CASE REPORT

Multiple haemangiomas, diaphragmatic eventration and Beckwith-Wiedemann syndrome: an unusual association

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To cite: Francisco T, Gonçalves RM, Borges C, *et al*. *BMJ Case Rep* Published online: [*please include* Day Month Year] doi:10.1136/bcr-2013-010077

SUMMARY

A 6-month-old girl with Beckwith-Wiedemann syndrome, multiple haemangiomas (axillary, laryngeal, pulmonary and hepatic) and diaphragmatic eventration was reported. All tumours responded to treatment with propranolol. The surgical correction of diaphragmatic eventration was crucial to a better outcome.

BACKGROUND

Beckwith-Wiedemann syndrome (BWS) is a growth disorder in which several malformations and embryonic tumours can be found.[1] However, vascular tumours are uncommon, and the presence of multiple haemangiomas is even rarer. Moreover, to our knowledge diaphragmatic eventration was never described in association with this syndrome.

This case highlights for the presence of some rare anomalies which may be associated with BWS.

CASE PRESENTATION

A female newborn infant was admitted to our neonatal intensive care unit (NICU) on her second day of life for surgical repair of omphalocele. She was delivered at 29 weeks of gestation by caesarean section due to acute fetal distress. Her 27-year-old mother had an uneventful pregnancy and diabetes was denied; she was admitted 4 days earlierdue to premature rupture of membranes and was medicated with ampicillin, erythromycin and β-methasone. Apgar score was 1′-6, 5′-8 and birth weight was 1670 g (90th centile). The newborn was ventilated and given surfactant and ampicillin and gentamicin were started. Besides macrosomia and omphalocele, supernumerary fingers, ear creases (figure 1), ocular protrusion, macroglossia and cardiomegaly were found.

Surgical correction of omphalocele was performed at 31 h of life. On day 12, still on the ventilator, she developed a profuse laryngeal haemorrhage with bradycardia and hypoxia, which prompt tracheal tube substitution. The rigid bronchoscopy performed 5 days later showed a friable and bleeding subglotic space and a granulation on the cricoid cartilage, later on admitted as haemangiomas; trachea and bronchial tree were normal.

At 1 month, a left axillary mass was found, with progressive increasing size (figure 2). The ultrasound showed a subcutaneous solid mass, highly vascularised, probably corresponding to a haemangioma.

At 2 months, owing to the persistent need of respiratory support and diffuse generalised opacity of the left lung and right mediastinum deviation (figure 3), a thoracic CT scan was performed, showing a mass at the left pulmonary lower lobe with heterogeneous contrast enhancement, and three nodular lesions on the left pulmonary parenchyma, the larger one on the rear side of the lung (figure 4);

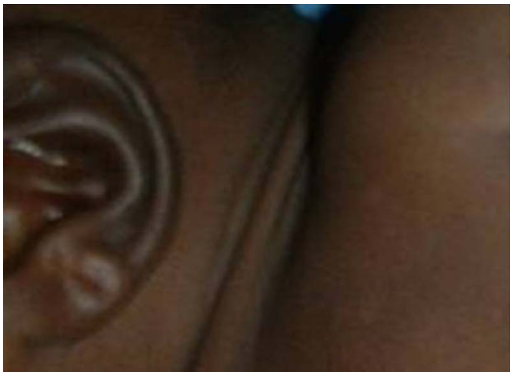

Figure 1 Ear creases (courtesy of Dr Maria João Lage).

