A Review of Granular Cell Tumours at the University Hospital of the West Indies: 1965–2006

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ABSTRACT

Objective: *Granular cell tumours are uncommon lesions that occur in a wide variety of sites. They are usually benign, but as they are infrequently diagnosed preoperatively, they may be confused clinically with malignant lesions. The objective of this study was to assess the relative frequency and the clinico-pathologic characteristics of granular cell tumours identified at the University Hospital of the West Indies (UHWI) over a 41-year period.*

Methods: *The archives of surgical pathology reports in the Department of Pathology at the UHWI from 1965 to 2006 were searched for all cases of granular cell tumour. From these records, a number of demographic and other data were recorded and analyzed.*

Results: *One hundred and thirty cases of granular cell tumours were found in 122 patients. Of these, 99 patients were female and 23 male, providing a male: female ratio of 1 to 4.3. The ages ranged from 5 days to 82 years with a mean age (excluding the 2 youngest cases) of 34.4 years.*

Lesions ranged in size from 0.2 cm to 10 cm in greatest dimension, the average size being 1.85 cm and were found in a diverse array of anatomic locations, the most common being the vulva, breast and tongue. The correct clinical diagnosis was proffered preoperatively in only one case. In contrast, a malignant diagnosis was suggested in 19 cases.

Conclusions: *Compared with other studies, there was a notable difference in the distribution of granular cell tumours in this series. In particular, lesions of the tongue accounted for fewer than expected, while lesions of the breast and vulva were considerably increased. The well-recognized female predominance was also substantially higher than in other studies.*

Un Estudio de los Tumores de Células Granulares en el Hospital Universitario de West Indies: 1965–2006

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RESUMEN

Objetivo: *Los tumores de células granulares son lesiones poco comunes que ocurren en una amplia variedad de lugares. Por lo general son benignos, pero como son raramente diagnosticados preoperativamente, puede confundírseles clínicamente con lesiones malignas. El objetivo de este estudio fue evaluar la frecuencia relativa y las características clínico-patológicas de los tumores de células granulares identificados en el Hospital Universitario de West Indies (HUWI) en un período de 41 años.*

Métodos: *Se investigaron los archivos de los reportes de patologías quirúrgicas en el Departamento de Patología de la UHWI, de 1965 a 2006, en busca de todos los casos de tumores de células granulares. A partir de estos archivos, se registraron y analizaron un número de datos demográficos y de otra índole.*

Resultados: *Se hallaron un total de ciento treinta casos de tumores de células granulares en 122 pacientes. De estos, 99 pacientes era mujeres y 23 hombres, para una proporción varón: hembra de 1 a 4.3 Las edades estuvieron en un rango de 5 días a 82 años con una edad promedio (excluyendo los dos casos de menos edad) de 34.4 años.*

El tamaño de las lesiones fluctuó de 0.2 cm a 10 cm como la mayor dimensión, siendo el tamaño promedio 1.85 cm. Estas lesiones se encontraban distribuidas en una variedad de lugares anatómicos,

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siendo los más comunes la vulva, el pecho y la lengua. El diagnóstico clínico correcto fue presentado preoperativamente sólo en un caso. En contraste con ello, se sugirió un diagnóstico maligno sólo en 19 casos.

Conclusiones: *En comparación con otros estudios, hubo una notable diferencia en la distribución de los tumores de células granulares en este serie. En particular, las lesiones de la lengua dan cuenta de menos casos de los que se esperaba, mientras que las lesiones del pecho y la vulva presentaban un aumento considerable. El bien reconocido predominio femenino fue sustancialmente más alto que en otros estudios.*

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INTRODUCTION

Granular Cell Tumour (GCT) is a lesion first described by Abrikossoff in 1926. Then called granular cell myoblastoma, the name has gone through several changes *en route* to its present nomenclature. These tumours occur in a wide variety of sites and the usual presentation is that of a painless 'lump'. However, because GCTs are uncommonly encountered and have no distinct clinical features, they may be clinically misdiagnosed as carcinoma. The objective of this study was to examine the frequency and clinicopathologic characteristics of these tumours at the University Hospital of the West Indies (UHWI).

MATERIAL AND METHODS

The files of the Department of Pathology of the UHWI were reviewed for all cases of GCT diagnosed over the period July 1965 to June 2006. The patients' age and gender, as well as the site and size of lesions were documented. Clinical diagnoses proffered, were also recorded, when available.

