7-20	1	1	1-2

deparaffinized in xylene and rehydrated using decreasing serial concentrations of alcohol. The tissue sections were then washed in Tris-Buffer-Saline (TBS) with a pH of 7.6 and incubated with 3% hydrogen peroxide followed by washing with TBS. The slides were then incubated with (i) prediluted antibody for 30 minutes, (ii) swine-anti-rabbit immunoglobulin for 20 minutes and (iii) rabbit PAP complex for 20 minutes. Washing between these steps was performed with TBS with a pH of 7.6. The reaction was developed with diamino-benzidine-hydrogen peroxide mixture in TBS, rinsed in running tap water, lightly stained with Gill hematoxylin, dehydrated in serial alcohols and xylene, and a coverslip was mounted using permanent mounting medium.

RESULTS

Port-of-Spain General Hospital caters for approximately 60% of the 1.2 million population predominantly of African (42%) and Indian (41%) descent with less than 1% whites in Trinidad. Thirty two granular cell tumours involving various anatomical sites were examined during the same 10-year period (table 2). Twenty seven of the patients were women and 5 were men; the age range of the patients was 7-73 years. Thirty of these patients were Negro while 2 were of Indian descent. The clinical diagnosis most frequently made was fibroma, lipoma or sebaceous cyst. In 17 patients the tumours originated in skin and subcutaneous tissues of the lower and upper extremities and trunk. The tongue was the site in only 2 cases. Breast accounted for 6 cases and in each the GCT was located within breast parenchyma. There were 7 women with a vulvar GCT, each being located in the dermal and subcutaneous tissues of the labia majora with the largest measuring 5cm in diameter (table 1).

All the patients presented with a solitary, mobile nodule; none had a correct preoperative diagnosis and local excision was curative in all.

Light microscopy: In all the tumours, the tumour cells were polyhedral with ill-defined cytoplasmic outline often arranged in clusters separated by thin fibrous septae. The tumour cells showed abundant slightly eosinophilic granular cytoplasm and small multiple dark staining nuclei (figure 1a). Mitoses were not found. The cytoplasmic granules showed diastase resistant PAS positivity. The tumours were encapsulated and were usually poorly demarcated from the adjacent tissue. In one, benign pseudocarcinomatous hyperplasia of the surface epithelium was noted (figure 1b).

Immunohistochemical findings: All tumour cells in the 7 GCT of the vulva examined showed both intracytoplasmic and nuclear positive staining with antiserum against S-100. The tissues adjacent to the tumour cells were not stained except for nerve bundles which also showed strong staining of the Schwann cell elements (figure 2). The tumour cells were negative for myoglobin, alpha-1-antitrypsin, and lysozyme.

DISCUSSION

The vulva is an infrequent location for GCT and constitutes about 7% of the reported cases (9). It has been noted that GCTs are more common in blacks; a review of reported cases of this entity in the vulva also showed a preponderence in blacks (3), and 6 of the 7 patients in our study were black. This racial predilection may be related to greater reactive potential of mesenchymal tissue among blacks (10), and may explain its relatively commoner occurrence in our predominantly Negro hospital population.

GCT of the vulva presents as a small, painless, poorly encapsulated mass resembling a fibroma or an inclusion cyst, and may be mistaken for carcinoma if the surface is ulcerated. Histological features of GCT, regardless of location, are characteristic. However, pseudocarcinomatous hyperplasia of the overlying epithelium, a common finding with GCT, may mislead the pathologist into a diagnosis of squamous cell carcinoma, especially if a superficial biopsy is submitted for interpretation.

The histogenesis of GCT has evoked considerable interest. After Abrikossoff's (4) descriptions of 'granular cell myoblastoma', histological observations (11), and tissue culture studies (12) were also interpreted to favour a muscle cell origin of GCT. However, ultrastructural (5), and immunohistochemical studies (6) failed to support this theory. Absence of myoglobin in all cases in our study further militates against a muscle cell origin.

