Article published online: 2020-12-31

Review Article

Giant solitary trichoepithelioma

Bhavuray Teli, P. B. Thrishuli[1], R. Santhosh, D. N. Amar[2], Shravan Rajpurohit

Abstract

Adnexal tumors like giant solitary trichoepitheliomas are uncommon to most of us to permit a ready familiarity with them. Information regarding the genesis, clinical profile, behavior, and management options for this tumor is limited. There are 18 cases reported in the world literature till date. This review attempts to provide insight to this rare tumor. Our search included indexed literature from Pubmed, Directory of Open Access Journals, Health Inter Network Access to Research Initiative and Google databases in addition to standard dermatology texts. Giant solitary trichoepithelioma is a rare trichogenic tumor with potential for local recurrence. It has predilection for the older age, but may present at any age including at birth. It has close resemblance to basal cell carcinoma and other skin adnexal tumors - clinically, cytologically, and histologically. CD10, CD 34, PHLDA1 but not p75NTR are useful adjunct markers. Surgical excision is the standard treatment. Recurrence and possible transformation into BCC cautions follow up at regular intervals.

Key words: Brooke-Spiegel syndrome, giant solitary trichoepithelioma, Rombo syndrome, trichogenic tumor

Introduction

Adnexal tumors like giant solitary trichoepitheliomas are uncommon to most of us to permit a ready familiarity with them. Information regarding the genesis, clinical profile, behavior and management options for this tumor is limited. This review attempts to provide insight into this rare tumor by compiling the available data, which is limited to case reports (including ours) and case series, the largest of which comprises only of three cases.

Our search included indexed literature from Pubmed, Directory of Open Access Journals, Health Inter Network Access to Research Initiative and Google databases in addition to standard dermatology texts between 01/01/2013 to 01/08/2013. Giant solitary trichoepithelioma, GST, trichoepithelioma, skin adnexal tumors, trichogenic tumors, multiple trichoepitheliomas were used as key words for literature search. All the articles are included and no language filters were used.

Genesis

Trichoepithelioma (TE) was first described by Brooke in 1892 as Epithelioma Adenoides Cysticum.[1] Brooke demonstrated the histogenesis of this tumor from epidermis and epithelium of hair sacs. Montgomery[2] believed that the tumor arose from the outer walls of the hair follicle and hair matrix. Lever[3] favored origin from a primary epithelial germ or a pluripotential embryonic cell. Pinkus[4] postulated that all epitheliomas of the skin originate from adult pluripotential cells rather than from one or the other specific part of the epithelial system or from embryonic rests.

The immunoreactivity of the epithelial nests and the keratinous cysts, in the classical solitary TE, desmoplastic TE, trichogenic trichoblastoma, trichoblastic fibroma, and giant solitary trichoepithelioma (GST) are similar to those of the outer root sheath and the infundibulum of normal hair follicles, respectively. It is speculated that all trichogenic tumors differentiate mainly toward the outermost layer of the outer root sheath and some parts of them towards other parts of the follicle. No specific immunoreactivity or staining pattern for each kind of trichogenic tumor is demonstrated. This supports the notion that all neoplasms of follicular germinative cells should be grouped as a single entity.[5]

Access this article online
Quick Response Code:
Website: www.sajc.org
DOI: 10.4103/2278-330X.149951

Department of Surgery, DMWIMS, Wayanad, Kerala, [1]JSS Medical College and Hospital, Mysore, [2]Srinivasa Institute of Medical Science, Mangalore, Karnataka, India
Correspondence to:
Dr. Bhavuray Teli,
E-mail: teli.bhavu@gmail.com

Thus, TE is widely thought to be a benign cutaneous appendageal tumor, which arises from hair follicles. A scanning electron microscopic study from India revealed that the basement membrane of TE and desmoplastic TE is similar to the basement membrane of sweat or sebaceous gland, thus, pointing to an exocrine differentiation.[6]

Classically, three clinical forms of TE are recognized:[7]

- A small solitary form
- A small multiple form, which is inherited in an autosomal-dominant fashion
- A rare giant solitary form.

The two clinical forms (multiple TE and GST) coexisting is also documented.[8] GST has been defined as a solitary trichoepithelioma with a diameter of 2 cm or more.

Clinical Profile

The clinical profile, anatomic distribution, and other data are summarized in Table 1.

