Vocal Cord Palsy in Children With Cancer: A 10-Year Analysis of UK Pediatric Intensive Care Admissions

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Summary: Vocal cord palsy (VCP) is a rare but potentially life-threatening complication in children with cancer. This study reviews UK Intensive Care admissions for children with cancer and VCP using data obtained from the Pediatric Intensive Care Audit Network (PICANet) database. 26 children with cancer and VCP were admitted to intensive care from 2002 to 2012. The majority of admissions (23/26) required respiratory intervention (17 invasive ventilation, 8 noninvasive ventilation, and 5 tracheostomy). VCP should be considered early in children with cancer who present with signs of upper airway obstruction, especially in those receiving vinca-alkaloids as VCP is likely to be reversible.

Key Words: vocal cord palsy, cancer, leukemia, child, intensive care

(*J Pediatr Hematol Oncol* 2017;39:293–295)

Vocal cord palsy (VCP) is defined as reduced or absent movement of the vocal cords due to dysfunction of the motor nerve supply to the laryngeal muscles. VCP may be unilateral or bilateral, and the most common presenting symptom in children is stridor.[1] Symptoms and signs range from dysphonia and mild feeding difficulties to severe respiratory distress requiring a tracheostomy. Children with cancer are most likely to present with VCP secondary to drug toxicity or central nervous system tumors. Vincristine, a vinca-alkaloid drug, used in many treatment regimes, is well known to cause peripheral neurotoxicity. In rare cases, vincristine can cause paralysis of the recurrent laryngeal nerve, a branch of the vagus nerve, causing vocal cord palsy.[2] VCP attributed to vinca-alkaloid drugs other than vincristine has been reported in adult patients only.[3,4]

The diagnosis of VCP can be made by bedside flexible fibreoptic endoscopy if tolerated by the child, or by microlaryngoscopy and bronchoscopy under general anesthesia. When a general anesthetic is required, vocal cord mobility is assessed by direct visualization of the larynx as the child is waking up. Laryngeal ultrasound imaging is an alternative method utilized to assess cord mobility in specialist centers. In cases resulting from vincristine toxicity, withdrawal of the drug leads to gradual resolution.[2,5–7] In a review of all published pediatric case reports by Latiff et al,[8] omission of vincristine led to clinical resolution in all 15 patients. In the largest published institutional case series, median time to resolution was 6.8 weeks.[2] Correct diagnosis of VCP, with omission of vincristine, is therefore essential as clinical presentation can mimic laryngomalacia, croup, and other upper airway infections, including pharyngeal abscess and fungal tracheitis, of which the treatment greatly differs.

Intervention is guided by the degree of airway compromise and a proportion of children will require admission to intensive care for monitoring and respiratory support. There are very few studies describing the requirement for respiratory support, airway intervention, and outcome for children with cancer and VCP. This is the first published series of UK pediatric intensive care unit (PICU) admissions for children with VCP and cancer.

METHODS

Data for children with VCP admitted to pediatric intensive care were obtained from the Pediatric Intensive Care Audit Network (PICANet) database managed by the Universities of Leeds and Leicester. PICANet is an audit database recording demographics and clinical details of all critically ill children admitted to 30 collaborating PICU across the UK and Ireland. Data collection started in 2002 from English and Welsh units with units from Scotland, Northern Ireland and the Republic of Ireland joining thereafter. The data collected is quality-controlled by regular staff training and site checks by the PICANet team, together with local and central validation procedures.[9]

Information from PICANet was obtained to include all children, younger than 16 years, admitted to PICU with VCP from 2002 to 2012. Patients with VCP were extracted from the database by diagnostic code, and cases reviewed for corresponding cancer diagnosis. Clinical information, patient characteristics, and nature of intervention were all obtained from the database. Collection of personally identifiable data were approved by the Patient Information Advisory Group (now the NHS Health Research Authority Confidentiality Advisory Group) and ethics approval granted by the Trent Medical Research Ethics Committee (ref. 05/MRE04/17 + 5). Data was analyzed using Microsoft Excel 2011 (Version 14.4.5).

RESULTS

From 2002 to 2012, there were 8573 children younger than 16 years admitted to collaborating PICU with a

Received for publication March 31, 2016; accepted December 12, 2016.
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current diagnosis of cancer. Out of a total of 416 admissions with a primary diagnosis of VCP, 26 (13 male and 13 female) had cancer (0.3%).