RESULTS

During the 41-year period, 130 excised lesions were found in 122 patients. Three patients had multiple tumours, including one patient with three lesions, while four patients had recurrent excisions. The average number of GCTs seen in the Department of Pathology annually was 3.2 cases.

Of the patients studied, 99 were female and 23 were male conferring a male: female ratio of 1 to 4.3. Patient ages ranged from five days to 82 years. Excluding the two youngest patients, a 5-day old infant and a 1-year old child, the mean age of patients was 34.4 years, with the modal and median ages both being 30 years. Information on size was available for 84 (64.6%) lesions. These ranged from 0.2 cm to 10 cm in largest dimension, the mean size being 1.85 cm and the mode, 1.5 cm.

The majority of lesions (56.2%) were located on the trunk, with the head and neck (26.9 %) next in frequency (Table 1). Table 2 shows a more detailed site of lesions within the broader anatomic locations. The commonest site overall was the vulva (23 cases) followed by the breast (22 cases) and tongue (15 cases). The location of the lesion in the 5-day old infant was the gingiva. Only four lesions occurred in internal organs, two in the respiratory tract including one in the trachea and the other in the bronchus.

Table 1: Main anatomical location of granular cell tumours

Anatomic Site	No of cases	(%)
Trunk	73	56.2
Head and Neck	35	26.9
Extremities	17	13.1
Miscellaneous *	4	3.1
Skin, NOS	1	0.8

* Located in internal organs
NOS = Not otherwise specified

Table 2: Detailed anatomical site of granular cell tumours

Location	Number of cases	% of total
TRUNK		
Vulva	**23**	**17.7**
Breast	**22**	**16.9**
Back	9	6.9
Abdomen	6	4.6
Chest	5	3.8
Groin	3	2.3
Scrotum/ perineum	2	1.5
Vagina	2	1.5
Buttock	1	0.8
HEAD and NECK		
Tongue	**15**	**11.5**
Neck	8	6.1
Scalp	3	2.3
Lip	3	2.3
Face, NOS	3	2.3
Eye/ ear	2	1.5
Gingiva	1	0.8
EXTREMITY		
Arm	8	6.1
Thigh/ hip	5	3.8
Hand	4	3.0
MISCELLANEOUS		
Respiratory tract	2	1.5
Pharynx/oesophagus	2	1.5

The clinical diagnoses proffered, with submission of the specimens, are detailed in Table 3. The most frequent clinical diagnosis for lesions occurring in the skin and subcutis was that of "fibroma". Those in the breast were most often diagnosed clinically as fibroadenoma but car-

Table 3: Diagnoses proffered by clinicians

Site	Diagnosis	Number
Skin, subcutaneous tissue &miscellaneous sites (66)*	Fibroma/neurofibroma/schwannoma	16
	Sebaceous/epidermal/dermoid cyst	13
	Miscellaneous malignant diagnoses	9
	Miscellaneous benign diagnoses	22
	No diagnosis	6
Vulva (23)	Cyst/tumour	13
	LGV / ulcer	6
	Bartholin's abscess	2
	Fibroma	1
	No diagnosis	1
Breast (22)	Fibroadenoma/ fibrocystic disease	9
	Carcinoma	7
	Sebaceous cyst	1
	Malignant melanoma	1
	Neoplasm, NOS	1
	No diagnosis	3
Tongue (15)	Granular cell tumour	1
	Fibroma	3
	Papilloma	2
	Carcinoma	2
	Inflammatory lesions	2
	No diagnosis	5

* Excluding cases of recurrent tumours
LGV = Lymphogranuloma venereum; NOS = Not otherwise specified

cinoma was a close second choice. Considering the entire series, a malignant diagnosis was suggested preoperatively in 19 cases including 8 with lesions from the breast. The correct clinical diagnosis was proffered preoperatively in a single case that occurred on the tongue.

DISCUSSION

The descriptive term granular cell tumour emphasizes the main histologic feature of the lesion which is characterized by large cells with coarsely-granular eosinophilic cytoplasm.

