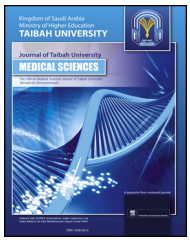
Journal of Taibah University Medical Sciences (2022) 17(6), 950–953

Taibah University

Journal of Taibah University Medical Sciences

www.sciencedirect.com



Case Report

A rare association of Down syndrome with Dandy–Walker variant, pulmonary hypertension and childhood interstitial lung disease: A case report of a prognostic dilemma

Anis M. Mohd Kori, MD [a,*], Amelia Alias, MD [a], Mariana Daud, MD [a], Nor A. Yahaya, MB BCh [a] and Muhamad A. Anuar, MBBS [b]

[a] *Department of Paediatrics, Hospital Raja Perempuan Zainab II, Jalan Hospital, Kota Bharu, Kelantan, Malaysia*
[b] *Department of Paediatrics, Kulliyyah of Medicine, International Islamic University Malaysia, Indera Mahkota, Kuantan, Malaysia*

Received 9 January 2022; revised 18 March 2022; accepted 25 May 2022; Available online 10 June 2022

الملخص

المقدمة: تعتبر العلاقة بين متلازمة داون، داندي- ووكر المتغير، ارتفاع ضغط الشريان الرئوي ومرض الرئة الخلالي في مرحلة الطفولة نادرة للغاية. تم الإبلاغ عن العديد من الحالات بين اضطرابات التثلث الصبغي مع تشوه داندي- ووكر ونتائج النمو العصبي. بصعوبة الحالة وتعقيدها مع القناة الشريانية السالكة، ارتفاع ضغط الشريان الرئوي ومرض الرئة الخلالي في مرحلة الطفولة، وجب علينا دراسة امتداد ارتفاع ضغط الشريان الرئوي سواء كان متوسطا الى شديدا والذي يؤدي الى امراض ووفيات كبيرة عند الرضع المصابين بمتلازمة داون وتشوه داندي- ووكر

تقرير حالة: نبلغ عن حالة لطفلة خديجة - تبلغ خمسة عشر- شهرا, تأكدت اصابتها بمتلازمة داون و داندي- ووكر المتغير والتي أصيبت بارتفاع ضغط الشريان الرئوي ومرض الرئة الخلالي في مرحلة الطفولة

الاستنتاجات: هذه هي الحالة الأولى من نوعها مع وجود العديد من الارتباطات المعقدة التي تم الإبلاغ عنها تتضمن متلازمة داون وداندي- ووكر المتغير. أدت هذه الحالة الى معضلة في التشخيص واستشارة الوالدين الرحيمة حيث ان المستقبل غير معروف

الكلمات المفتاحية: متلازمة داون؛ داندي- ووكر المتغير؛ ارتفاع ضغط الشريان لرئوي؛ رض الرئة الخلالي في مرحلة الطفولة؛ التنبؤ

Abstract

Associations among Down syndrome (DS), Dandy–Walker variant (DWv), pulmonary hypertension (PH) and childhood interstitial lung disease (chILD) are extremely rare. Several cases of trisomy disorders with Dandy–Walker malformation (DWM) and neuro-developmental outcomes have been reported. The extent to which moderate to severe pulmonary hypertension with complications of patent ductus arteriosus (PDA), PH and chILD leads to substantial morbidity and mortality in infants with DS and DWM should be studied. We report the case of an ex-premature 15-month-old girl with confirmed DS with DWv, who developed PH and chILD. This is the first case study reporting the complexity of multiple associations involving DS and DWv. This case led to a prognostic dilemma and required compassionate parental counselling because of the child's uncertain future.

Keywords: Childhood interstitial lung disease; Dandy–Walker variant; Down syndrome; Prognosis; Pulmonary hypertension

* Corresponding address: Department of Paediatrics, Hospital Raja Perempuan Zainab II, Jalan Hospital, 15586 Kota Bharu, Kelantan, Malaysia.
E-mail: anismun88@gmail.com (A.M. Mohd Kori)

Peer review under responsibility of Taibah University.

Production and hosting by Elsevier

 https://doi.org/10.1016/j.jtumed.2022.05.005

Introduction

Down syndrome (DS) is the most common chromosomal aneuploidy disorder. The incidence rate of DS according to the World Health Organization is between 1 and 10 per 1000 live births worldwide.[1] In Malaysia, the prevalence has been estimated to be 1.25 per 1000 live births.[1] The association of DS with Dandy–Walker malformation (DWM) is rare. Among the reported cases, only one had a good neurodevelopmental outcome, given the absence of systemic involvement and acute malformation.[2–5]

DS is commonly associated with congenital heart disease (CHD). In a 10-year survival study of DS with CHD in Malaysia, more than half of cases of DS had co-morbid CHD, of which 30% had spontaneous closure of cardiac lesions, and the majority (35%) underwent intervention, 9% resulted in death before intervention, and 10% were treated with comfort care.[6] However, no case of an association of DS with DWM, patent ductus arteriosus (PDA), pulmonary hypertension (PH) and childhood interstitial lung disease (child) had been reported. Here, we report a case of such rare associations, which presented a prognostic dilemma.

