The Egyptian Journal of Hospital Medicine (October 2019) Vol. 77 (5), Page 5677-5680

Adult Hepatoblastoma: an Update

Bilal O Al-Jiffry
Department of surgery, Taif University

Abstract: Diagnostic and therapeutic protocols of adult hepatoblastoma are lacking because it is a rare condition, though, the pediatric one is the commonest hepatic tumor in children. The present study aimed at revision of the English literature of the published case reports and the systematic reviews of this rare tumor to elucidate the recent trends and update the etiological, pathological, diagnostic, and therapeutic concerns of hepatoblastoma in adult.
Keywords: adult, hepatoblastoma, update, English literature.

Introduction:
Adult hepatoblastoma is a rare hepatic neoplasm though this tumor is the commonest pediatric hepatic tumor [1, 2]. The etiology of the tumor is not quit known though many authors correlated the development of the tumor with genetic factors and underlying liver diseases as hepatitis B, liver fibrosis, and cirrhosis [1-3]. Diagnosis is difficult because no specific signs and symptoms are present [1-4]. Workup may show increased level of alpha fetoprotein with normal or mild derangement of liver function [4]. Computed tomography scan (CT) usually shows stippling calcification more than other hepatic tumors [4, 5]. Some authors advocated needle biopsy which is not accepted by the majority of other investigators for the fear of bleeding due to hypervascularity in addition to the possibility of dissemination [1-6]. The main lines of treatment include preoperative chemotherapy for tumor down staging followed by partial or total hepatectomy with orthotopic liver transplantation and postoperative chemotherapy [7-15]. Successful local control is reported after trans-arterial chemo-embolization (TACE), radiofrequency ablation, or ethanol injection [1, 4, 7]. Recent reports found that one year survival is around 25% with expected worse outcome in patients above 45 years [1, 3, 16-19]. The present study aimed at revision of the English literature of the published case reports and the systematic reviews of this rare tumor to elucidate the recent trends and update the etiological, pathological, diagnostic, and therapeutic concerns of hepatoblastoma in adult.

Etiology: Adult hepatoblastoma is a rare condition and to date only 64 cases were reported in 59 articles from 1958 to 2019 [1, 2, 4]. The etiology of the disease is not exactly known and further investigations are required to correlate the reported risk factors with the pathogenesis of the tumor [2]. **Wang and Liu** reported in their systematic review that genetic abnormalities are found in both childhood and adult types with various gene expression patterns [1]. Though infantile hepatoblastoma occurs in normal liver, some cases of adult type are associated with cirrhosis (11/64, 17.2%) and chronic viral hepatitis B infection (10/64, 15.6%). **Rougemont *et al.*** recorded the association of liver cirrhosis or fibrosis with adult hepatoblastoma in about 30% of cases and this difference may be related to smaller number of cases studied by the author [3].

Demographic data: Adult hepatoblastoma may occur at any age and the reported mean age is about 40 years; however, the majority of cases were recorded in young adults [1]. Males are slightly more affected than females (1.14:1) [2].

Pathological features:
Histologically; **Ishak** modified the original classification of hepatoblastoma as follow: predominant epithelial cells (epithelia type) and mixed mesenchymal and epithelial components (mixed type) [17].
Gross appearance: About 50% of the reported cases were capsulated and two thirds of cases had nodular surface [3]. The tumor consistency was described to be firm, soft, or mixed which was the commonest form [17]. The majority of the tumors had yellowish to grayish cut surface with scattered necrotic and hemorrhagic foci and was divided into lobules by white fibro-collagenous strands [3, 17].

Diagnosis: Vishnoi *et al.* emphasized that the diagnosis of the adult hepatoblastoma is difficult due to lack of clinical, laboratory, and imaging specificity and diagnoses were settled in the majority of the reported cases after surgery or autopsy [4]. There are no specific presenting symptoms or signs [1-6]. The most common presentation in the recorded cases was abdominal pain followed by enlarging

Received:16/8/2019
Accepted:16/9/2019

abdominal swelling; however, other abdominal and extra-abdominal presenting symptoms are also recorded (Table 1) [5]. Similar to other hepatic neoplasms, abdominal examination would show localized hepatic mass which was large in the majority of the reported case [1, 2, 4]. The mass was reported in both lobes equally and usually solitary [1]. Diffuse hepatic enlargement was also common and other less common findings were recorded in Table 2 [1-6, 18, 19].