Histiocytic origin for GCT has been proposed (13). However, failure to demonstrate the histiocytic markers such as lysozyme and alpha-1-antitrypsin do not support the histiocytic origin of GCT. It has been suggested that GCT might arise from an uncommitted

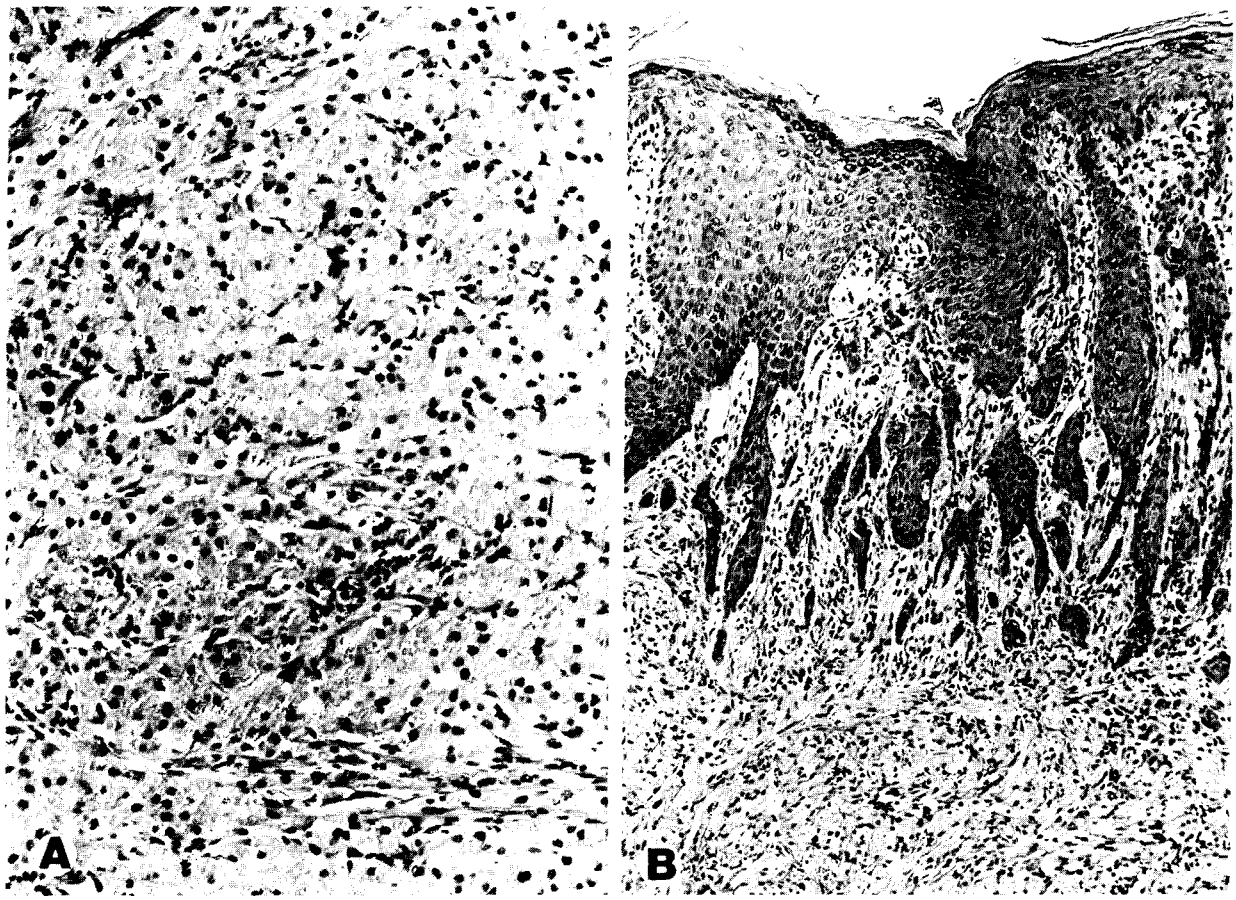

Figure 1. A) Tumour cells in GCT showing abundant granular cytoplasm and small nuclei (H&E × 120); B) Pseudocarcinomatous hyperplasia of the surface epithelium (H&E × 80).

