HEPATOBLASTOMA AS A RARE CAUSE OF PRECOCIOUS PUBERTY

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Abstract

A 15-month old boy presented with an abdominal swelling and early development of secondary sexual characteristics for the last 5 months. The mass was initially suspected to be of adrenal origin. Radiological and biochemical (hormonal) findings diagnosed the case to be a hepatoblastoma later confirmed by histopathological examination. Hepatoblastoma, an aggressive primary liver tumor, is a rare form of childhood malignancy and a rare cause of precocious puberty compared to the more common adrenal causes including congenital adrenal hyperplasia, adrenal tumors and the testicular tumors. Thus, when virilization occurs postnatally in boys, or girls presenting with ambiguous genitalia at birth, a virilizing adrenocortical tumor is usually given the first consideration (according to its frequency of incidence), followed by CNS causes. Rarely does one think of the other possibilities. This report describes the typical presentations and clinical features of hepatoblastoma highlighting its usual radiological features.

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Key Words: Hepatoblastoma, precocious puberty, imaging features.

Introduction

Precocious puberty is said to occur when secondary sexual characteristics develop in girls less than 8 years of age and boys before 9 years of age. In boys, 25-75% are found to have an underlying organic cause advocating the need for further investigations including CT & MRI of the abdomen and brain. Precocious puberty in them may be of a) true / central type which is gonadotropin dependent, due to the premature activation of the hypothalamic-pituitary axis (ie. CNS cause). These causes include hamartoma of the tuber cinereum (most common), midline mass lesions in and around the hypothalamus (including the pituitary), and the various causes of raised intracranial pressure. On the other hand, b) incomplete / pseudo-precocious puberty is due to the autonomous secretion of sex steroids (i.e. androgens) or hCG. Its causes include congenital adrenal hyperplasia (CAH, due to deficiency of 21- & 11-β hydroxylase in 95% and 5% cases respectively), adrenal tumors (adenoma-30%, carcinoma-60%), and testicular tumors. The rarer causes of precocious puberty in boys are the hCG-secreting tumors (eg. hepatoblastoma, teratoma, germinoma of the pineal gland) and the McCune-Albright Syndrome.

The present case

A boy aged 15 months, was admitted into the BIRDEM Hospital with the complaints of swelling in the right side of the abdomen associated with local pain noticed for the past 5 months, development of secondary sexual characteristics for past 3 months (manifested by penile enlargement, growth of pubic hair, deepening of voice, growth of fine hair above the upper lip). There was no history of consanguinity of marriage, no positive family history, and his elder brother was normal. On general examination, he had a mature looking face relative to his age (Fig-1). There were no features of dysmorphism. Thyroid gland was not enlarged and the lymph nodes were not palpable. His anthropometric measurements (height, weight) and

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milestones of development were normal for his age. Pubertal staging showed penile (P4) and testicular enlargement (vol-3-4ml) with the presence of pubic hair (PH3). Abdominal examination revealed a mass producing a visible bulge in the right hypochondriac and lumbar regions, firm to touch, not mobile and tender (Fig-1). Other systems revealed no significant abnormality.

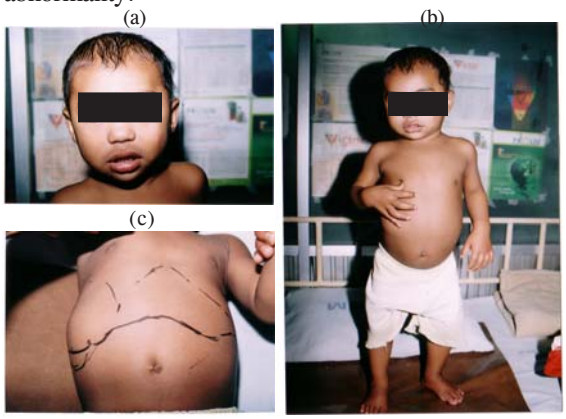

Fig-1: *A 15 months old boy with precocious puberty showing in (a) a mature looking face with fine moustache, in (b) distended abdomen and (c) a mass producing a visible bulge in the right hypochondrium.*

Based on the above findings, some investigations were carried out.