Case report

A 35-gestational-week baby girl was born via caesarean section. An antenatal detail scan showed multiple structural anomalies including severe bilateral ventriculomegaly, and hydrops fetalis with pleural and pericardial effusion. Amniocentesis for karyotyping confirmed trisomy 21. Her mother had polyhydramnios and gestational diabetes on diet control.

The patient had a good Apgar score at birth; however, she required supplementary oxygen because of mild desaturation. She had clinical features of DS with macrocephaly. An echocardiography examination revealed patent ductus arteriosus (PDA) with patent foramen ovale (PFO). A diagnosis of PH was made on the basis of echocardiography findings of dilated right heart chambers, a bidirectional shunt in PDA colour flow, moderate tricuspid regurgitation (TR) and minimal pericardial effusion. Her right ventricular systemic pressure (RSVP) on echocardiography was 44 mmHg. Thoracic ultrasonography showed minimal right plural effusion. She had generalised hypotonia with no symptoms of increased intracranial pressure. Her serial head circumferences were normal. MRI of the brain revealed Dandy–Walker variant (DWv) with communicating hydrocephalus (Figure 1). A neurosurgical opinion was obtained, which advised regular follow-up, given the absence of elevated intracranial pressure and the concerns regarding the prognosis of co-morbidities. The patient was considered for later endoscopic third ventriculostomy (ETV). She was enrolled in an early intervention program including rehabilitation and speech therapy.

The patient remained oxygen dependent for more than 3 months. Sildenafil therapy for PH was started on the basis of the echocardiography study. She was started on diuretics for clinical features of heart failure. Her pleural and pericardial effusion resolved by 2 weeks of age. Her serial echocardiography mainly showed a bidirectional shunt in PDA, thus leading to conservative management for 3 months with watchful waiting regarding the progression of the pulmonary hypertension and the PDA. She had persistent mild respiratory distress and remained oxygen dependent despite being free of pneumonia. Her highest level of oxygen support was continuous positive airway pressure of 6 mmHg and FIO_2 of 30%. Serial chest radiographs and high-resolution computed tomography (HRCT) of the thorax (Figure 2) were suggestive of chILD. However, lung biopsy and genetic study were not performed because of limited resources.

A multidisciplinary team meeting was held to discuss the prognosis and possible treatments that could be offered, given that the patient had a prolonged stay, and was oxygen dependent and in heart failure. The patient weighed 3.7 kg at the time of the meeting. She might have required ETV, but

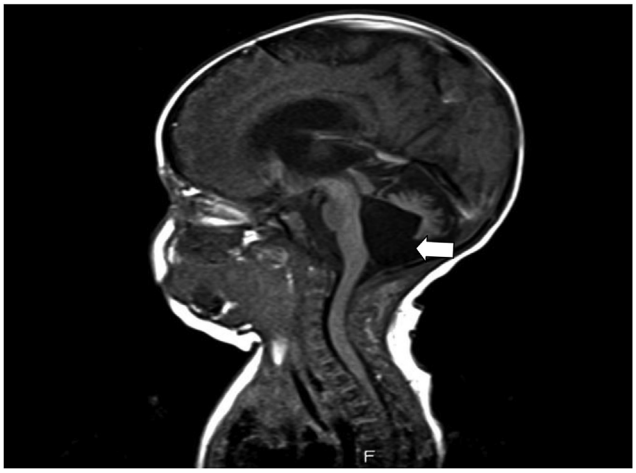


Figure 1: Sagittal view of brain MRI, showing features suggestive of the Dandy–Walker variant with communicating hydrocephalus, and no torcula, tentorium elevation or posterior fossa expansion.

