The Journal of Laryngology & Otology (2007), ***121***, *506–509*.

doi:10.1017/S0022215107005701
Printed in the United Kingdom
First published online 25 January 2007

Clinical Record

Paediatric granular cell tumour of the larynx: case report of laser resection with frozen section

C Holton, H E Cruickshank*, A S High†, K Maclennan†, Z G G Makura

Abstract

Granular cell tumours of the larynx are a very rare cause of persistent hoarse or husky voice in children. We report the case of a 13-year-old girl who presented with a three-year history of progressively huskier voice. We discuss the presentation, location and diagnosis of the tumour. In addition, we present a method of surgical treatment of the tumour, involving the hitherto unreported technique of laser excision and frozen section of the lesion.

Key words: Granular Cell Tumour; Larynx; Child; Frozen Sections

Introduction

Granular cell tumours are uncommon, usually benign neoplasms.[1] They can be found all over the body, although they are most common in the head and neck region of the aero-digestive tract.[1]

Whilst granular cell tumours of the larynx are uncommon in adults, they are rarer still in children – a literature search revealed only 20 reported cases of laryngeal granular cell tumours in the paediatric population.[2] The age range for this group was four to 16 years.[2]

We describe a further case of a 13-year-old girl with a three-year history of progressively huskier voice, who was surgically treated with laser excision and frozen section.

Case report

A 13-year-old Caucasian girl presented to the otolaryngological out-patient clinic with a three-year history of progressively huskier voice. No stridor was present. She was otherwise medically well, with no history of asthma, voice trauma or intubation. She had never smoked.

Indirect laryngoscopy revealed a smooth swelling on the right vocal fold, extending back to the arytenoid cartilage but not quite reaching the anterior commissure.

Microlaryngoscopy and biopsy was performed. Histological examination revealed a granular cell tumour.

Further management of the patient's tumour was discussed with the pathologists, the patient and her family. It was decided to perform a laser excision of the lesion with frozen section.

Laser excision was performed with a CO_2 laser, model 315M Superpulse class 4 (Irradia AB, Stockholm, Sweden). A maximum of 15 W CO_2 laser beam power and a maximum of 5 MW Gallium-aluminium-arsenate (GaAIAs) laser guide were used. The Wolfgang Steiner transoral tumour resection technique[1] was performed with the CO_2 laser at 6 W continuous power setting. The Wolfgang Steiner technique involved a vertical split in the midline of the tumour until the tumour muscle boundary was reached. The anterior portion of the tumour was resected, followed by the posterior portion. Frozen sections were obtained after tumour removal was completed. Sections were taken from the anterior margin and from the right mid-vocal fold deep margin. Haemostasis was achieved using the laser and adrenaline-soaked patties. Frozen sectioning revealed the anterior portion to be clear of tumour, whilst there was a suspicion that granular cells were present in the deep mid-vocal fold section. However, on formalin section of the mid-vocal fold section, it was found be clear of tumour cells.

Four weeks following surgery, the patient's voice was returning to normal. Eight months after surgical excision, her vocal quality was improved compared with her first presentation, although it remained slightly husky and breathy. She will be reviewed indefinitely to monitor for recurrence.

Discussion

Granular cell tumours are usually benign neoplasms which are thought to originate from Schwann cells.[2] Granular cell tumours are most commonly reported in the head and neck, with the anterior part of the tongue being the commonest site.[3] About 10 per cent of patients may have synchronous granular cell tumours at other anatomic sites.[4] Laryngeal lesions account for 7 to 10 per cent of all reported cases of granular cell tumours.[5,6] They most commonly affect adults between 20 and 50 years of age and only rarely occur in children.[2,7] They predominantly affect females of African descent.[7]

Granular cell tumours in adults, throughout the whole body, have a 1–2 per cent malignancy rate,[8–11] although there is currently only one reported case of a malignant laryngeal granular cell tumour.[12] Malignancy is characterised by rapid growth, a tumour size greater than 5 cm^3

From the Department of Otolaryngology and Head & Neck Surgery, Leeds General Infirmary, Leeds, UK.
Presented at the 26th Annual Meeting of the American Society for Laser Medicine and Surgery, 5–9 April 2006, Boston, Massachusetts, USA.
Accepted for publication: 30 October 2006.