Hormonal assay revealed raised S.testosterone level-3.15 ng/ml (normal post pubertal level is 3.4–14.0 ng/ml, pre pubertal level being barely recordable), S. Cortisol & DHEAS were within normal limits. The patient also had very high S. AFP (alpha-feto protein)-27900ng/dl (normal level is 0.6-6.0ng/dl) and high β-hCG level -123.94μU/ml (normal is < 7μU/ml).

Radiological findings included

a) CxR- A small nodular shadow in the periphery of the lower zone of right lung (Fig-2).

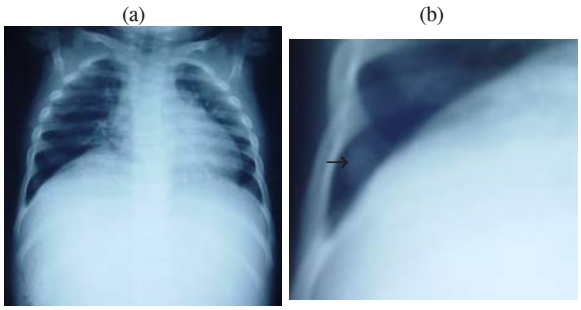

Fig-2: (a) *CxR- shows a small nodular shadow in periphery of lower zone of right lung. (b) Close up view of the right costophrenic angle with the nodule.*

b) USG- A large, irregular, mixed echogenic mass measuring about 98 x 48mm, with calcifications was noted in the right hypochondriac region adjacent to the upper pole of the right kidney, and it could not be separated from the right lobe of the liver. The possibilities were- hepatoblastoma or neuroblastoma (Fig-3).

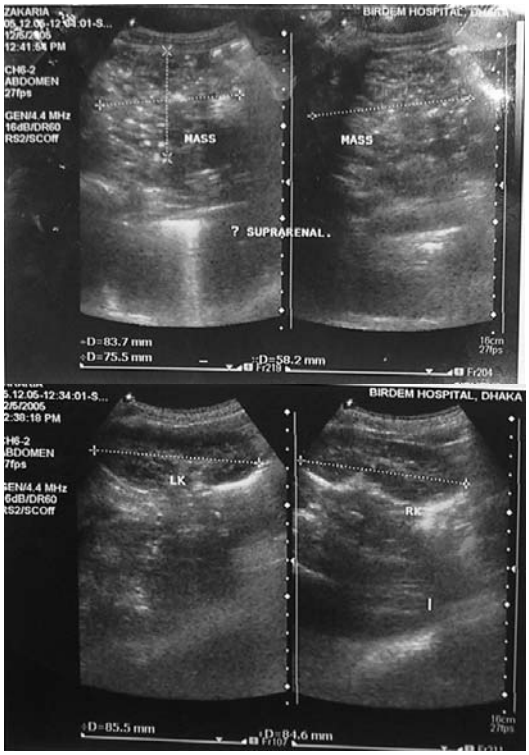

Fig-3: *USG abdomen shows a large heterogeneous mass with calcifications in the liver. The kidneys appear clear from invasion.*

c) IVU- normal.

d) CT-Abdomen and Lower Chest- A huge heterogeneous mass with scattered flecks of calcifications was found occupying almost the whole of the right lobe of the liver. On post contrast CT it showed heterogeneous enhancement with intervening lakes of hypodense areas possibly due to necrosis. The interface between the mass and skin and the diaphragm could not be well delineated and a spicule could be traced direct up through the diaphragm into the right lung field in the sagittal reconstructed view. Chest cuts also revealed numerous metastatic nodules in both lung fields. (Fig-4).

e) CT brain- No pituitary enlargement or focal lesions were found.