The mean age of the presentation is 60 years with a predilection for the older age group. Tumor may appear at any age as it was present at birth in our case. They are known to affect both sexes equally[24] in contrast to female preponderance in multiple TEs.[25] But, our review suggests that males outnumber females. Most cases were seen in the perianal and groin region. It is important to distinguish it from basal cell carcinoma (BCC) of the perineum and malignant basaloid (cloacogenic) carcinoma of the anal canal. Ours [Figure 1] is an index case that presented in the mammary region. TE arising from facial scar is also documented.[26] The majority of the GST have been subcutaneous, but pedunculated,[21] ulcerated,[22] and cystic[15] forms appear as well.

TEs are associated with Brooke-Spiegel syndrome and Rombo syndrome. The Brooke-Spiegel syndrome inherited by autosomal-dominant transmission consists of multiple TEs, cylindromas (type of epithelial tumor characterized by islands of neoplastic cells embedded in a cylindrical hyalinized stroma formed from ducts of glands), and spiradenomas (benign tumor of eccrine sweat gland origin). CYLD gene on chromosome 16q12-13 is responsible for this syndrome.[27] The Rombo syndrome is dominantly inherited disorder characterized by vermiculate atrophoderma (symmetrical vermiform facial atrophy with time, the lesions develop into pit-like depressions), milia (benign, keratin-filled cysts), hypotrichosis (less than normal amount of hairs), TEs, BCC, and peripheral vasodilation with cyanosis.[28] Unlike trichoblastic carcinoma associated with multiple familial TEs, no such association found in the review literature with GSTs.[29]

Table 1: Clinical profile of patients with GST from 1972 to 2013

Case reports/series	Age*/ sex	Duration (years)	Size (cm)	Anatomical location	Treatment	Recurrence/ follow up
Czernobilsky *et al*.[9]	58/M	20	8	Thigh	Excision	No/?
Dvir *et al*.[10]	70/M	?	2.5	Nose	Excision	No/1 year
Filho *et al*.[11]	53/M	3.5	6.5	Thigh	Excision	No/9 months
Tatnall *et al*.[12]	77/F	7	3.5	Natal cleft	Excision	No/18 months
Tatnall *et al*.[12]	71/M	?	5	Buttock	Excision	No/1 year
Tatnall *et al*.[12]	70/F	10	3.5	Natal cleft	Excision	No/6 months
Beck *et al*.[13]	31/M	?	2	Scrotum	Excision	Yes/17 years
Oursin *et al*.[14]	67/F	15-20	17	Abdomen	-	No/?
Lorenzo *et al*.[15]	-	-	9	Thigh	Excision	?
Jemec *et al*.[16]	48/M	?	4	Shoulder	Excision	No/3.5 years
Ohnishi *et al*.[5]	-	-	-	-	-	-
Kazakov *et al*.[17]	52/F	-	2	Scalp	Excision	?
Abdelmoula *et al*.[18]	-	-	-	Perianal	Excision	?
Hanumanthaiah[19]	71/M	5	2	Nose	RFA	?
Patrocinio *et al*.[20]	56/M	5	3	Nose	Excision	No/4 years
Krishnamurthy *et al*.[21]	80/M	1	3	Nose	Excision	No/?
Goyal *et al*.[22]	45/F	25	9.5	Forearm	Excision	No/6 months
Bedir *et al*.[23]	82/F	10	5	Groin	Excision	?
Our case	3/M	3	6	Mammary	Excision	No/2 years

*Age in years. M: Male, F: Female. Ohnishi *et al*.[5] m had studied the immunophenotypes of 13 cases of trichogenic tumors werein there was only one giant solitary trichoepithelioma. They have described regarding the possible origin, differentiation and immunoreactivities of these tumors. However since the onus was on Immunohistochemical analysis, the patient characters and tumor size were not highlighted. But since our study is a compilation of all the available literature on GST, we feel it is prudent to include it in the review, that also credits the authors original contributions

Cytology

Fine needle aspiration cytology shows highly cellular aspirate consisting of frond-like pattern of basaloid cells and papillary mesenchymal bodies. The epithelial component consists of uniform basaloid cells with scant cytoplasm and darkly stained nucleus arranged in nests and adenoid pattern. The mesenchymal component consists of spindle-shaped cells in a myxoid stroma. The spindle-shaped cells may also be seen traversing the epithelial component. Acellular eosinophilic bodies, which represents abrupt keratinization, favors the diagnosis.[21]

The cytological differential diagnoses of GST are keratotic BCC, trichoblastoma, and microcystic adnexal carcinoma. Scanty mitotic activity and apoptotic cells favor TEs. The absence of papillary mesenchymal bodies, presence of peritumoral lacunae detected only around the solid areas, undifferentiated basaloid cells, parakeratotic cells and accumulation of amyloid-like hyalinized material favors BCC.[30] Trichoblastoma (trichoblastic fibroma) lacks keratinizing cysts.[31] Microcystic adnexal carcinoma is a poorly circumscribed invasive dermal tumor with pleomorphic ductal epithelial cells and basaloid keratinocytes.[32]

Some authors opine that TEs and BCC are two ends of same spectrum, whereas others believe that giant TEs (both solitary and non-solitary) can transform into BCC. There is no strong evidence in literature to support either.