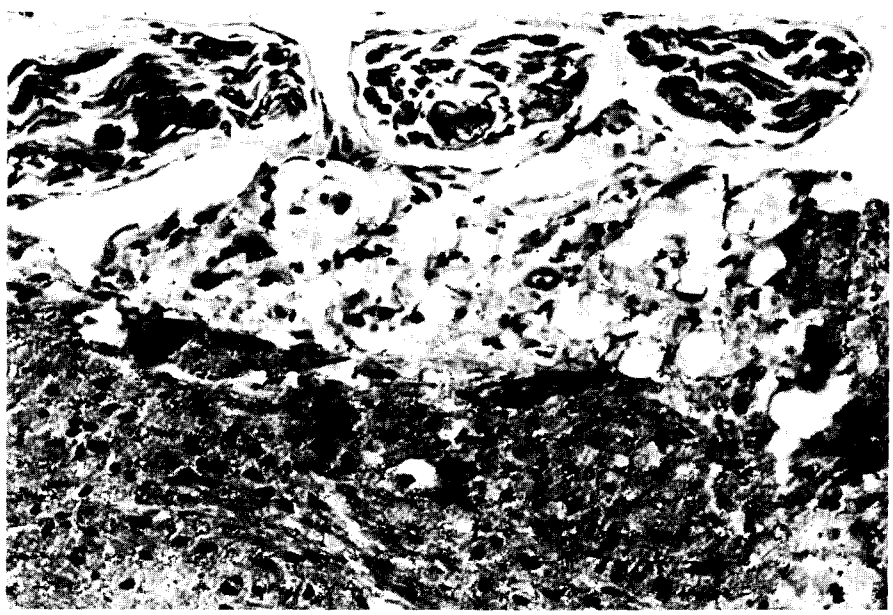

Figure 2. S-100 positive staining of cytoplasm and nuclei of granular tumour cells and similar staining of peripheral nerve bundles. Note apparent granular change in few cells of nerve bundles (immunoperoxidase-haematoxylin × 250).