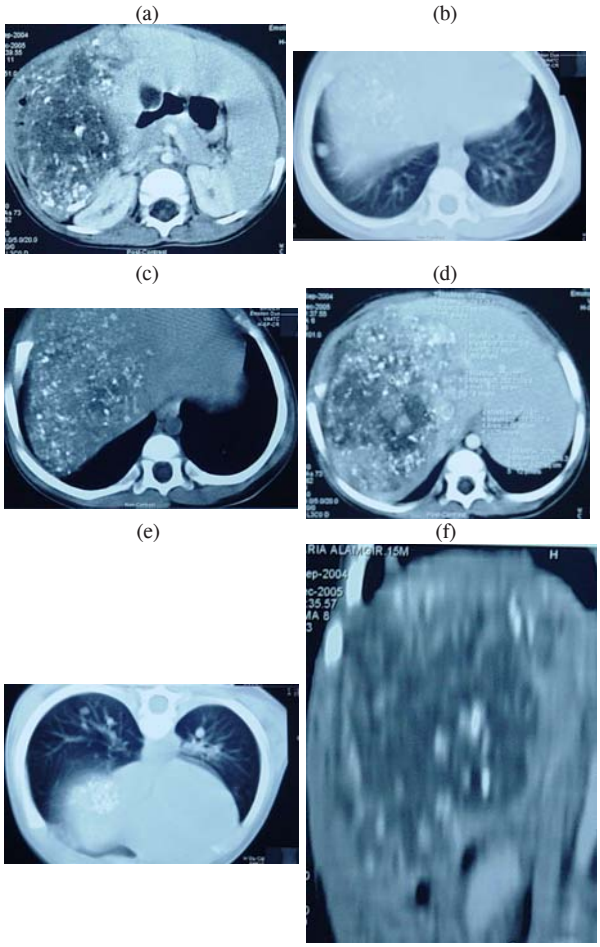

Fig-4: *CT abdomen and lower chest: (a) CE-CT shows a heterogeneous mass occupying almost the whole of the right lobe of the liver with flecks of calcifications. (b) CE-CT shows heterogeneous enhancement of the lesion with intervening hypodensities denoting lakes of necrosis. (c) CE-CT- Involvement of anterior abdominal wall by the lesion and right kidney is separate. (d) and (e) CT lower chest shows distinct nodules indicative of pulmonary metastasis in both lungs. (f) Sagittal reconstruction of CE-CT delineates the vertical extension of the mass lesion with upward protrusion through the diaphragm.*

In conformity with these typical imaging features, the impression was that it was a hepatoblastoma with probable extension into the anterolateral abdominal wall and lung metastasis.

Based on the radiological and clinical diagnosis, laparotomy was done. The tumor was excised. During surgery, ascitic fluid was found. The huge mass, occupying almost the whole of the right lobe of the liver, was found to be adherent to the diaphragm and abdominal wall. Porta hepatis and gall bladder were normal. No nodal involvement was found and no other metastatic focus was found in the abdominal cavity. Right lobectomy of the liver was done during which the right dome of the diaphragm had to be incised and then closed. The tissue was sent for histopathology where it was confirmed that it was a hepatoblastoma (mixed variety). The deep resected margin of the tumor was found to be involved by the tumor indicative of an incomplete resection together with distant metastasis in the lungs. It was thus staged to be at Stage-IV B. Following recovery from surgery, the boy was advised for chemotherapy.

Discussion

In children, most hepatic neoplasms are malignant[1]. The hepatoblastoma (HB) is an extremely rare, highly aggressive primary liver tumor of childhood. Among the childhood hepatic neoplasms it is the most common one -54%, followed by HCC –35% and others –11%[2]. It is a tumor of embryonal hepatocytes or mesenchymal cells, histologically classified into a) epithelial and b) mixed varieties- which is useful for prognosis[3,4]. It forms 0.2-5.8% of all primary pediatric malignancies[5]. The majority appear within the first 3 years of life (rarely thereafter)[1]. They are more frequent in boys and occur most often in the right lobe of the liver (60%)[6].

They usually develop as a large, solitary (in 20% multifocal), well circumscribed mass with a nodular / lobulated surface. Epithelial tumors are homogeneous whereas mixed variety ones are overall heterogeneous with large calcifications (50%) and fibrotic bands. The mass may be massive (upto > 22cm)[6]. Patients usually present with a large palpable right upper quadrant abdominal mass. Systemic signs include anorexia, vomiting, weight loss, and fatigue. Rarely, hormone-related presentations occur such as – male sexual precocity, hypoglycaemia, hypercalcaemia, and thrombocytosis. It has been reported to be associated with Beckwith-Wiedeman syndrome, polyposis coli, trisomy 18, in patients whose mothers were exposed to metal and petroleum products, mothers taking oral contraceptive pills and gonadotropins, and in the fetal alcohol syndrome[1].

Regarding the pathophysiology of the precocious pseudo-puberty in hepatoblastoma - the primitive hepatoblastoma cells secrete hCG which acts on LH-receptor of the testes, inducing them to release

increased amounts of testosterone which results in sexual precocity in these patients [7-11] (Fig-5).