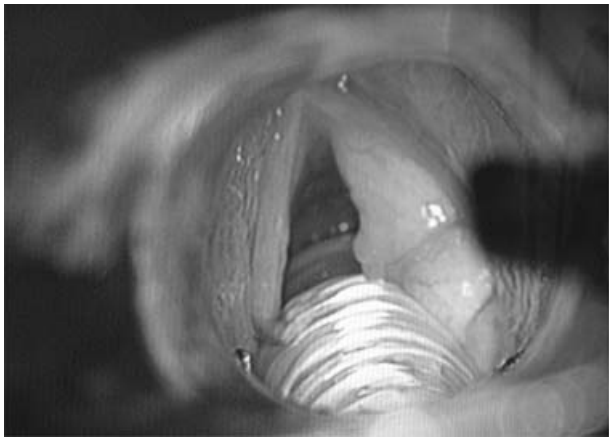

FIG. 1

Microlaryngoscopy revealed a smooth swelling on the right vocal fold, extending back to the arytenoid cartilage.

and local recurrence.[13] Thunold highlighted these factors as being of greater prognostic significance than histology alone in suggesting the likelihood of malignancy.[5] Malignant lesions usually result in death within two years of diagnosis.[14] There have been six reported cases of malignant granular cell tumours within the head and neck region, and 83 per cent of these cases died within five years of diagnosis.[15] Fortunately, no malignant cases have been reported in the paediatric population.[15]

Twenty cases of paediatric laryngeal granular cell tumours have been documented in the literature so far. These patients ranged in age from four to 16 years, with a mean age of 9.7 years.[3,16] Granular cell tumours of the larynx are painless;[15] presenting symptoms have included: dyspnoea, cough and/or globus sensation, airway obstruction, stridor, wheezing, increasingly hoarse voice, and referred otalgia.[14,17,18] The commonest presentation is hoarseness.[19] The diagnosis is usually made on the basis of the histopathology. Very rarely, a pre-operative diagnosis has been established due to previous granular cell tumours in other sites.[12,14]

Granular cell tumours were originally thought to be derived from skeletal muscle cells, as first described by Abrikossoff in 1926.[20] However, this has been subsequently corrected, and the origin of this tumour is now proven to be neuroectodermal cells.[12,21] The neural theory was first proposed in 1952 by Fust and Custer.[22] It was later confirmed by Sobel and Marquet,[23] through their use of microscopic and cytochemical stains which proved the derivation to be mesenchymal cells or Schwann cells. These lesions are thus now referred to as 'granular cell tumours' rather than the old term 'myoblastoma'.

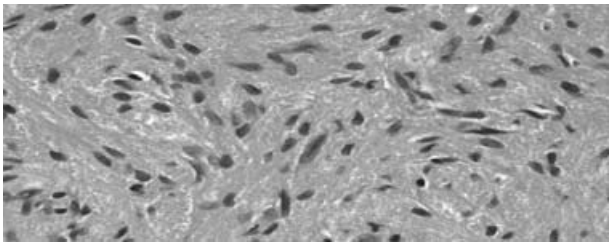

FIG. 3

High power photomicrograph of granular cell tumour pattern, with granulated cytoplasm and small, basophilic nuclei (H&E; × 400).

Histopathological and immunohistochemical evaluation is required for definitive diagnosis of granular cell tumours. Histologic evaluation under the light microscope reveals granular cell tumours to exhibit large, polyhedral cells with characteristic intracytoplasmic granules, small or oval nuclei, and absent mitosis.[18,24] Distinct intercellular borders were noted in these closely packed cells, with the granular cells being infrequently spindled and elongated.[18] The occasional normal mitosis and presence of epithelial downgrowths, along with the florid pseudoepitheliomatous hyperplasia which often accompany these lesions, have fooled some pathologists into reporting these lesions as squamous cell carcinomas,[19] although pseudoepitheliomatous hyperplasia is not a common feature in paediatric lesions.[6] Cree *et al.* point out the need for good communication between the surgeon and pathologist, especially in cases in which the initial biopsy is superficial or few granular cells are present, so that a correct diagnosis can be made.[19] These authors add that pathologists should also question a diagnosis of squamous cell carcinoma in a clinically benign-looking lesion.[19] Immunohistochemical investigation reveals reactivity with antibodies to S-100 protein, laminin, neuron-specific enolase and various myelin proteins.[21,25] These immunohistochemical investigations are helpful in the diagnosis of granular cell tumour if doubt exists over the lesion.[21,25]