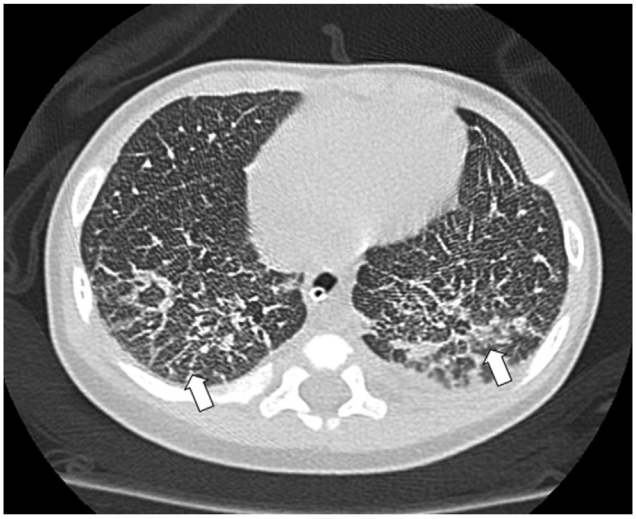


Figure 2: Thorax HRCT showing a diffuse ground glass appearance, particularly in both lower lobes, with thickened intralobular and interlobular septa suggestive of childhood interstitial lung disease.

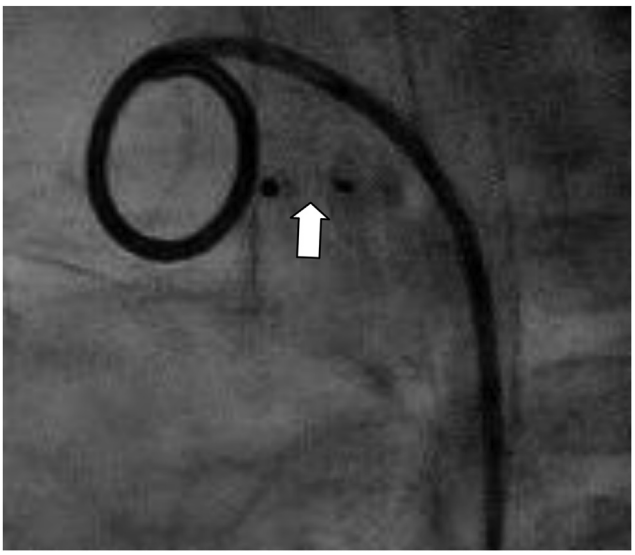


Figure 3: Lateral 90-degree projection angiogram showing the PDA device in situ.

her co-morbidities might have prevented the procedure. She was also at risk of recurrent nosocomial infection. Before the meeting, her echocardiography results indicated dilated bilateral cardiac chambers, no effusion, significant PFO shunted left to right, and PDA with bilateral shunt but left to right dominant. Her RSVP remained less than 40 mmHg. Cardiac catheterisation with a possible trial of occlusion if the haemodynamics permitted was offered to her parents. The high risk and grave prognosis were explained. A conservative option was also offered. The parents opted for the procedure despite the poor odds.

An angiogram study indicated a PDA isthmus diameter of 1.18 mm, ampulla of 8.6 mm and length of 3.47 mm. A preprocedural haemodynamic study showed a mean pulmonary pressure of 48 mmHg. Her pulmonary pressure was 69/30 mmHg, and her systemic blood pressure was 63/27 mmHg. A trial of occlusion with an Amplatzer piccolo occluder 5−2 mm was performed to occlude the PDA. The device was kept in place for 10 min, while the patient's haemodynamic and general well-being were monitored. Her systemic blood pressure improved to 74/28 mmHg. Her pulmonary pressure was 48/23 mmHg, and the mean was 35 mmHg. Echocardiography showed reasonable PFO flow of the left to right shunt with good function. The patient was clinically stable throughout. The device was then released (Figure 3). Post procedure care and ventilation were uneventful.

At 2 weeks after PDA device occlusion, her heart failure was ameliorated, and oxygen was discontinued. She was discharged in a well condition after 4 months in the hospital. Sildenafil therapy was continued because of a risk of PH of DS in subsequent visits despite an absence of evidence of PH on echocardiography. Sildenafil was discontinued at the age of 14 months. On neurodevelopmental follow-up, she was able to sit without assistance, wave goodbye, and feed herself at 15 months of age. She remains in mild respiratory distress but maintains good oxygen saturation on air.

Discussion

DS is extremely rarely associated with DWv. Estroff et al.[3] and Imataka et al.[7] have indicated that several types of chromosomal abnormalities are associated with DWM, but none have been reported with trisomy 21.[3,7]

Compared with classic DWM, DWv is a less severe posterior fossa anomaly. Our patient met the criteria for DWv, in view of the absence of torcular-lambdoid inversion and no clear posterior fossa expansion. Interestingly, half of all patients with DS and DWv have normal neurodevelopmental outcomes.[3] Our patient's development was comparable to those typical in children of the same age with DS.