A review of the literature revealed that studies reporting GCTs from all anatomical sites were generally confined to the older literature (1–3). In contrast, the recent literature has been replete with case reports documenting the occurrence of GCT in an increasing variety of locations throughout the body, or limited to series confined to localized regions of the body such as the head and neck (4). Three studies, that included lesions from all anatomical sites, cited prevalence rates between 2 and 3.7/year (1–3). In the present study, the prevalence of 3.2 per year is, therefore, in keeping with that recorded in the literature, making it an uncommon tumour despite occasional references to the contrary (5). The relative rarity of this tumour is further supported by the sample size of most of those series, with only 2 of the 3 studies amassing more than 100 cases, the largest with only 118 cases (2), still less than the number reported in the present series. These lesions have consistently been reported to show a higher frequency among blacks (2, 5). This study, as far as we can ascertain, is the first such series of GCTs reported in a predominantly black population.

Almost all studies cite that the incidence of GCT is more common in females, with a ratio of females, on average, twice that in men (3, 5). This female preponderance was, however, overwhelming in our series which recorded more than four females to each male. A notable exception to this female preponderance is the slight male prevalence reported in one of the larger series where the authors quoted a male: female ratio of 1.8:1 (2). Granular cell tumours have been reported to occur more commonly in the 4^{th}, 5^{th} and 6^{th} decades of life (2, 5). The average age of patients in this study was 34.4 years which accords well with nearly all the other reports (2, 3). Although GCTs can occur at any age, they are usually less common in children with some authors even suggesting that this is a rare occurrence (5). In the present study, 19 tumours were found (14.6%) in children 16 years or younger. This included the tumour in the 5-day old child that occurred in the mouth. The latter category of tumours, designated congenital GCT or congenital epulis, is considered a unique variant and has been well described (6).

Granular cell tumours continue to be reported from a diverse array of anatomical sites throughout the body. An almost consistent feature of studies, with sufficiently large numbers, is the prevalence of lesions in the region of head and neck, mostly due to lesions in the tongue (2 – 4). In fact, the head and neck region represented the site of almost 50% of all lesions, with the tongue accounting for approximately one-third of these lesions, in two of these studies (3, 4). In the present series, lesions in the head and neck were less prominently represented, amounting to 26.9% overall and, while many of these did occur on the tongue, their contribution to the total number was less than previously reported. In contrast to the findings in other series, however, lesions in the vulva and breast were significantly represented in this study, accounting for 17.7% and 16.9% of all cases respectively. These proportions are considerably higher than that reported elsewhere for vulva and breast (2, 3). In recent times, however, small series of GCTs in these latter sites are increasingly being reported (7, 8). In general, the occurrence of GCT in internal organs is much less common. However, reports of their occurrence in the respiratory and gastrointestinal tracts, similar to this series, have been previously reported in the literature (2, 9, 10). There were three cases (2.3%) of multiple tumours, which is less than the generally quoted frequency that ranges from 5 to 10% (2, 3). Interestingly, one of the previously cited papers described an unusually high frequency of multiple lesions at 29.8% (1).

The histogenesis of GCT has been a source of controversy since its recognition as an entity by Abrikossoff in 1926. Then thought to be of muscular origin, he termed it granular cell myoblastoma. These early suggestions of myoblastic origin were later discounted and use of the term

granular cell myoblastoma as a designation for this tumour was discouraged. Most investigators currently favour a schwann cell derivation based on electron microscopic (11) and immunohistochemical (12) findings and, in view of this, some advocate the designation of granular cell schwannoma. However, some investigators believe that GCT is not a specific entity as many different neoplastic and non-neoplastic lesions show granular cell changes (13, 14), a result of a possibly degenerative cytoplasmic change due to still unknown metabolic alterations that may occur in various cell types. Until more information becomes available, perhaps that derived from cytogenetic studies, this lesion should be considered a separate entity and the descriptive designation of granular cell tumour continues to be recommended.

Preoperative diagnoses in this study were incorrect in all but one case, a proportion only marginally better in those studies that recorded such information (2, 3). This abysmal level of concordance is not unexpected, since there are no distinct clinical features with which to diagnose these lesions. Although the lone case with a correct clinical diagnosis was submitted in a lesion from the tongue, we thought it surprising that this diagnosis was not proffered in other tongue lesions, given the recognized propensity for GCTs to occur in this location. The wide range of diagnoses submitted might also reflect the infrequency with which these tumours are seen. Compared to other studies, our series had an increased number of cases thought clinically to be malignant. One reason was clearly due to the fact that many of these lesions were located in the breast, where GCTs are well known to simulate breast cancer (15).

