

## The Role of Radiopathological Evaluation in Diagnosis of Beckwith-Wiedemann Syndrome

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### Abstract

Beckwith-Wiedemann Syndrome (BWS), an overgrowth syndrome is associated with early development of embryonal tumours usually in the first four years of life. Hepatoblastoma is observed in 1% to 3% of persons with Beckwith-Wiedemann Syndrome or isolated hemihypertrophy(HH). We report a case of hepatoblastoma associated with both BWS and HH with raised serum alpha-feto protein levels and hypoglycaemia.

**Keywords:** Beckwith-Wiedemann syndrome, Hemihypertrophy, Hepatoblastoma

### Case Report

A 6 month old male presented with complaints of abdominal swelling, large tongue, asymmetrical in size of limbs and excessive crying. He was only child born to a couple with 3rd degree consanguineous marriage without any significant family history but with a perinatal history suggestive of large for gestational age and intra-partal history of prolonged labour. Although birth weight was unknown, also with no history suggestive of hypoglycaemia. On examination, child was alert but irritable, weighted 12kg and 70 cm in height (more than 90 percentile for age). He had significant macroglossia, hemihypertrophy of right side of body, with normal developmental milestones. On systemic examination, abdomen was

protruberant with gross hepatomegaly crossing the umbilicus with mild splenomegaly. Other systemic examination was unremarkable.

MDCT evaluation with 64 slice GE Scanner revealed a large heterogenous peripherally enhancing mass lesion with multiple streaky linear internal enhancing foci and multiple non-enhancing necrotic foci without any evidence of calcifications noted involving right hepatic lobe with sparing of segment 6. Mass causing splaying of portal veins and extending anteriorly upto anterior abdominal wall with peripheral normal rim of liver parenchyma causing thinning of abdominal wall in subchondral and umbilical region on right side. Also noted a small defect in umbilical region without any evident herniating contents. Bilateral adrenals and kidney were normal with mild splenomegaly.

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Fine needle aspiration was carried out which yielded high cellularity of variable sized, with three dimensional clusters, loose sheets with prominent rosette formation by uniform population of cells of epithelial component with high N:C ratio and hyperchromasia with moderate amount of cytoplasm, intermingled with mesenchymal fragments. Overall features along with the location of mass favoured the diagnosis of hepatoblastoma.

Laboratory examinations revealed haemoglobin 8g/dl, total leukocyte count  $13,000/\text{mm}^3$ , platelets  $2.0 \times 10^5/\text{mm}^3$  and bone marrow aspiration was normal. Serum alpha feto-protein was elevated to 1500 ng/mL.



**Fig 1: Axial CECT of abdomen revealing a large heterogeneous mildly enhancing mass lesion with multiple streaky linear internal enhancing foci and multiple non-enhancing necrotic foci without any evidence of calcifications noted involving right hepatic lobe causing splaying of left portal vein. Also noted normal right adrenal gland.**

## Discussion

Beckwith-Wiedemann syndrome (BWS) is a congenital over-growth syndrome characterized by some or all of the following features: gigantism, macroglossia,