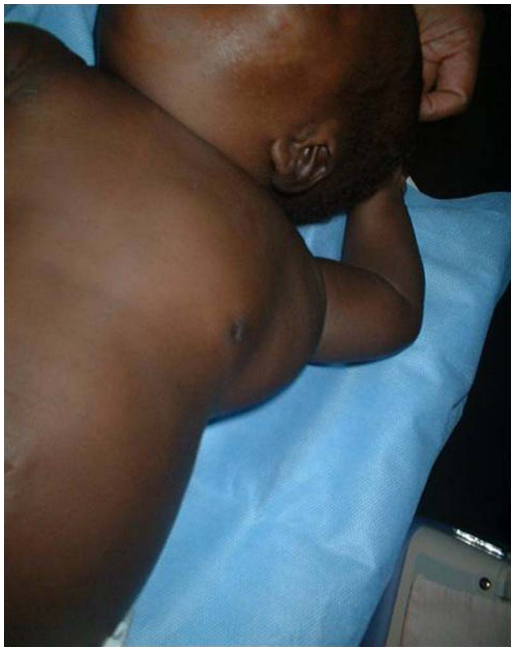

Figure 2 Axillary haemangioma, 45×22 mm (courtesy of Dr Maria João Lage).

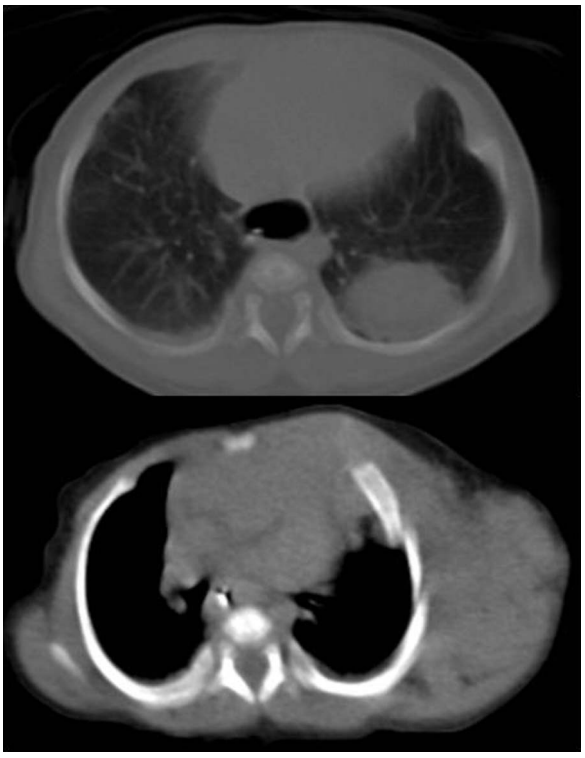

Figure 3 Thoracic CT scan showing three nodular lesions on the left pulmonary parenchyma, the larger with 34 mm and located on the rear side of the lung.

an ultrasound scan revealed vascular characteristics. Because a sarcoma with pulmonary metastasis could not be excluded, an aspiration biopsy was performed; blood and scarce endothelial cells were obtained, suggesting of a vascular mass.

Thoracic, abdominal and pelvic MR, performed soon after the thoracic CT scan, showed several vascularised tumours: axillary, pulmonary apex and hepatic, all of them with T2 hyperintensity. A cystic lesion on right ovary was also found (figure 5). Serum α-foetoprotein level was 206 µg/L (reference range <9 µg/L)

By 5 months, owing to persistence of the previously described lung condensation on the lower left lobe and extubation failure,

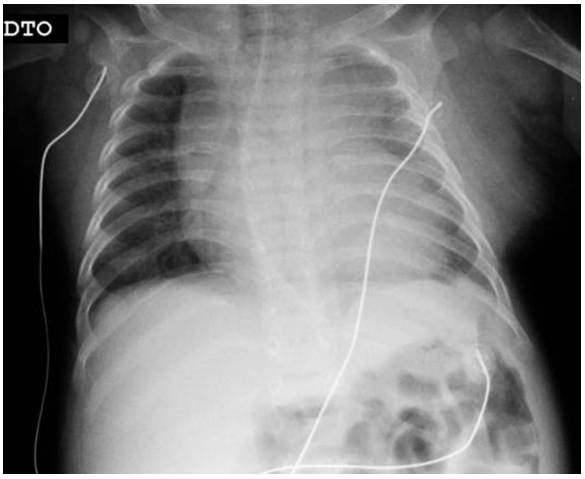

Figure 4 Thoracic radiograph showing diffuse generalised opacity of the left lung and right mediastinum deviation.

a thoracic angioressonance was performed. A solid supra diaphragmatic left mass, supplied by a vascular structure originating in descending thoracic aorta, possibly corresponding to pulmonary or extra pulmonary sequestration was found (figure 6). On surgery a diaphragmatic eventration with intrathoracic spleen was diagnosed.