Granular cell tumours are generally benign although a few have been classified as malignant and have been known to metastasize. Compared with the benign tumours, malignant GCTs are usually larger and display necrosis, cytological atypia and mitoses (16). Malignant or probably malignant tumours accounted for 1.6% of all lesions in this series, which compares with the 2% prevalence normally quoted (5).

Treatment of GCTs is surgical and, despite frequent involvement of surgical margins, recurrences are uncommon (2). Although 22 tumours (16.9%) in this series were reported as "incompletely excised", there were only 4 (3%) recurrences noted, comparing well with recurrence rates reported in the literature (1, 2).

This series of GCTs is the first report from a predominantly black population. It has documented a considerable difference in the anatomical distribution of the lesions when compared with previous similar studies. In particular, lesions of the tongue accounted for fewer than expected, whereas, lesions of the breast and vulva were far more common. An overwhelming female preponderance was demonstrated, substantially more marked than most other studies reporting this lesion.

REFERENCES

1. Khansor T, Balducci L, Tavassoli M. Granular cell tumor. Clinical spectrum of the benign and malignant entity. Cancer 1987; **60:** 220–2.
2. Lack EE, Worsham GE, Callihan MD, Crawford BE, Klappenbach S, Rowden G et al. Granular cell tumor: a clinicopathologic study of 110 patients. J Surg Oncol 1980; **13:** 301–16.
3. Strong EW, McDivitt RW, Brasfield RD. Granular cell myoblastoma. Cancer. 1970; **25:** 415–22.
4. Alessi DM, Zimmerman MC. Granular cell tumors of the head and neck. Laryngoscope 1988; **98:** 810–4.
5. Weiss SW, Goldblum JR. Granular cell tumor. In Enzinger and Weiss's soft tissue tumors, 4th edition. Mosby, 2001, 1178–88.
6. Lack EE, Worsham GF, Callihan MD, Crawford BE, Vawter GF. Gingival granular cell tumors of the newborn (congenital "epulis"): a clinical and pathologic study of 21 patients. Am J Surg Pathol. 1981; **5:** 37–46.
7. Levavi H, Sabah G, Kaplan B, Tytiun Y, Braslavsky D, Gutman H. Granular cell tumor of the vulva: six new cases. Arch Gynecol Obstet. 2006; **273:** 246–9.
8. Adeniran A, Al-Ahmadie H, Mahoney MC, Robinson-Smith TM. Granular cell tumor of the breast: a series of 17 cases and review of the literature. Breast J. 2004; **10:** 528–31.
9. Redjaee B, Rohatgi PK, Herman MA. Multicentric endobronchial granular cell myoblastoma. Chest. 1990; **98:** 945–8.
10. David O, Jakate S. Multifocal granular cell tumor of the esophagus and proximal stomach with infiltrative pattern: A case report and review of the literature. Arch Pathol Lab Med 1999; **123:** 967–73.
11. Sobel HJ, Marquet E, Avrin E, Schwarz R. Granular cell myoblastoma: An electron microscopic and cytochemical study illustrating the genesis of granules and aging of myoblastoma cells. Am J Pathol 1971; **65:** 59–78.
12. Le BH, Boyer P, Lewis JE, Kapadia SB. Granular cell tumor: immunohistochemical assessment of Inhibin alpha, protein gene product 9.5, S100 protein, CD68, and Ki-67 proliferative index with clinical correlation. Arch Pathol Lab Med 2004; **128:** 771–5.
13. Mentzel T, Wadden C, Fletcher GD. Granular cell change in smooth muscle tumours of skin and soft tissue. Histopathology 1994; **24:** 223–31.
14. LeBoit PE, Barr RJ, Burall S, Metcalf JS, Yen TS, Wick MR. Primitive polypoid granular-cell tumor and other cutaneous granular-cell neoplasms of apparent nonneural origin. Am J Surg Pathol. 1991; **15:** 48–58.
15. Damiani S, Koerner FC, Dickersin GR, Cook MG, Eusebi V. Granular cell tumour of the breast. Virchows Arch A Pathol Anat Histopathol. 1992; **420:** 219–26.
16. Fanburg-Smith JC, Meis-Kindblom JM, Fante R, Kindblom LG. Malignant granular cell tumor of soft tissue; diagnostic criteria and clinicopathologic correlation. Am J Surg Pathol 1998; **22:** 779–94.