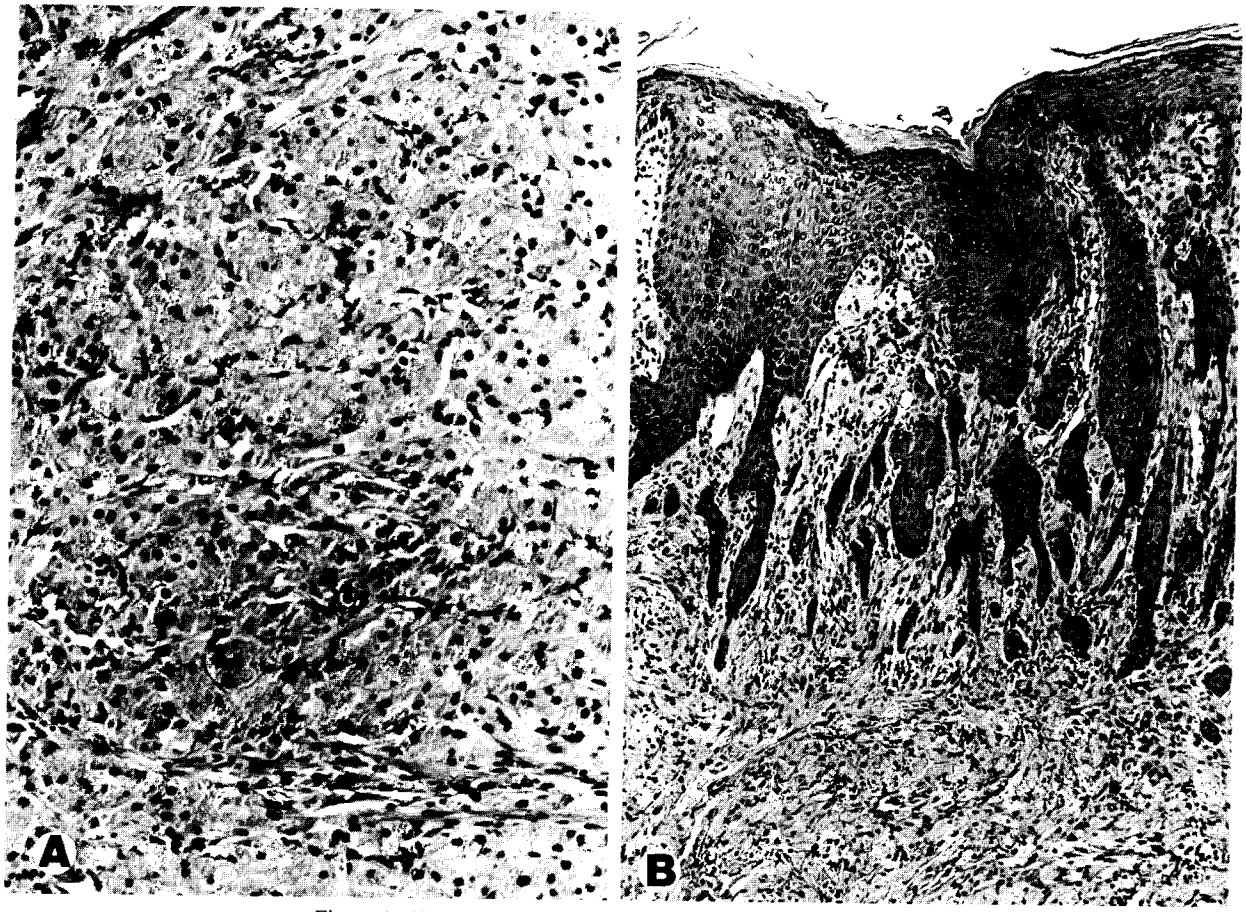

Figure 1. A) Tumour cells in GCT showing abundant granular cytoplasm and small nuclei (H&E × 120); B) Pseudocarcinomatous hyperplasia of the surface epithelium (H&E × 80).

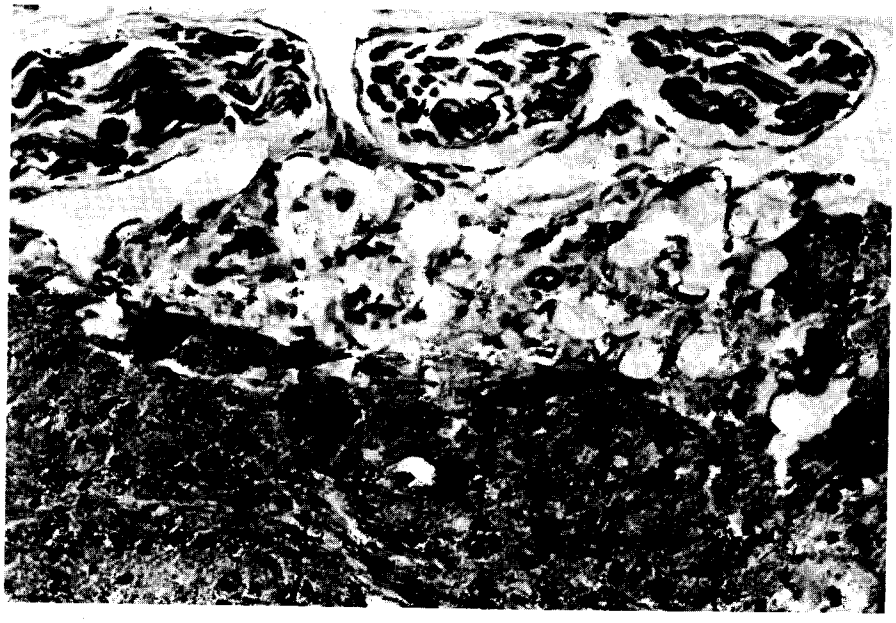

Figure 2. S-100 positive staining of cytoplasm and nuclei of granular tumour cells and similar staining of peripheral nerve bundles. Note apparent granular change in few cells of nerve bundles (immunoperoxidase-haematoxylin × 250).

cell (14). This cell type might be related to nerve cells or their precursors as GCT cells contain neural markers.