Histopathology

The tumors of hair follicle can be categorized according to their predominant lines of differentiation. The term "Solitary Trichoepithelioma" is used as histological designation only for lesions showing a high degree of differentiation toward hair structures.[33,34] TE and giant TE represent the more mature end of the spectrum of trichoblastoma.[24]

Grossly, the tissue is solid in consistency, skin-colored, and lobulated in nature with sharp demarcation. The lobularity is

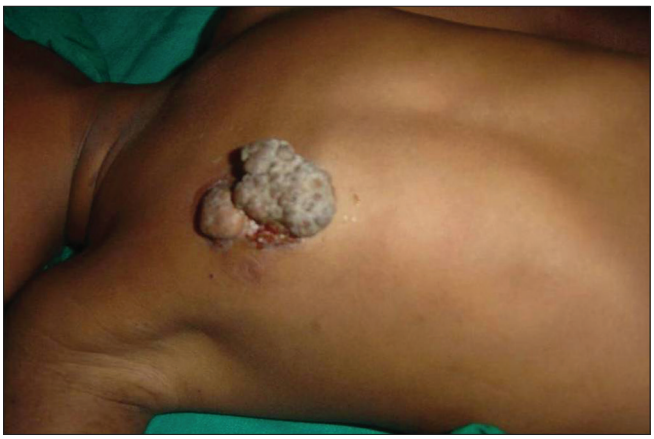

Figure 1: Pedunculated 6 × 4 cm GST with lobular surface in right mammary area with broad base of 1.5 cm

described to have 'pushing borders' (where the margin of the tumor mass is well defined, curvilinear, pushing the surrounding normal tissue).

Microscopy of hematoxylin and eosin stained paraffin sections showed a subcutaneous tumor with a normal overlying epidermis. At scanning magnification, dome shaped epithelial neoplasm within the dermis is seen. The tumor shows islands of uniform basaloid cells with scant cytoplasm and darkly stained nucleus arranged in nests and adenoid pattern with epithelial islands. The epithelial islands may not connect to the overlying epidermis. The stroma may be fibromyxoid or fibrocellular.[21,23] Various stages of follicular differentiation are identified. Mitotic figures are frequent, but abnormal mitoses are not seen.[24] Immature hair appears as keratinous cysts. These horn cysts are the characteristic features in most GST. They consist of fully keratinized center surrounded by basophilic cells that lack high-grade atypia and mitosis. The keratinization is abrupt and complete – the so called trichilemmal keratinization, which differentiates it from

squamous cell carcinoma having gradual and incomplete keratinization in horn pearls.[35] Unusually, multinucleated giant cells may be present.

The focal presence of pleomorphic giant cells is believed to have no clinical or prognostic implications. It does not denote its "malignant transformation" in a low proliferative index tumor.[17] GST may present as a pigmented lesion because of the increased activity of melanocytes or increased retention of pigments in the basal keratinocytes.[36] Additional findings, such as amyloidosis, inflammation, granulomas, foreign-body giant cell reactions, calcification, and apoptotic bodies, are seen in GST.[30]

Immunohistochemistry

IHC can be handy in differentiating GST from BCC. The follicular stem cell marker pleckstrin homology-like domain, family A, member 1 (PHLDA1) also known as T-cell death-associated gene 51 (TDAG51) labels TE but not BCC.[37] CD34 is an antigen known to stain the spindle-shaped cells located around the middle portion of normal hair follicles. Trichoepithelioma cells are positive for CD34, whereas, in all BCCs, the spindle-shaped cells surrounding the nests of tumor cells are negative.[38] Condensation of CD10-positive stromal cells around basaloid nests as was in our case favors TE over BCC.[39] p75 neurotrophin receptor (p75NTR) is expressed in sclerosing neoplasms like desmoplastic TE, infiltrative BCC, and microcystic adnexal carcinoma of the skin. But, its use as an adjunct marker in the differential diagnosis is limited because of significant overlap in amount of p75NTR immunoreactivity.[40] Thus, CD10, CD34, PHLDA1 but not p75NTR are useful adjunct markers in distinguishing TE from BCC.