The median age at admission for children with VCP and cancer was 3 years and 5 months (Table 1), 8 children were below 12 months old. Of the 26 children, 9 had acute lymphoblastic leukemia (ALL) (34.6%), 10 had brain tumors (38.5%) and 7 had "unspecified" tumors (26.9%). There were 9 children with VCP and Down syndrome admitted to PICU, and 3 of these children had ALL.

The mean length of PICU stay was 7.8 days. Twenty-three children (88.5%) required respiratory support or tracheostomy (17 with endotracheal ventilation, 8 with noninvasive ventilation, and 5 with tracheostomy) (Fig. 1). Of the 5 children requiring a tracheostomy, 3 had a diagnosis of ALL and 2 had brain tumors. The average duration of invasive ventilation was 7.2 days. Eight children received noninvasive ventilation for an average of 6.4 days. All were alive on discharge from PICU.

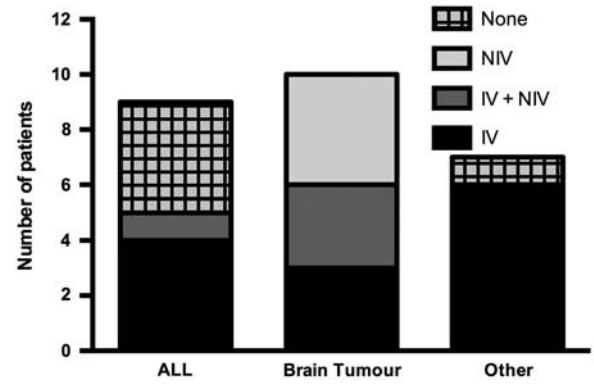

FIGURE 1. Proportion of patients with acute lymphoblastic leukemia (ALL), brain tumor or other tumor requiring invasive ventilation (IV), noninvasive ventilation (NIV), both forms of ventilation, or neither.

DISCUSSION

This study describes the proportion of intensive care admissions for VCP among all intensive care admissions for children with cancer and the requirement for airway intervention and respiratory support. The median age of patients admitted to PICU with VCP and cancer (41 mo) was significantly higher than previously reported for all causes of pediatric VCP where most children (68%) were diagnosed younger than 12 months.[1] This difference is explained by an older peak age of onset of childhood cancer and related comorbidity compared with the most common aetiologies of VCP in noncancer patients being iatrogenic as a result of cardiac surgery or idiopathic where the majority present at birth.[1]

Nineteen of 26 children with cancer and VCP had ALL (34.6%) or brain tumors (38.5%). The higher incidence of VCP in children with brain tumors compared with leukemia is most likely due to either direct or indirect infiltration by the tumor, associated hydrocephalus, or iatrogenic as a result of surgical debulking. The relatively high rate in those with leukemia can be explained by the use of vincristine in current treatment protocols leading to neurotoxicity.[2] One third of children with VCP and ALL had Down syndrome. Children with Down syndrome and leukemia are likely to require intensive monitoring and airway support due to greater airway compromise caused by underlying hypotonia.

Only 5 children with cancer and VCP (19.2%) required airway intervention with tracheostomy and is considerably lower than in previous pediatric series for all children with VCP (57%),[1] but higher than that previously reported for cancer patients with VCP (13%).[8] The lower rate of tracheostomy in children with cancer may be due to the fact that VCP is potentially reversible if due to vincristine therapy, usually only requiring supportive management and omission of vincristine.[8]

Limitations of PICANet data did not allow for exact causality of VCP, nor whether VCP was unilateral or bilateral. VCP prevalence is likely to be higher than that reported as cases were extracted using a primary diagnosis of VCP whereas VCP may have been coded as a condition secondary to the reason for admission such as cancer. In addition, not all PICUs participated over the complete time period. A detailed prospective study is required to determine the effect of vincristine dose, number of exposures, concomitant therapy, and time to resolution of symptoms.