Table 1: the main presenting symptoms

Clinical presentation	Number (%)
Abdominal pain	29/64 (45.3)
Site of pain:	
Epigastric	18/29 (62.1)
Right upper quadrant	10/29 (34.5)
Diffuse abdominal	1/29 (3.4)
Enlarging abdominal mass	20/64 (31.3)
Gastrointestinal symptoms:	10/64 (15.6)
Anorexia, nausea, and vomiting	8/10 (80.0)
Gastrointestinal bleeding	2/10 (20.0)
Extra-abdominal symptoms	3/64 (4.7)
Back pain	1/3 (33.3)
Leg swelling	1/3 (33.3)
Dyspnea	1/3 (33.3)
Incidentally discovered	2/64 (3.1)

Table 2: physical signs

Physical signs	Number (%)
Present	41/64 (64.1)
Absent	23/64 (35.9)
Diffuse hepatic enlargement	13/41 (31.7)
Localized liver mass (usually> 5 cm, mean 15.3 cm)	12/41 (29.3)
Weight loss	10/41 (24.4)
Anemic signs	3/41 (7.3)
Lower limb edema	2/41 (4.9)
Icterus	1/41 (2.4)

Workup: In most of the recorded cases the liver profile and other laboratory findings were within normal; however, alpha feto protein was high in about 40% of the reported cases [2].

Imaging is the keystone for preliminary diagnosis and in most of the cases a plain radiograph was performed where elevated hemidiaphragm, liver enlargement, and calcification with stippling or chunky pattern were detected [5, 6].

In most of the reported cases, ultrasound showed a solid liver mass with increased echogenecity; however, hypoechoic septated lesions were also recorded [6].

Kishimoto *et al*.[5] reported a pattern of calcification in CT scan especially in mixed hypervascular tumors which may help in diagnosis and differentiation of other hepatic neoplasms. Even though, this pattern of calcification is considered to be non specific by most of the authors [1-4, 6, 18-19]. **Wang and Liu** found in their study that calcification did not exceed 20% [1]. Computed tomography angiography and selective arteriography would detect in the majority of cases a large tumor mass with prominent hypervascularity [3]. Magnetic resonance imaging was also performed in the recently recorded cases without recorded specific features [2]. **Harada *et al.*** advocated needle biopsy for diagnosis of the tumor, though the reported success rate of such procedure does not exceed 2% [18]. **Al-Jiffry** insisted in his report that needle aspiration biopsy has low positivity and carries the risk of tumor dissemination and hemorrhage [16].

Differential diagnosis: Adult hepatoblastoma has to be differentiated from hepatocellular carcinoma which is the commonest adult tumor and both tumors usually present as a nodule and commonly a histological overlap is found [17]. Though it is still confusing, immunohistochemical (IHS) staining for CK19, EpCAM and beta catenin may help an expert pathologist to differentiate between both tumors [3, 6, 18].Mixed hepatocellular carcinoma and adult hepatoblastoma were reported, in addition, after chemotherapy the histological pattern of hepatoblastoma might be changed to resemble hepatocellular carcinoma [3].Thorough histological examination and IHS would help to exclude other tumors which carry histological similarities as; Teratomatous liver tumors, carcinosarcoma, calcifying stromal - epithelial tumor, malignant mesenchymal tumor [7].

Treatment: There is no standard therapeutic protocol for treatment of adult hepatoblastoma and all the recommended protocols are based on that of pediatric tumors [4-7]. Down staging using neoadjuvant chemotherapy followed by radical tumor resection is considered to be the mainstay in the treatment in the recently reported cases [4]. Cis-platinum is considered to be the most effective chemotherapeutic agent; however, irinotecan, adriamycin, and pirarubicin had been tried with limited success in some cases [4, 8, 13]. **Al-Jiffry** emphasized in his report that preoperative chemotherapy decreases the vascularity of the tumor and adjacent tissues which facilitates tumor

resection in addition to its cyto-reductive effect [6]. Following neoadjuvant therapy, partial hepatectomy is advocated for localized peripheral tumors and orthotopic liver transplantation for central and multifocal lesions that involve both hepatic lobes [11, 19]. Liver transplantation can be performed in presence of venous invasion but the survival is expected to be shorter in such patients [1-6, 11]. **Nakamura *et al*.** reported a 4 year survival in adult patient presented with locally advanced tumor and treated by neoadjuvant chemotherapy, partial hepatectomy, and postoperative combination chemotherapy [16].

In presence of pulmonary secondaries, all the metastases would be widely excised with partial hepatectomy or liver transplantation followed by post-operative chemotherapy [7, 13]. However, liver transplantation is contraindicated in presence of viable irresectable secondary lesions after pre-operative chemotherapy and in such patients palliative combination chemotherapy can be tried [3]. Palliative regimen included doxorubicin, cisplatin, five fluorouracil, cyclophosphamide, and vincristine [13]. Other therapeutic modalities were tried in multifocal tumors where partial hepatectomy was done to remove a large tumor and in some cases, smaller lesions were controlled by radiofrequency, trans-arterial chemo-embolization, or ethanol injection [19]. **Ortega *et al*.** reported a 151 months survival in a case treated by hepatic resection and ethanol injection for recurrence [13].