INVESTIGATIONS

Owing to the association of omphalocele, prematurity, macrosomia, ear creases and cardiomegaly, genetic tests were performed in order to confirm BWS. Hypomethylation of gene KCNQ1OT1 in imprinting centre 2 and normal methylation of gene H19 in imprinting centre 1 confirmed the diagnosis. Several transfontanelar US were performed without significant findings.

DIFFERENTIAL DIAGNOSIS

The presentation of a newborn with macrosomia, macroglossia and dysmorphic features should prompt a comprehensive clinical investigation and genetic testing for several syndromes, including Simpson-Golabi-Behmel syndrome, Costello syndrome, Maroteaux-Lamy syndrome, as well as mosaicism for trisomy 8.

Perlman syndrome may also include renal hamartomas. In our patient, the presence of omphalocele and characteristic facial features, raised the suspicion of BWS, confirmed by molecular testing.

The mass found on the left pulmonary lower lobe could correspond to an angioma, adenoma, hamartoma or malignant neoplasm.

TREATMENT

Treatment with prednisolone and propranalol was started after the finding of multiple haemangiomas.

OUTCOME AND FOLLOW-UP

- Hypoglycaemia episodes were never found.
- Global reduction in the size of all haemangiomas was observed after propranolol treatment.
- Diaphragmatic eventration correction was followed-up by prompt respiratory recovery.
- The patient has been followed-up in the outpatient clinic of our hospital. Growth percentiles are over P95. A mild developmental delay, mainly affecting language has been observed.
- One episode of respiratory viral infection with respiratory distress needing hospital admission occurred at 2 years of life, with full recovery.
- Ovarian cyst dimensions remained stable, so, for the moment, it is under observation. If it shows significant enlargement probably it will be considered surgery or aspiration.

DISCUSSION

BWS is a growth disorder characterised by macrosomia, visceromegaly, macroglossia, neonatal hypoglycaemia, omphalocele or umbilical hernia, ear pits and creases, adrenocortical cytomegaly and renal abnormalities (eg, medullary dysplasia, nephrocalcinosis, medullary sponge kidney and nephromegaly).[1] Also, embryonal tumours (eg, Wilms tumour, hepatoblastoma, neuroblastoma and rhabdomyosarcoma) are among the most common features of this syndrome[1] and angiomas are rarely found.

On the basis of the radiological, MR and ultrasound features and on the response to propranolol and prednisolone treatment it was admitted that pulmonary, axillary and hepatic masses corresponded to haemangiomas. In fact, treatment with propranolol has been increasingly used in management of infantile haemangiomas, with encouraging results.[2]