TABLE 1. Demographics, Number of Ventilated Days, Length of PICU Stay, and Outcome for Children (Under 16 y) With Cancer and VCP Admitted to Pediatric Intensive Care

		n (%)		
	All Children With Cancer and VCP	ALL	Brain Tumor	Other Malignancy
No. patients	26	9 (34.6)	10 (38.5)	7 (26.9)
Sex				
Male	13 (50)	5 (55.6)	6 (60)	2 (28.6)
Female	13 (50)	4 (44.4)	4 (40)	5 (71.4)
Age (mo) (median, IQR)	41 (4-73)	41 (10.5-95)	65 (25-81)	2.5 (0.5-16.5)
No. days of ventilation (median, IQR)				
IV	4 (1-11)	6 (1-24)	3.5 (1.8-6.8)	5.5 (1-12)
NIV	4 (2-7.8)	4	4 (2-8)	—
No. patients without the need for ventilatory support	5	4	0	1
Length of PICU stay (d) (median, IQR)	5.3 (1.0-10.4)	4.7 (1.3-7.9)	6.4 (1.0-17.0)	9.6 (0.8-11.2)
Alive at discharge from PICU	26 (100)	9 (100)	10 (100)	7 (100)

ALL indicates acute lymphoblastic leukemia; IQR, interquartile range; IV, invasive ventilation (children requiring mechanical ventilation by endotracheal tube or tracheostomy); NIV, noninvasive ventilation (children receiving continuous positive airway pressure, CPAP); PICU, pediatric intensive care unit; VCP, vocal cord palsy.

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Early otolaryngology review and endoscopic inspection is advised for all children with cancer presenting with signs of upper airway obstruction. For children receiving vincristine, timely diagnosis of VCP is essential as withdrawal of the drug is generally associated with spontaneous resolution.[2] Patients admitted to PICU had a good prognosis with no deaths reported and a relatively short length of stay. Intensive care management is guided by degree of airway compromise, voice and swallowing impact, underlying comorbidity, and potential for reversibility.

ACKNOWLEDGMENTS

The authors would like to thank Dr Roger Parslow and the PICANet team for provision of data, review of methodology, and final manuscript approval. PICANet is commissioned by the Healthcare Quality Improvement Partnership (HQIP) as part of the National Clinical Audit Program (NCA). HQIP is led by a consortium of the Academy of Medical Royal Colleges, the Royal College of Nursing and National Voices. PICANet is funded by NHS England, NHS Wales, NHS Lothian/National Service Division NHS Scotland, the Royal Belfast Hospital for Sick Children, The National Office of Clinical Audit (NOCA), Republic of Ireland, and HCA Healthcare.

REFERENCES

1. Daya H, Hosni A, Bejar-Solar I, et al. Pediatric vocal fold paralysis: a long-term retrospective study. *Arch Otolaryngol Head Neck Surg*. 2000;126:21–25.
2. Kuruvilla G, Perry S, Wilson B, et al. The natural history of vincristine-induced laryngeal paralysis in children. *Arch Otolaryngol Head Neck Surg*. 2009;135:101–105.
3. Cherif S, Danino S, Yoganathan K. Autonomic neuropathy resulting in recurrent laryngeal nerve palsy in an HIV patient with Hodgkin lymphoma receiving vinblastine and antiretroviral therapy. *Int J STD AIDS*. 2015;26:206–208.
4. Choi BS, Robins HI. Reversible paclitaxel-induced vocal cord paralysis with later recall with vinorelbine. *Cancer Chemother Pharmacol*. 2008;61:345–346.
5. Annino DJ Jr, MacArthur CJ, Friedman EM. Vincristine-induced recurrent laryngeal nerve paralysis. *Laryngoscope*. 1992;102:1260–1262.
6. Ahmed A, Williams D, Nicholson J. Vincristine-induced bilateral vocal cord paralysis in children. *Pediatr Blood Cancer*. 2007;48:248.
7. Tobias JD, Bozeman PM. Vincristine-induced recurrent laryngeal nerve paralysis in children. *Intensive Care Med*. 1991;17:304–305.
8. Latiff ZA, Kamal NA, Jahendran J, et al. Vincristine-induced vocal cord palsy: case report and review of the literature. *J Pediatr Hematol Oncol*. 2010;32:407–410.
9. Paediatric Intensive Care Audit Network National Report 2006 - 2008 (published August 2009): Universities of Leeds and Leicester. ISBN 978 0 85316 283 4.