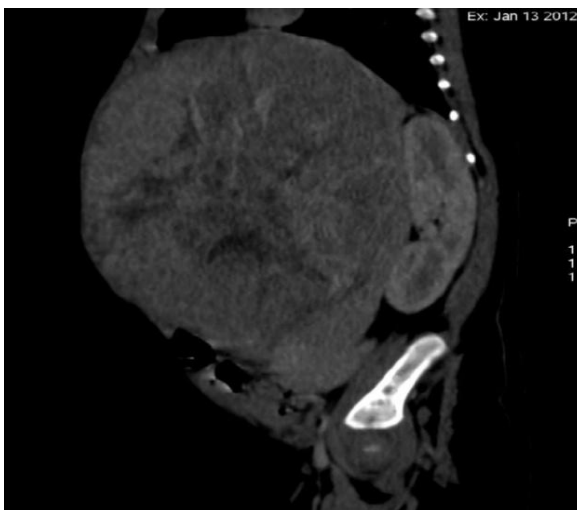
omphalocele, hemihypertrophy, and neonatal hypoglycaemia.<sup>1</sup> The association between embryonal cancer and BWS has been widely reported.<sup>2, 3</sup> A significant relative risk has been reported for Wilms' tumor, neuroblastoma, and hepatoblastoma (HBL).<sup>4</sup> In addition, children with BWS may also exhibit organomegaly, ear pits or creases.<sup>5</sup> Vaughan et al.<sup>6</sup> reported that HH may be an incomplete form of BWS that shares with it a similar increased risk of developing intra-abdominal malignancy. BWS occurs due to perturbations of the normal dosage balance of a number of genes clustered at 11p15 (organized in 2 separate domains). Domain 1 contains paternally expressed insulin like growth factor (IGF2) as well as genes and transcripts that control expression of IGF2. Domain 2 contains several imprinted genes including CDKN1C and KCNQ10T1 (L1T1).<sup>1,7</sup>



**Fig 2: Axial CECT of abdomen revealing a large heterogeneous mildly enhancing mass lesion with multiple streaky linear internal enhancing foci and multiple non-enhancing necrotic foci without any evidence of calcifications noted involving right hepatic lobe with apparent involvement of right portal main branch. Also noted bilateral normal kidneys with mild splenomegaly.**



**Fig 3: Coronal CECT of abdomen revealing a large heterogeneous mildly enhancing mass lesion with multiple streaky linear internal enhancing foci and multiple non-enhancing necrotic foci without any evidence of calcifications noted involving right hepatic lobe with apparent involvement of right portal main branch. Also noted B/L normal kidneys with mild splenomegaly.**



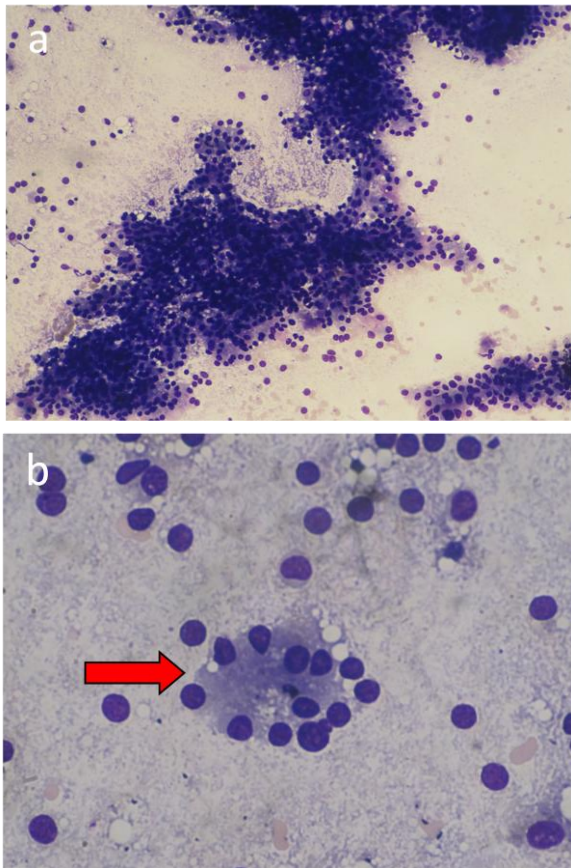
**Fig 4: Sagittal CECT of abdomen revealing a large heterogeneous mildly enhancing mass lesion with multiple streaky linear internal enhancing foci and multiple non-enhancing necrotic foci without any evidence of calcifications noted involving right hepatic lobe with peripheral rim of normal hepatic tissue.**