Diagnosing granular cell tumours on frozen section can be difficult. There are often artefactual changes in cells

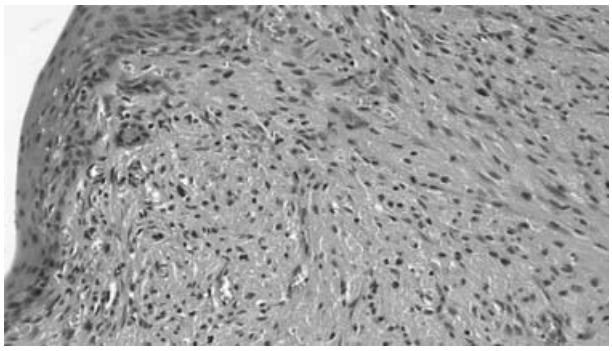

FIG. 2

Photomicrograph showing benign squamous epithelium and underlying tissue containing diffuse deposits of granular cells (H&E; × 250).

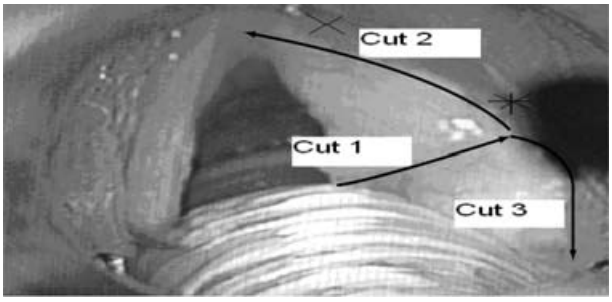

FIG. 4

The surgical technique used. × = first anterior margin of frozen section biopsy; ∗ = second right mid-vocal fold deep margin biopsy

https://doi.org/10.1017/S0022215107005701 Published online by Cambridge University Press

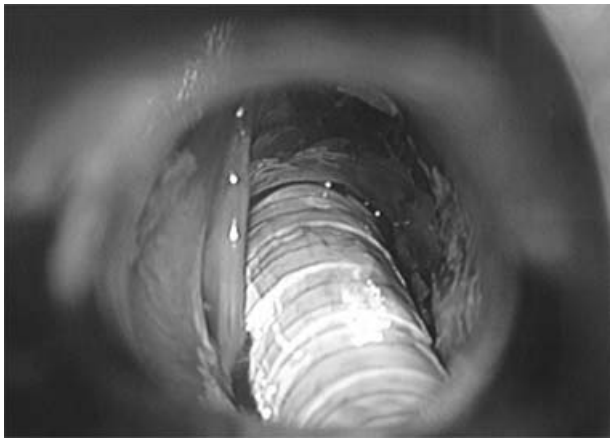

FIG. 5
Intra-operative view of laser-resected lesion.

(due to ice crystal formation) which can give them a rather granular appearance. It is sensible to do a periodic acid Schiff stain at the same time as a haematoxylin and eosin or alcian blue stain, as this is often helpful in confirming true granular cells. Pseudoepitheliomatous hyperplasia is another confirmatory feature to look for, although not noted in the present case.

The true vocal folds are the commonest site for laryngeal granular cell tumours; more than 50 per cent of reported cases were found at this location.[26] Holland *et al.*[3] and Lazar *et al.*[26] both commented on the location of the lesions in relation to the vocal folds. They noted the difference between adult laryngeal lesions and those in the paediatic population. Adult lesions were noted to predominantly involve the posterior portion of the true vocal folds and arytenoid areas, with only two reported cases occurring subglottally. However, paediatric lesions mainly occurred in the anterior and subglottic regions, with 58 per cent seen within the vocal folds.[3,5]

Our patient presented with a tumour mimicking the appearance of an adult type lesion. However, the prolonged history (three years' hoarse voice) was unusual. Initial endoscopy and biopsy was performed to rule out squamous cell carcinoma. Once this was excluded by histopathological examination of the biopsy, further management of the granular cell tumour was required.

