Dilated cardiomyopathy in a child with abdominal neuroblastoma and normal serum catecholamine levels: anaesthetic management and review of literature

Anuradha Ganigara*, Chandrika Yabagodu Ramavakoda, Chandana M Srinivasan and Madhusudan Ganigara

*Department of Pediatric Anesthesiology, Indira Gandhi Institute of Child Health, Bangalore, India

Department of Pediatrics, Mount Sinai Medical Center, New York, NY, USA

*Corresponding author, email: anuradhasudhir@gmail.com

Introduction

Neuroblastoma is the most common extracranial solid tumour of childhood. Dilated cardiomyopathy as an initial presentation of neuroblastoma is rare. We report the case of a three-year-old child with giant abdominal neuroblastoma encasing the abdominal aorta who presented with dilated cardiomyopathy in heart failure without hypertension or elevated serum catecholamine levels. The probable pathophysiological mechanism for such an occurrence and review of similar cases along with perioperative management is presented.

Keywords: anaesthesia, catecholamines, child, dilated cardiomyopathy, neuroblastoma

Neuroblastoma is the most common extracranial solid tumour of childhood. It arises from the neural crest cells of the sympathetic nervous system. Usual clinical presentation is a palpable mass in the abdomen (60%), but it may rise from any site in the sympathetic nervous system including the cervical, thoracic and pelvic regions. Of interest to the anaesthesiologist is the fact that these intriguing tumours have a potential to produce excess catecholamines and thus, mimic pheochromocytoma perioperatively.

Systemic hypertension has an incidence of 10–27% on presentation. Dilated cardiomyopathy (DCM) secondary to catecholamine secretion is a rare presentation with seven case reports so far in the medical literature. The clinical picture and perioperative anaesthetic management of a child with abdominal neuroblastoma and dilated cardiomyopathy with normal serum catecholamine levels is described.

Case report

A three-year-old female presented with a two-week history of fever, easy fatigability and abdominal pain associated with gradual distension of abdomen. Contrast-enhanced computed tomography showed a large, heterogeneous mass lesion measuring 11.5 × 8.4 × 8 cm in the right suprarenal region with displacement of adjacent viscera (Figure 1). Laterally and posteriorly, the tumour encased and stretched the right renal vessels throughout their course up to the hilum. Medially, the tumour extended to the midline with encasement of the abdominal aorta, coeliac and mesenteric arteries and compression and displacement of the inferior vena cava. Fine-needle aspiration cytology was consistent with neuroblastoma of undifferentiated type. She was normotensive on presentation with blood pressure ranging between 90–110 mm Hg systolic pressure and 54–70 mm Hg diastolic pressure. Chest X-ray revealed cardiomegaly. 2D echocardiography identified dilated cardiomyopathy with reduced global left ventricular systolic function (ejection fraction of 41%) in the interim period. Her blood pressure remained within normal limits and 24-hour urinary VMA levels were normal throughout her hospital course (0.31 mg/24 hour urine. Reference range 0–13.6 mg/24 hour urine).

Preoperatively the child was started on intravenous dobutamine infusion at 7 μg/kg/min and maintenance of intravenous fluids for 12 hours prior to surgery. Slow titrated induction of anaesthesia was achieved with intravenous morphine 0.1 mg/kg, propofol 2 mg/kg and atracurium 0.5 mg/kg was used to aid muscle relaxation and endotracheal intubation. Continuous invasive arterial blood pressure monitoring and central venous pressure monitoring was carried out. Other parameters monitored included ECG, EtCO2, oxygen saturation and urine output and oesophageal temperature monitoring. She was ventilated with a mixture of oxygen and isoflurane 1% end-tidal concentration. The intraoperative course was uneventful apart from two transient episodes of desaturation and hypotension which responded to gentle hand ventilation and removal of the optimisation. Six months later, after a reduction of the tumour size to 3.6 × 2.6 × 3.4 centimetres, she was scheduled for surgical excision of the tumour. There was an improvement of cardiac function (ejection fraction of 41%) in the interim period. Her blood pressure remained within normal limits and 24-hour urinary VMA levels were normal throughout her hospital course (0.31 mg/24 hour urine. Reference range 0–13.6 mg/24 hour urine).