Imaging

Radiology is not routinely needed as these tumors are superficial tumors. Magnetic resonance imaging may aid in depicting the extent and depth, if the tumor is large and the diagnosis is uncertain. But, the signal intensity is non-specific and does not allow histological classification.[14]

Treatment

Treatment for multiple TEs include excision, electrodessication, dermabrasion, cryotherpy, radiotherapy, Argon, Carbon dioxide, erbium-YAG lasers. Surgical excision, with or without flap used by most of the authors, is the standard treatment for most of GSTs. Radio-surgical ablation can be considered for cosmetic reasons when the tumor is situated over face. It helps in accurate removal of the tumor with minimal bleeding without destroying the underlying structures like cartilage. Malignant transformation into BCC after surgical excision requires adjuvant radiotherapy.[8] Recurrence and possible transformation into BCC cautions follow up at regular intervals.

Conclusions

GST is a rare trichogenic tumor with potential for local recurrence. It may present at any age including at birth with predilection for old age. It has close resemblance to BCC and other skin adnexal tumors - clinically, cytologically, and histologically. CD10, CD34, PHLDA1 but not p75NTR are useful adjunct markers. Surgical excision is the standard treatment. Recurrence and possible transformation in to BCC cautions follow up at regular intervals.

References

1. Anderson DE, Howell JB. Epithelioma adenoides cysticum: Genetic update. Br J Dermatol 1976;95:225-32.
2. Lever WF. Histopathology of skin, 4th ed. Philadelphia: J.B. Lippincott Company; 1967. p. 557.
3. Montgomery H. Dermatopathology, Vol. 2. New York: Hoeber Medical Division, Harper and Row Publishers; 1967. p. 887.
4. Pinkus H. Premalignant fibroepithelial tumors of skin. AMA Arch Derm Syphilol 1953;67:598-615.
5. Ohnishi T, Watanabe S. Immunohistochemical analysis of cytokeratin expression in various trichogenic tumors. Am J Dermatopathol 1999;21:337-43.
6. Mandal AK, Mandal A. Exocrine differentiation of trichoepithelioma and desmoplastic trichoepithelioma: A scanning electron microscopic study. Indian J Pathol Microbiol 1993;36:101-3.
7. Rosen LB. A review and proposed new classification of benign acquired neoplasms with hair follicle differentiation. Am J Dermatopathol 1990;12:496-516.
8. Martinez CA, Priolli DG, Piovesan H, Waisberg J. Nonsolitary giant perianal trichoepithelioma with malignant transformation into basal cell carcinoma: Report of a case and review of the literature. Dis Colon Rectum 2004;47:773-7.
9. Czernobilsky B. Giant solitary trichoepithelioma. Arch Dermatol 1972;105:587-8.
10. Dvir E. Solitary trichoepithelioma in a 70-year-old man. Arch Dermatol 1981;117:455-6.
11. Filho GB, Toppa NH, Miranda D, Matos MP, da Silva AL. Giant Solitary Trichoepithelioma. Arch Dermatol 1984;120:797-8.
12. Tatnall FM, Jones EW. Giant solitary trichoepitheliomas located in the perianal area: A report of three cases. Br J Dermatol 1986;115:91-9.
13. Beck S, Cotton DW. Recurrent Solitary Giant Trichoepithelioma located in the perianal area: A case report. Br J Dermatol 1988;118:563-6.
14. Oursin C, Krüger HJ, Sigmund G, Hellerich U. MR imaging of a giant solitary trichoepithelioma of the skin. Radiologe 1991;31:574-6.
15. Lorenzo MJ, Yebra-Pimentel MT, Peteiro C, Toribio J. Cystic giant solitary trichoepithelioma. Am J Dermatpathol 1992;14:155-60.
16. Jemec B, Lovgreen Nielsen P, Jemec GB, Balsev E. Giant solitary trichoepithelioma. Dermatol Online J 1999;5:1.
17. Kazakov DV, Michal M. Trichoepithelioma with giant and multinucleated neoplastic epithelial cells. Am J Dermatopathol 2006;28:63-4.
18. Fraoua Abdelmoula F, Lahmar Boufaroua A, Goutallier C, Khalfallah MT, Mzabi Regaya S. An uncommon trichoepithelioma: The giant solitary trichoepithelioma. Tunis Med 2006;84:503-5.
19. Hanumanthiah HC. Radiosurgical ablation of solitary trichoepithelioma. J Cutan Aesthet Surg 2008;1:27-8.
20. Patrocinio LG, Damasceno PG, Patrocinio TG, Patrocinio JA. Solitary nasal Trichoepithelioma. Rev Bras Otorrinolaringol 2008;74:637.
21. Krishnamurthy J, Divya KN. The cytology of giant solitary trichoepitheliomas. J Cytol 2010;27:99-101.
22. Goyal S, Mahajan NC, Garg M, Goyal S. Giant solitary nodular trichoepithelioma: A case report and review of literature. Arch Clin Exp Surg 2012;1:58-60.
23. Bedir R, Pergel A, Gucer H. Giant solitary trichoepithelioma: A Case report. [Article in Turkish] Dicle Med J 2013;40:137-40.
24. Colenje E. Tumours of the skin appendages. In: Burns T, Breathnach S, Cox N, Griffiths C, editors. Rook's Textbook of Dermatology, 8th ed. Vol. 3. West Sussex: Wiley-Blackwell Publishing; 2010.
25. Kim C, Kovich OI, Dosik J. Brooke Spiegler syndrome. Dermatol Online J 2007;13:10.
26. Yong LJ, Jin KD, Ho K, Sung-No J. Trichoepithelioma arising from facial scar tissue. J Craniofac Surg 2013;24:292-4.
27. Duparc A, Lasek-Duriez A, Wiart T, Duban-Bedu B, Gosset P, Modiano P. Multiple familial trichoepithelioma: A new CYLD gene mutation. Ann Dermatol Venereol 2013;140:274-7.
28. Michaelsson G, Olsson E, Westermark P. The Rombo syndrome: A familial disorder with vermiculate atrophoderma, milia, hypotrichosis, trichoepitheliomas, basal cell carcinomas and peripheral vasodilation with cyanosis. Acta Derm Venereol 1981;61:497-503.
29. Kirby JS, Siebert Lucking SM, Billingsley EM. Trichoblastic carcinoma associated with multiple familial trichoepithelioma. Dermatol Surg 2012;38:2018-21.
30. Gray HR, Helwig EB. Epithelioma adenoides cysticum and solitary trichoepithelioma. Arch Dermatol 1963;87:102-14.
31. Gilks CB, Clement PB, Woods WS. Trichoblastic fibroma. Am J Dermatopathol 1989;11:397-402.