Wiedemann<sup>3</sup> noted that approximately 7.5% of patients with BWS develop malignant tumors. The most common is Wilms' tumor, followed by adrenocortical carcinoma, HB, and neuroblastoma.<sup>5</sup> Data reported from the National Cancer Institute's Beckwith-Wiedemann support group indicate a relative risk of hepatoblastoma as 2,280, higher than that for other embryonal tumors, including Wilms' tumor. The relative risk for all cancers in this group was 676.<sup>4</sup>

Hepatoblastoma (HBL) occurs in only one in a million children, 1% to 3% of which are observed with Beckwith-Wiedemann syndrome (BWS) or isolated hemihypertrophy (HH)<sup>1</sup>. It has been suggested that HH is an under appreciated diagnostic feature of the over growth syndrome of BWS.<sup>8</sup>

The CT appearances of hepatoblastoma usually confined to a single lobe, with the right lobe affected twice as often as the left, but they may involve both lobes or they may be multicentric. They generally have a density equal to or lower than that of normal hepatic parenchyma on unenhanced scans. On arterial phase imaging, they enhance more than adjacent normal liver. They become hypointense to liver on portal venous phase imaging. They often are heterogeneous because they contain hemorrhage, necrosis, or focal steatosis. Calcifications occur in approximately 50% of hepatoblastomas. Tumor thrombus appears as a low-attenuation area within the portal or hepatic veins.<sup>9,10</sup>

Malignant hepatic lesions are hypointense with respect to liver on T1-weighted MR images and hyperintense on T2-weighted



**Fig 5a:** Fine needle aspiration smears showing variable sized uniform population of cells, with three dimensional clusters, loose sheets with prominent rosette formation, with high N:C ratio and hyperchromasia with moderate amount of cytoplasm. (May-Grunwald-Giemsa  $\times$  Lp). **Fig 5b:** high power of same smear showing rosette formation (May-Grunwald-Giemsa  $\times$  Hp).

sequences. On gadolinium-enhanced images, hepatoblastoma demonstrate diffuse, heterogeneous enhancement. Tumor thrombus is seen as a hyperintense focus within a normally signal-free vessel on spin-echo images or as a hypointense area on GRE imaging. Hemorrhage can appear hypo- or hyperintense on T1-weighted pulse sequences, depending on the age of the blood; it usually is hyperintense on T2-weighted images. Focal steatosis produces signal hyperintensity on both T1- and T2-

weighted pulse sequences and low signal intensity on fat-suppressed images. Calcifications are hypointense on all sequences.<sup>11, 12</sup>



**Fig 6:** Photograph of the child showing macroglossia and obesity.

The hepatoblastoma are classified as epithelial, mixed epithelial, and mesenchymatic. The epithelial variant (56% of cases) is subclassified as fetal, embryonary, macrotrabecular, and made up of small cells. The fetal variant shows a disperse and uniform population of cells with abundant cytoplasm, well-defined plasma membranes, and large hyperchromatic nuclei, as in our case. Cells are small and spindled, with hyperchromatic nuclei and poorly defined plasma membranes in embryonary subtype, whereas, cells of small cell subtype have scarce cytoplasm and hyperchromatic nuclei, arranged in masses with little or no cohesiveness.<sup>13, 14</sup>

Infant mortality rate is estimated to be as high as 21 %. Fortunately, affected individuals who survive infancy generally are healthy. Mental capacity may be normal though some cases show mild to moderate mental deficiency.<sup>7</sup> Screening for HBL every two to three months upto age four years with Serum AFP measurement in conjunction with hepatic US is a reasonable strategy for children with BWS or HH.<sup>15</sup>

### Conclusion

Infants with BWS should be screened for hepatoblastoma as early as the third month of life with abdominal ultrasounds at three monthly intervals. Alpha fetoprotein levels if elevated beyond the norm for age would warrant a biopsy for histological confirmation. Early treatment and total resection of hepatoblastoma has an excellent prognosis.<sup>16</sup>

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