The frequent association of GCT with nerves and immunohistochemical localization of S-100 in the tumour cells strongly suggest that GCT represent neural or Schwann cell origin (6,15). S-100 protein although initially thought to be 'brain specific', has been found in a wide variety of other cells indicating that S-100 may be more widespread in human tissues (16). Although it is evident that S-100 protein is not specific for any particular tissue, it is generally recognized as a useful marker of neural tissues, especially Schwann cells, and the tumours derived from these cells. Positive staining by immunoperoxidase techniques in granular cell tumours for the S-100 protein from various locations suggest a neural cell origin for these lesions (6). Our study using PAP method for S-100 protein showed a uniform localization of strong intensity in all granular cell tumours. Immunohistochemical localization of myoglobin, lysozyme and alpha-1-antitrypsin using the PAP method in all cases demonstrated the absence of staining in tumour cells. These observations support the concept of neurogenic origin for granular cell tumours irrespective of their location. Whatever the origin and nature of this interesting entity, granular cell tumour will continue to interest clinicians and pathologists alike because of its varied sites of occurrence and its mimicry of other lesions both benign and malignant.

References

1. Lack E.E., Warsham G.F., Callihan M.D. et al. Granular cell tumour: a clinicopathological study of 110 patients. J Surg Oncol 1980; 13: 301-316.
2. Dgani R., Czernobilsky B., Borenstein R., Lancet M. Granular cell myoblastoma of the Vulva: report of 4 cases. Acta Obstet Gynecol Scand 1978; 57: 385-387.
3. King D.F., Bustillo M. Broen E.N., Horose F.M. Granular cell tumours of the Vulva: A report of three cases. J Dermatol Surg Oncol 1979; 5: 794-797.
4. Abrikossoff A. Uber Myome, ousgehend von der quergestreiften wilkurlichen muskulatur. Virchow Arch Pathol Anat Physiol 1926; 260: 215-233.
5. Fisher E.R., Wechsler H. Granular cell myoblastoma: a misnormer: Electron microscopic and histochemical evidence concerning its Schwann cell derivation and nature (granular cell Schwannoma). Cancer 1962; 15: 936-954.
6. Armin A., Connelly E.M, Rowden G. An immunoperoxidase investigation of S-100 protein in granular cell myoblastomas: evidence for Schwann cell derivation. Am J Clin Pathol 1983; 79: 37-44.
7. Sobel H.J., Schwarz R., Marquet E. Light and electron microscopic study of the origin of granular cell myoblastoma. J Pathol 1973; 109: 101-111.
8. Sterberger L.A. Immunohistochemistry. 2nd Ed. New York, J. Wiley and Sons 1979; pp 104-130.
9. Gifford R.R.M., Birch H.W. Granular cell myoblastoma of multicentric origin involving the vulva: a case report. Am J Obstet Gynecol 1973; 117: 184-187.
10. Mascovic E.A. Azar H.A. Multiple granular cell tumours ("myoblastomas"). Case report with electron microscopic observations and review of the literature. Cancer 1967; 20: 2032-2047.
11. Shear M. The histogenesis of the so-called granular cell myoblastoma. J Pathol Bact 1960; 80: 225-228.
12. Murray M.R. Cultural characteristics of 3 granular cell myoblastomas. Cancer 1951; 4: 857-765.
13. Azzopardi J.G. Histogenesis of granular cell "myoblastoma". J Pathol Bacteriol 1957; 71: 85-94.
14. Miettinen M., Lehtonen E., Lehtola H., Ekblom P., Lehto V.P., Virtanen I. Histogensis of granular cell tumour — an immunohistochemical and ultrastructural study. J Pathol 1984; 142: 221-229.
15. Bangle R. Jr. An early granular cell myoblastoma confined within a small peripheral myelinated nerve. Cancer 1953; 6: 790-793.
16. Vanstapel M.J., Gatter K.C., Wolf-peeters, C., Mason D.Y., Desmet V.D. New sites of Human S-100 immunoreactivity detected with monoclonal antibodies. Am J Clin Pathol 1986; 85: 160-168.