Figure 1: Neuroblastoma.
offending surgical stimulus. Intraoperative analgesia was supplemented with an epidural infusion of 3 ml/hour of 0.2% ropivacaine at the T12–L1 epidural space. She was discharged at the end of one week and unfortunately lost to follow-up.

Discussion
Neuroblastoma remains an enigmatic tumour known for its variable clinical presentation ranging from a benign incidental finding to life-threatening posterior mediastinal tumours causing a compression effect on major structures. To the anaesthesiologist, the concerns while dealing with cases of neuroblastoma for excision include the site of the tumour and its attendant clinical presentation, size of tumour and its consequent effects and, third, its catecholamine secretory or non-secretory nature. Chemotherapy details and pertinent drug history need to be reviewed as well.5–7

Systemic hypertension as a clinical marker of catecholamine excess in children with neuroblastoma has a reported incidence of 10–27%. Kwok et al., in their study of neuroblastoma and its myriad cardiac-related presentations, reported DCM to be the commonest cardiac abnormality and attributed elevated catecholamines to the same cause.8 They suggested catecholamine-induced vasoconstriction, coronary vasospasm, tachycardiomyopathy caused by a hyper-adrenergic state and down-regulation of beta-adrenergic receptors as factors for cardiac muscle damage and subsequent DCM. Interestingly, they found that not all children with neuroblastoma and DCM had hypertension but invariably all of them had elevated urinary catecholamine levels.

Our patient had an undifferentiated type of neuroblastoma with DCM, normal blood pressure and normal serum catecholamine levels. We propose the presence of pre-existing idiopathic cardiomyopathy or mechanical pressure effect of the tumour on vascular structures such as the renal artery and aorta activating the RAAS (renin angiotensin aldosterone system) or release of vasoactive mediators other than catecholamines such as renin and angiotensin as probable causes for the presence of DCM without hypertension or elevated catecholamines.

Pre-existing cardiomyopathy was unlikely given that the child presented with a history of recent onset of symptoms. Mechanical compression of the renal artery or aorta by the tumour or release of vasoactive mediators like renin and angiotensin seemed plausible. Unfortunately, facilities to detect serum concentrations of renin and angiotensin were not an affordable option in our institution. Venkataraman and Martin described a 13-month-old child with DCM and huge neuroblastoma encircling the abdominal aorta. They attributed the resultant cardiac failure to both catecholamine-induced myocyte damage and massive mechanical pressure by the tumour.4

Sanchez Andres et al. and Chalavon et al. reported DCM without elevated catecholamines in children with retroperitoneal tumours.9,10

DCM due to elevated serum renin and angiotensin II levels secondary to mechanical compression of the renal artery by the huge renal tumour was considered as the pathophysiological mechanism in a seven-month infant with right renal tumour.

Similarly, the authors described DCM in a two-month-old infant with immature Norris grade 2 teratoma without hypertension or elevated catecholamine levels. They suggested release of pro-inflammatory cytokines such as INF-alpha, IL-1, IL-6 by the tumour, promoting fibroblast activity and inducing myocardial cell apoptosis and myocardial fibrosis as the cause for DCM.

The pathogenesis of DCM in children with retroperitoneal tumours is unclear and warrants more physio-pathological studies to understand the mechanisms for the resulting DCM in infants with retroperitoneal tumours. Anaesthetic management of children with a neuroblastoma and associated DCM requires a well-planned anaesthetic technique that results in minimal imbalance of the already compromised physiology.

Children with DCM accounted for 13% of entries in the paediatric perioperative cardiac arrest registry.11 Keeping in view this increased risk of morbidity and mortality in addition to the presence of a retroperitoneal neuroblastoma in this child, the anaesthesia management was tailored to meet the following goals: avoidance of drug-induced myocardial depression, avoidance of increase in afterload along with maintenance of normovolemic status, and adequate perioperative analgesia by judicious use of regional anaesthesia.