Outcome: The analysis of the reported cases shows a median survival of 6 months with about 25% one year survival [1, 2]. Young patients shows a better prognosis than older patients where an 80% one year survival has been recorded in pediatric hepatoblastoma, 42% in adult patients below 45 years, and 0% in the patient group above 45 years .Patients treated by liver transplantation have shown a better survival but due to the limited number an accurate survival rate can't be established [11, 13, 19]. To conclude; more studies are required to establish a therapeutic protocol; however, multimodal treatment with preoperative cytoreductive chemotherapy, radical resection particularly total hepatectomy with orthotopic liver transplantation, and postoperative chemotherapy is advisable.

References:

1. **Wang YX, Liu H (2012):** Adult hepatoblastoma: systemic review of the English literature. Dig Surg., 29: 323–30.
2. **Celotti A, D'Amico G, Ceresoli M, Tomasoni M, Raimondo S, Baggi P *et al*. (2016):** Hepatoblastoma of the adult: a systematic review of the literature. Surg Oncol., 25: 339–47.
3. **Rougemont AL, McLin VA, Toso C, Wildhaber BE (2012):**Adult hepatoblastoma: Learning from children. Journal of Hepatology, 56: 1392-403.
4. **Vishnoi JR, Sasidhar A, Misra S, *et al*. (2019):**Hepatoblastoma in a Young Adult: a Rare Case Report and Review of the Literature. J Gastrointest Canc., 2019: e1.
5. **Kishimoto Y, Hijiya S, Nagasako R (1984):** Malignant mixed tumor of the liver in adults. Am J Gastroenterol., 79: 229–35.
6. **Al-Jiffry B O (2013):** Adult hepatoblastoma: A case report and literature review. International journal of surgery case reports, 4: 204–7.
7. **Al-Sinani S, Al-Naamani K (2015) :**Adult Hepatoblastoma: What do we know?. Sultan Qaboos University medical journal, 15: 155–6.
8. **Lim I, Bondoc AJ, Geller JI, Tiao GM (2018):** Hepatoblastoma-The Evolution of Biology,Surgery, and Transplantation. Children (Basel, Switzerland), 6: 1-5.
9. **Venkatramani R, Stein JE, Sapra A *et al*. (2015):**Effect of neoadjuvant chemotherapy on resectability of stage III and IV hepatoblastoma. Br J Surg., 102:108-13.
10. **Vinayak R, Cruz RJ Jr, Ranganathan S, *et al* (2017).** Pediatric liver transplantation for hepatocellular cancer and rare liver malignancies: US multicenter and single-center experience (1981-2015). Liver Transpl., 23:1577-88.
11. **Triana Junco P, Cano EM, Dore M *et al*. (2019):** Prognostic factors for liver transplantation in unresectable hepatoblastoma. Eur J Pedatr Surg., 29:28-35.
12. **van Gulik TM, Westermann AM, Phoa SSKS, Verheij J, Oomen M, de**

Bree K *et al*. (2018): Two cases of hepatoblastoma in young adults. J Adolesc Young Adult Oncol., 7: 404–8.

13. **Ortega JA, Douglass EC, Feusner JH, Reynolds M, Quinn JJ, Finegold MJ *et al*. (2000):** Randomized comparison of cisplatin/vincristine/fluorouracil and cisplatin/continuous infusion doxorubicin for treatment of pediatric hepatoblastoma: a report from the Children's Cancer Group and the Pediatric Oncology Group. J Clin Oncol., 18: 2665–75.
14. **Zheng MH, Zhang L, Gu DN, Shi HQ, Zeng QQ, Chen YP (2009):** Hepatoblastoma in adult: review of the literature. Journal of Clinical Medicine and Research, 1: 13–16.
15. **Remes-Troche JM, Montano-Loza A, Meza-Junco J, Garcia-Leiva J, Torre-Delgadillo A (2006):** Hepatoblastoma in adult age. A case report and literature review. Annals of Hepatology, 5: 179–81.
16. **Nakamura S, Sho M, Kanehiro H, Tanaka T, Kichikawa K, Nakajima Y (2010):** Adult hepatoblastoma successfully treated with multimodal treatment. Langenbecks Arch. Surg., 395: 1165–8.
17. **Ishak KG, Glunz PR (1967):** Hepatoblastoma and hepatocarcinoma in infancy and childhood. Report of 47 Cases. Cancer, 20: 396–422.
18. **Harada T, Matsuo K, Kodama S, Higashihara H, Nakayama Y, Ikeda S (1995):** Adult hepatoblastoma: case report and review of the literature. Aust N Z J Surg., 65: 686–8
19. **Bee K, Westerman A, klumpen H *et al*. (2018):** Two cases of hepatoblastoma in young adults. Journal of adolescent and young adult oncology, 3: e1.