Schottenfeld and Marsh commented that the ideal treatment of these tumours is local excision with histologically negative margins.[27] Proposed treatments for these lesions have included local 'cold steel' excision with or without laser excision,[14] laryngofissure for large lesions, and, rarely, laryngectomy.[26] Granular cell tumours are radioresistant therefore radiation therapy is not indicated in the treatment of these benign lesions.[14,28]

Our case highlights the use of endoscopic laser excision with frozen section for a granular cell tumour, without requiring local cold steel excision. Piazza *et al.*[13] proposed endoscopic laser excision of hypopharyngeal granular cell tumours in the adult population. Wight *et al.* first proposed CO_2 excision of laryngeal granular cell tumours in the paediatric population.[29] Both groups commented that laser excision allowed surgeons precise excision of the lesion while working in a bloodless field and causing minimal thermal damage to surounding tissues. Piazza *et al.* also noted the advantage of an endoscopic approach which would allow further procedures to be carried out if local recurrence did occur.[13]

- **Granular cell tumours are uncommon, usually benign neoplasms. They are most commonly found in the head and neck region of the aero-digestive tract**
- **A literature search revealed only 20 reported cases of laryngeal granular cell tumours in the paediatric population**
- **This paper describes the case of a 13-year-old girl with a three-year history of progressively huskier voice, who was surgically treated with laser excision and frozen section**

Intra-operative frozen section allows clear resection margins to be gained, so the extent of surgical resection can be minimised. In two paediatric cases, incomplete excision of a laryngeal granular cell tumour has led to further surgical treatment being required.[28,30] Recurrence occurred in only one of 36 adequately resected cases of laryngeal lesions reviewed by Campagno *et al.*[10] However, recurrence has been reported in up to 8 per cent of adult cases following adequate resection of lesions elsewhere in the body.[12,31] If excision of the primary lesion is found to have positive margins on pathological examination further growth of the remaining lesion is reported in 21 to 50 per cent of these case.[31,32]

There are no reports documenting recurrence rates in the paediatric population following granular cell tumour excision with clear resection margins. However, it would seem reasonable to propose that complete excision of the lesion would reduce the risk of recurrence in this age group. We therefore propose laser resection with frozen section as a suitable treatment for paediatric granular cell tumour of the larynx, one which minimises the extent of surgery required and the recurrence rate of these rare, benign lesions.

Acknowledgement

The authors would like to thank Dr Judith Short, who administered the general anaesthetic.

References

1 Steiner W and Ambrosch P. Laser microsurgery for laryngeal carcinoma. *Endoscopic Laser Surgery of the Upper Aerodigestive Tract: With Special Emphasis on Cancer Surgery*. New York: Thieme Medical Publishers, 2000;47–50
2 Sobol SE, Samadi DS, Wetmore RF. Pediatric subglottic granular cell myoblastoma. *Otolaryngol Head Neck Surg* 2005;**132**:655–7
3 Holland RS, Abaza N, Balsara G, Lesser R. Granular cell tumour of larynx in a six-year-old child: case report and review of the literature. *Ear Nose Throat J* 1998;**77**:652–4
4 Gleason-Jordan IO, Mirra JM, Mahendra T, Pathmarajah C. Case report 676. *Skeletal Radiol* 1991;**20**:529–32
5 Thunold S, Von Eyden FE, Maehle B. Malignant granular cell tumour of the neck: immunohistochemical and ultrastructural studies. *Histopathology* 1989;**14**:655–62
6 Har-El G, Shviro J, Avidor I, Segal K, Sidi J. Laryngeal granular cell tumour in children. *Am J Otolaryngol* 1985; **6**:32–4
7 Ipakchi R, Zager WH, de Baca ME, Bloedon E, McCue PA, Zwillenberg D. Granular cell tumour of the trachea in pregnancy: a case report and review of literature. *Laryngoscope* 2004;**114**:143–7
8 Victoria LV, Hoffman HT, Robinson RA. Granular cell tumour of the larynx. *J Laryngol Otol* 1998;**112**:373–4
9 Michaels L. *Pathology of the Larynx*. Berlin: Springer Verlag, 1984;285–300