Schechter et al. advocated the prophylactic use of inotropic agents like dobutamine, amrinone or milrinione in patients with DCM before administration of anaesthesia. The combinations have been shown to have a beneficial effect on the failing ventricle without causing an increase in myocardial oxygen consumption or lactate production.12

Placement of an epidural catheter at the lower thoracic segments helped us achieve the pharmacological goals in this child during both the intraoperative and postoperative periods.

To summarise, we successfully managed a case of DCM with neuroblastoma without hypertension and with normal serum catecholamine levels by strict adherence to known protocols and by maintaining near normal physiology with the judicious use of an anaesthetic pharmacological armamentarium even during the stressful times of anaesthetic induction and tumour resection.

Conclusion
Children with neuroblastoma can have varied presentation. As anaesthesiologists we need to be familiar with both pertinent medical issues and the perioperative anaesthetic challenges that could be encountered while handling these children. This case report highlights the unique presentation of neuroblastoma in a child with DCM without elevated catecholamine levels. This case report also warrants further studies regarding the possible pathophysiological mechanisms of development of DCM in children.

Acknowledgment – The authors would like to thank Dr Yaduraj, postgraduate resident, Department of Anaesthesia, MVJ Medical College, Bangalore, Karnataka for his help in procuring pertinent patient details.

Conflict of interest – None reported.

Authorship statement – All the authors involved in the preparation of this manuscript have read and submitted the article, which represents honest work and has not been published or presented elsewhere.
References

1. Henry MCW, Tashjian DB, Breuer CK. Neuroblastoma update. Curr Opin Oncol. 2005;17:19–23. http://dx.doi.org/10.1097/01.cco.0000147901.12325.90

2. Madre C, Orbach D, Baudouin V, et al. Hypertension in childhood cancer: a frequent complication of certain tumour sites. J Pediatr Hematol/Oncol. 2006;28:659–64. http://dx.doi.org/10.1097/01.mph.0000212995.56812.bb

3. Kako H, Taghon T, Veneziano G, et al. Severe intraoperative hypertension after induction of anaesthesia in a child with a neuroblastoma. J Anesth. 2013;27:464–7. http://dx.doi.org/10.1007/s00540-012-1544-x

4. Venkataraman R, Martin S. Metastatic neuroblastoma presenting as dilated cardiomyopathy and hypertensive emergency. Critical Care Medicine. 2014;42(12):p A1633. http://dx.doi.org/10.1097/01.ccm.0000458634.07381.e9

5. Creagh-Barry P, Sumner E. Neuroblastoma and anaesthesia. Pediatr Anesth. 1992;2:147–52. http://dx.doi.org/10.1111/pan.1992.2.issue-2

6. Kain ZN, Shamberger RS, Holzman RS. Anaesthetic management of children with neuroblastoma. J Clin Anesth. 1993;5:486–91. http://dx.doi.org/10.1016/0952-8180(93)90066-N

7. Haberkern CM, Coles PG, Morray JP, et al. Intraoperative hypertension during surgical excision of neuroblastoma. Anesth Analg 1992;75:854–8.

8. Kwok SY, Cheng FWT, Cheung AF, et al. Variants of cardiomyopathy and hypertension in neuroblastoma. J Pediatr Hematol Oncol. 2014;36:e158–61. http://dx.doi.org/10.1097/MPH.0b013e318290c628

9. Sanchez Andres A, Valdes Dieguez E, Marco Macian A, et al. Immature ovarian tumour and dilated myocardopathy. An Pediatr (Barc). 2010;73(6):347–51. http://dx.doi.org/10.1016/j.anpedi.2010.06.011

10. Chalavon E, Lampin ME, Lervat C, et al. Dilated cardiomyopathy caused by Wilm's tumour. Pediatr Emerg Care. 2017;33(1):41–2.

11. Gottlieb EA, Andropoulos DB. Anesthesia for the patient with congenital heart disease presenting for non-cardiac surgery. Curr Opin Anesthesiol. 2013;26:318–26. http://dx.doi.org/10.1097/ACO.0b013e328360c50b

12. Schechter WS, Kim C, Martinez M, et al. Anaesthetic induction in a child with end stage cardiomyopathy. Can J Anaesth. 1995;42(5):404–8. http://dx.doi.org/10.1007/BF03015486

Received: 10-08-2016 Accepted: 16-01-2017