32. Sahin MT, Demir MA, Kaya Y, Can M, Inanir I, Oztürkcan S. Inguinal keratotic Basal cell carcinoma mimicking giant solitary trichoepithelioma. J Dermatol 2003;30:395-9.
33. Elder D, Elenitsas R, Ragsdale BD. Tumors of the epidermal appendages. In: Elder D, Elenitsas R, Jaworsky C, Johnson Jr B, editors. Lever's Histopathology of the Skin. Philadelphia: Lippincott-Raven; 1997. p. 747-803.
34. Ho VC. Benign epithelial tumors. In: Freedberg IM, Eisen AZ, Wolff K, Austen KF, Goldsmith LA, Katz SI, editors. Dermatology in General Medicine. New York: McGraw-Hill; 1999. p. 873-914.
35. David E Elder, Rosalie Elenitsas, Adam I Rubin, Michal Ioffreda, Jeffrey Miller, O Fred Miller III. Atlas and Synopsis of Lever's Histopathology of the Skin. Chapter 6, Tumors and Cyst of epidermis and subcutis. 3rd ed. Philadelphia: Lippincott-Raven; 2012. p. 364.
36. Rosai J. Rosai and Ackerman's surgical pathology. 9th ed. St Louis: Mosby; 2004. p. 176.
37. Sellheyer K, Cribier B, Nelson P, Kutzner H, Rütten A. Basaloid tumors in nevus sebaceus revisited: The follicular stem cell marker PHLDA1 (TDAG51) indicates that most are basal cell carcinomas and not trichoblastomas. J Cutan Pathol 2013;40:455-62.
38. Kirchmann TT, Prieto VG, Smoller BR. CD34 staining pattern distinguishes basal cell carcinoma from trichoepithelioma. Arch Dermatol 1994;130:589-92.
39. Sari Aslani F, Akbarzadeh-Jahromi M, Jowkar F. Value of CD10 expression in differentiating cutaneous basal from squamous cell carcinomas and basal cell carcinoma from trichoepithelioma. Iran J Med Sci 2013;38:100-6.
40. Jedrych J, McNiff JM. Expression of p75 neurotrophin receptor in desmoplastic trichoepithelioma, infiltrative basal cell carcinoma, and microcystic adnexal carcinoma. Am J Dermatopathol 2013;35:308-15.

How to cite this article: Teli B, Thrishuli PB, Santhosh R, Amar DN, Rajpurohit S. Giant solitary trichoepithelioma. South Asian J Cancer 2015;4:41-4.

Source of Support: Nil. **Conflict of Interest:** None declared.