The child has clinical manifestation of persistent respiratory distress with serial abnormal chest X-rays, as well as HRCT findings suggestive of chILD due to structural changes associated with trisomy 21.[13] Alveolar growth abnormalities are seen in 86%−88% cases, on the basis of lung biopsy in patients with trisomy 21 syndrome.[14]

DS is known to be associated with the risk of PH. Ongoing increased pulmonary flow from left to right cardiac lesions such as PDA in DS may lead to an imbalance in vasoactive mediators in the pulmonary lung vasculature leading to worsening PH.[8−10] PDA occlusion in PH is debatable, because it is associated with a high risk of pulmonary hypertensive crisis and worsening right heart failure. Staged management involving medical treatment of PH and subsequent closure has been applied in several centres and has shown reasonable outcomes. Responses to balloon occlusion testing of the PDA may provide clues regarding which patients may tolerate PDA occlusion. The timing of PDA occlusion in PDA with PH, and patient selection play major roles in the outcome. Our patient responded well to PDA occlusion. Serial echocardiography parameters were negative for PH, and oxygen was successfully discontinued.

Conclusion

Associations among DS, DWv, PH and chILD are extremely rare. This case report described our experience in a complex and individualised approach to DWv in DS. A multidisciplinary approach was important in this patient's care. Although our patient is currently thriving and developing well according to DS developmental milestones, we remain circumspect regarding the prognosis of the child's progression, which will probably determine her overall well-being.

Source of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors have no conflict of interest to declare.

Ethical approval

Ethical Approval statement was not applicable for the case report.

Authors contributions

All authors are contributing in writing the case report.

Acknowledgements

We thank the patient's parents for providing verbal consent and cooperating with us in completing this case report.

References

1. Al-Biltagi M. Down syndrome from epidemiologic point of view. **EC Paediatr 2015 Sep**; 2(1): 82–91.
2. Constantini S, Pomeranz S, Hoffman B, Martin O, Rappaport Z. Coexistence of Dandy-Walker syndrome and Down's syndrome. **Neurochirurgia 1989 Mar**; 32(2): 56–57. https://doi.org/10.1055/s-2008-1054003.
3. Estroff JA, Scott MR, Benacerraf BR. Dandy-Walker variant: prenatal sonographic features and clinical outcome. **Radiology 1992 Dec**; 185(3): 755–758. https://doi.org/10.1148/radiology.185.3.1438757.
4. Love K, Huddleston L, Olney P, Wrubel D, Visootsak J. Developmental outcomes of Down syndrome and Dandy-Walker malformation. **J Pediatr Neurol 2011 Jan**; 9(3): 405–408. https://doi.org/10.3233/JPN-2011-0500.
5. Goyal S, Nayak VH, Meena R. Rare association of Down syndrome with Dandy Walker malformation. **Nitte Univ J Health Sci 2014 Jun 1**; 4(2): 140. https://doi.org/10.1055/s-0040-1703784.
6. Zahari N, Mat Bah MN, Razak HA, Thong MK. Ten-year trend in prevalence and outcome of Down syndrome with congenital heart disease in a middle-income country. **Eur J Pediatr 2019 Aug**; 178(8): 1267–1274. https://doi.org/10.1007/s00431-019-03403-x. Epub 2019 Jun 20.
7. Imataka G, Yamanouchi H, Arisaka O. Dandy-Walker syndrome and chromosomal abnormalities. **Congenit Anom 2007 Dec**; 47(4): 113–118. https://doi.org/10.1111/j.1741-4520.2007.00158.x.
8. Alam A, Chander BN, Bhatia M. Dandy-walker variant : prenatal diagnosis by ultrasonography. **Med J Armed Forces India 2004 Jul**; 60(3): 287–289.
9. Colvin KL, Yeager ME. What people with Down Syndrome can teach us signs about cardiopulmonary disease. **Eur Respir Rev 2017 Feb;26**; 143: 160098. https://doi.org/10.1183/16000617.0098-2016.
10. Bush D, Abman SH, Galambos C. Prominent intrapulmonary bronchopulmonary anastomoses and abnormal lung development in infants and children with Down syndrome. **J Pediatr 2017 Jan**; 180: 156–162.e1. https://doi.org/10.1016/j.jpeds.2016.08.063.
13. Semple TR, Ashworth MT, Owens CM. Interstitial lung disease in children made easier…well, almost. **Radiographics 2017**; 37(6): 1679–1703. https://doi.org/10.1148/rg.2017170006.
14. Chen J, Ma H, Zheng Y, Cao J, Zeng H, Zhang Q. Trisomy 21 syndrome associated interstitial lung disease: a case report. **Zhonghua Er Ke Za Zhi 2015 Oct**; 53(10): 771–774 [in Chinese. PMID: 26758114].

How to cite this article: Mohd Kori AM, Alias A, Daud M, Yahaya NA, Anuar MA. A rare association of Down syndrome with Dandy –Walker variant, pulmonary hypertension and childhood interstitial lung disease: A case report of a prognostic dilemma. J Taibah Univ Med Sc 2022;17(6):950–953.