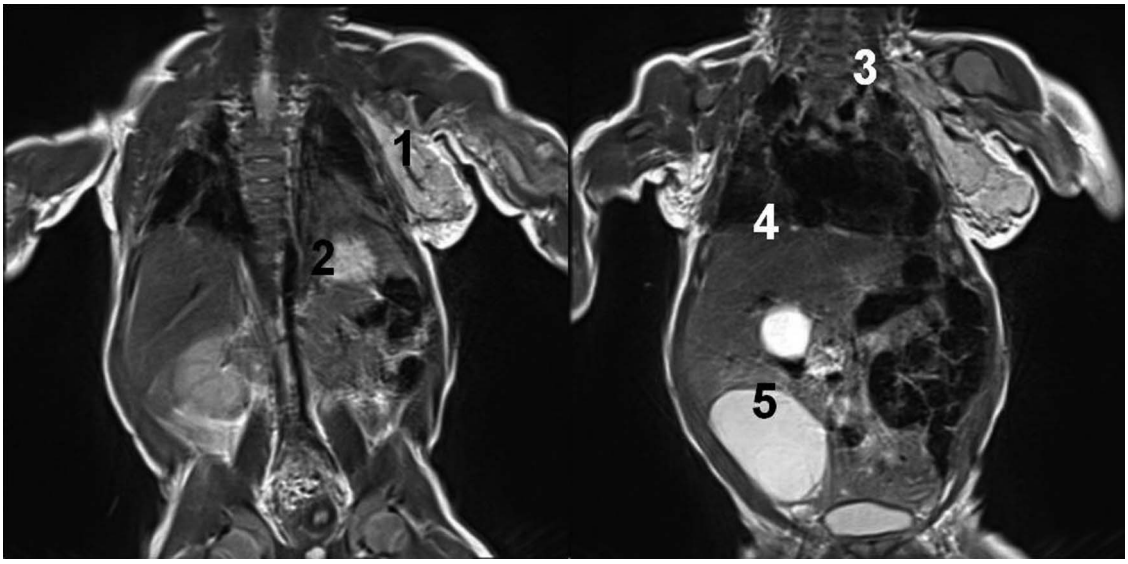

Figure 5 Thoracic, abdominal and pelvic MR showing axillary (1) pulmonary (2 and 3) and hepatic (4) vascularised tumours and ovarian cyst 50×30 mm (5).

To our knowledge, this is the first described association of BWS with multiple haemangiomas. As previously stated, isolated angiomas are rarely found (reports being limited to spleen,[3] liver[4 5] and placenta[5]) which is supposed to be due to BWS mosaic associated molecular changes, that is, many cells with BWS-associated changes may reside in organs 'at risk' for tumour development such as liver or kidneys. The genetic variations found in the patient (hypomethylation of gene KCNQ1OT1 in imprinting centre 2 and normal methylation of gene H19 in imprinting centre 1) are known to be associated with low risk of developing Wilms tumour and moderate risk of hepatoblastoma and thyroid carcinoma,[6 7] so a better prognosis may be expected.

Importantly, diaphragmatic eventration was not yet described, and early clinical awareness to this condition may have a profound impact on the prognosis, as was the case of our patient.

The high serum α-foetoprotein level could be explained by the presence of omphalocele and by the fact that children with BWS have higher reference values.[8]

This clinical report has the purpose to alert for other features which may be associated with BWS phenotypic spectrum.

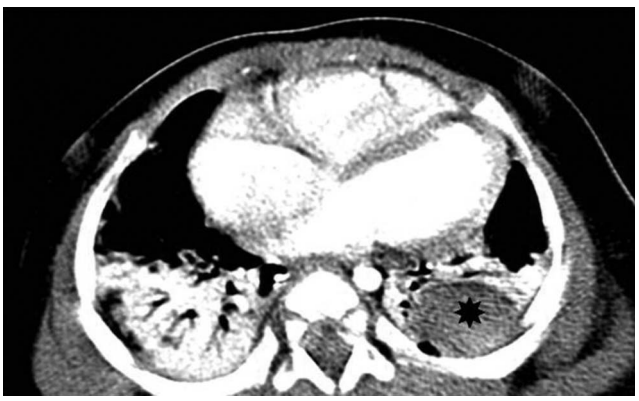

Figure 6 Thoracic angioressonance showing a solid supradiaphragmatic left node 27×32×25 mm (*).

Learning points

- Beyond all tumours associated with Beckwith-Wiedemann syndrome (BWS), multiple haemangiomas may also be part of it. Genetic variations may be responsible for the presence or absence of different tumours, and this may influence the prognosis.
- Diaphragmatic eventration should be suspected in a patient with BWS and pulmonary consolidation.
- It is important to be aware of several new features that may be associated with BWS.

Contributors All the authors are responsible for the research and participated in concept and design, analysis and interpretation of the data, writing and editing of the manuscript and approved the final text.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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