10 Campagno J, Hyams VJ, Ste-Marie P. Benign granular cell tumours of the larynx: a review of 36 cases with clinicopathologic data. *Ann Otol Rhinol Laryngol* 1975;**84**:308–14
11 Booth JB, Osborn DA. Granular cell myoblastoma of the larynx. *Acta Otolaryngol* 1970;**70**:279–93
12 Conley SF, Milbrath M, Beste D. Pediatric laryngeal granular cell tumour. *J Otolaryngol* 1992;**21**:450–3
13 Piazza C, Casirati C, Peretti G, Battaglia G, Manfredini C, Nicholai R. Granular cell tumor of the hypopharynx treated by endoscopic carbon dioxide laser excision: report of two cases. *Head Neck* 2000;**22**:524–9
14 Sataloff RT, Ressue JC, Portell M, Harris RM, Ossoff R, Merati AL *et al*. Granular cell tumours of the larynx. *J Voice* 2000;**14**:119–34
15 Kershisnik M, Batsakis JG, Mackay B. Granular cell tumors. *Ann Otol Rhinol Laryngol* 1994;**103**:416–19
16 Hamid AM, Alshaikhly A. Granular cell tumour of the larynx in an eight year girl. *J Laryngol Otol* 1993;**107**:940–1
17 Farmer RW, Scher RL. Granular cell tumour of the larynx presenting with airway obstruction. *Otolaryngol Head Neck Surg* 1998;**118**:874–6
18 Fliss DM, Puterman M, Zirkin H, Leiberman A. Granular cell lesions in the head and neck: a clinicopathological study. *J Surg Oncol* 1989;**42**:154–60
19 Cree IA, Bingham BJ, Ramesar KC. Granular cell tumour of the larynx. *J Laryngol Otol* 1990;**104**:159–61
20 Abrikossof A. Review of myotomes within striated muscle [in German]. *Virchows Arch* 1926;**260**:215–33
21 Weiss SW, Goldblum JR. *Enzinger and Weiss's Soft Tissue Tumours*, 4th edn. St Louis: Mosby, 2001;1178–87
22 Fust JA, Custer RP. On the neurogenesis of so-called granular cell myoblastoma. *Am J Clin Path* 1952;**22**:1044–53
23 Sobel HJ, Marquet E. Granular cells and granular cell lesions. *Path Ann* 1974;**9**:43–79
24 Mills SE, Gaffey MJ, Frierson HF. *Tumours of the Upper Aerodigestive Tract and Ear*, 3rd series. Washington, DC: Armed Forces Institute of Pathology, 2000
25 Fisher ER, Wechsler H. Granular cell myoblastoma – a misnomer: EM and histochemical evidence concerning its Schwann cell derivation and nature (granular cell schwannoma). *Cancer* 1962;**15**:936–44
26 Lazar RH, Younis RT, Kluka EA, Joyner RE, Storgion S. Granular cell tumour of the larynx: report of two pediatric cases. *Ear Nose Throat J* 1992;**71**:440–3
27 Schottenfeld R, Marsh B. Granular cell tumour of the larynx. *Ear Nose Throat J* 1986;**65**:554–7
28 Torsiglieri AJ Jr, Handler SD, Uri AK. Granular cell tumours of the head and neck in children: the experience at the Children's Hospital of Philadelphia. *Int J Ped Otorhinolarnygol* 1991;**21**:249–58
29 Wight RG, Variend S, Bull PD. Granular cell tumour of the larynx in childhood. *J Laryngol Otol* 1989;**103**:880–1
30 Royal SA. Pediatric laryngeal granular cell tumour. *Pediatr Radiol* 2000;**30**:869–70
31 Alessi DM, Zimmerman MC. Granular cell tumours of the head and neck. *Laryngoscope* 1988;**98**:810–14
32 Kamal SA, Othman EO. Granular cell tumour of the larynx. *J Laryngol Otol* 1998;**112**:83–5

Address for correspondence:
Mr Colin Holton,
Department of Otolaryngology and Head & Neck Surgery,
Leeds General Infirmary,
Leeds LS1 3EX, UK.

Fax: 0113 392 3165
E-mail: colinsholton@doctors.org.uk

Mr C Holton takes responsibility for the integrity of the content of the paper.
Competing interests: C Holton was awarded a travel grant to present this case at the 26th Annual Meeting of the American Society for Laser Medicine and Surgery, 5–9 April 2006, Boston, Massachusetts, USA.

Online Only Paper

Clinical Record
Oropharyngeal and hypopharyngeal myxoma: case report and literature review, *S Ayache, D Chatelain, B Tramier, V Strunski*, E5

https://doi.org/10.1017/S0022215107005701 Published online by Cambridge University Press