A flow-diagram for the pathophysiology of the precocious pseudo-puberty in hepatoblastoma

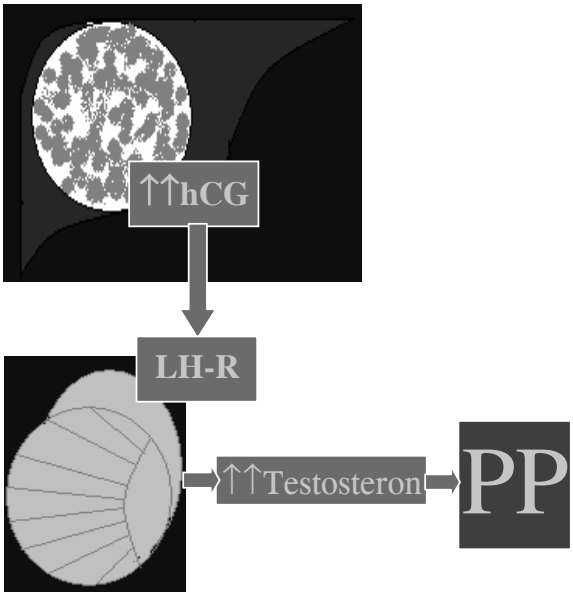

Fig-5: *The primitive hepatoblastoma cells secrete hCG which acts on LH-receptor (LH-R) of the testes, inducing them to release increased amounts of testosterone which results in precocious pseudo-puberty (PP) in these patients.*

Common sites of metastasis include the lungs (most common, and often present- in 10-20% at presentation), brain, bone, bone marrow, ovary, orbit[6].

The initial screening test for suspected cases should be – assessment of the serum α-fetoprotein (AFP), which is abnormally elevated in the vast majority of cases together with β-hCG which is also raised[1]. Both AFP and β-hCG are useful as monitors of potential tumor recurrence[12].

Imaging modalities and features

Typically, ultrasonography (USG) is the initial imaging evaluation in these children. The usual sonographic and CT findings are those that were found in our patient. Because these lesions can invade vascular structures such as the portal and hepatic veins, careful assessment of these structures by color flow Doppler is essential. One literature describes the prenatal diagnosis of a case at 37 weeks gestational age by USG[13]. However, it is not an adequate method of image staging of the neoplasm. CT is done for staging to assess the feasibility of surgery both before and after chemotherapy. One group[1] states that to assess the liver, CT is to be done by using biphasic (hepatic arterial and portal venous) dynamic contrast-enhanced spiral CT, followed by standard axial CT imaging of the remainder of the abdomen and chest. As in USG, thrombus may be found in the hepatic vein, portal vein and IVC. Metastases to bone and brain are rare, and therefore imaging is advised only if clinical signs and symptoms warrant doing so[1].

MRI can be used to determine the extent of the tumor, assess vascular structures, and detect secondary tumor nodules. However, it is not ideal in the detection of associated lymphadenopathy, and pulmonary metastases, which must also be excluded. Thus CT is preferred[1]. Staging of hepatoblastoma is done at the initial surgery [6]. Chemotherapy and complete surgical resection are both crucial in the cure of hepatoblastoma. Radiological interventions are optional[14,15]. Chemotherapy may reduce tumor size, allowing for complete conventional resection. If aggressive resection is necessary or bilobar disease persists, primary transplantation is recommended[16]. Prognosis depends on complete surgical resectability[4,12]. However, in most cases the tumor is unresectable because of its extensive hepatic involvement[17]. Prognosis for survival beyond 1-2 years from the time of diagnosis is poor.

Conclusion

Precocious pseudo puberty due to hepatoblastoma is extremely rare. A high index of suspicion is necessary on the part of the radiologists and endocrinologists by excluding usual causes like diseases of the adrenocortico-hypothalamo-pituitary axis. When a boy of 1-3 years presents with a mass in the right upper abdomen with typical physical and radiological features and hormonal assay findings, the possibility of this rare tumor should be kept in mind. Early diagnosis of hepatoblastoma is indispensible due to its highly aggressive nature. Appropriate and timely surgical and oncological interventions are worthwhile only in the early stages of the disease, which could lead to substantial reduction in the mortality and morbidity of the patient. Radiology and imaging plays a key role in the diagnosis adjuvant to biochemical parameters.

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