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Case Report Open Access

Hepatocellular Carcinoma with McCune Albright Syndrome

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Abstract

Cyprostate acetate (CPA) has been used in the treatment of hyper sexuality, which is considered as carcinogenic agent and its use has been prohibited for children. We presented young patient having hepatocellular carcinoma (HCC) with medication history of CPA during childhood, which arose from normal background liver without virus infections and other causes of liver dysfunction. The patient had multiple tumours in the liver, and only the largest one was diagnosed as HCC and other resected ones were hemangioma and hamartoma.

Keywords McCune albright syndrome; Hepatocellular carcinoma (HCC); Cyprostate acetate (Androcure); Young adult HCC; Hepatectomy

Introduction

Cyprostate acetate (CPA) is a synthetic progestagen to suppress gonadotropin secretion and blocks androgen action as a competitive inhibitor of androgen receptors. CPA had been used in the treatment of hypersexuality, deviationism, and prostatic carcinoma. In Japan, CPA had been introduced in 1983 to treat precocious puberty. However, its sale has been forbidden since 2001 because CPA administration had been considered probably carcinogenic to humans. Reviewing literature, 5 cases of HCC in the patients with CPA administration have been reported. In this case report, we investigate HCC patient with a medical history of CPA.

Case Report

A 34 years old female with medication history of cyprostate acetate (CPA) (Androcure®) for three years (Cumulative dosage: 300 g), until she was eight years old to treat precocious puberty due to McCune-Albright syndrome, was presented with multiple liver tumors. On examination, café au lait spot and polyostotic fibrous dysplasia were observed. She did not report any family history of hepatocellular carcinoma (HCC), any history of excessive alcohol intake, and hepatitis B and C infection. The laboratory data at administration showed that serum des-gamma-carboxyprothrombin (DCP) level was significantly high (Table 1).

Peripheral Blood		Coagulation	
White blood cell	5900 g/μl	APTT	28.4 second
Red blood cell	13.1 g/dl	PT	86.40%
Platelet	268000 g/μl	PT-INR	1.15
Liver Function Panel		**Endocrinological Ecamination**	
AST	75 IU/L	GH	73.8 ng/ml
ALT	145 IU/L	IGH-1	746 ng/ml
ALP	560 IU/L	Tumor Marker	
LD	138 IU/L	AFP	3 μg/l
YGT	138 IU/L	AFP L-3	<0.5%
ICG-R15	2%	DCP	1597 AU/L
Total Bililubin	1.2 mg/dl		
NH3	37 μg/dl		

Table 1: Serum des-gamma-carboxyprothrombin (DCP) level was high.

The dynamic CT scan, CT-angiography, and contrast MRI showed multiple liver tumors presented in bilobulary. Despite multiple tumors in the liver, only the largest tumor located in Couinoud's segment 8 showed typical enhancement pattern of HCC (Figures 1 and 2).

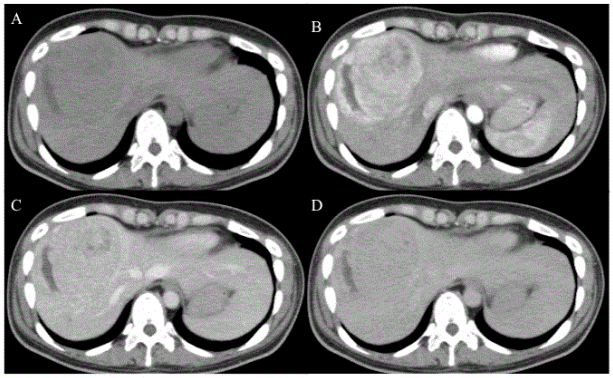

Figure 1: (A) plain CT image. (B) contrast CT at the early arterial phase, (C) contrast CT at the late arterial phase and (D) contrast CT at equivalent phase. These revealed that tumor showed at intense enhancement in the arterial phase and a contrast wash-out in late venous contrast phase.

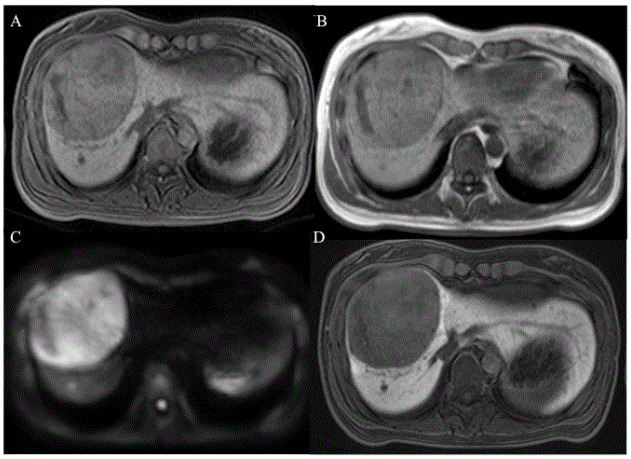

Figure 2: (A) T1 weighted image (B) T2 weighted image (C) EOB-MRI image (D) diffusion weighted image. These images showed liver tumor in segment 4, which was 91 mm in size, hypointense on EOB-MRI and highintense on diffusion weighted image.

Because other small tumors did not show typical enhancement pattern of HCC, and the size of those tumors was too small to evaluate and differentiated them from malignancy, we supposed that those tumors were large solitary HCC with multiple adenomas. For the purpose of diagnostic and therapeutic intention, we performed excisional biopsy via laparotomy. During the operation, using intraoperative ultrasonography, excisional biopsies of two tumors located on the surface of liver were performed. The intraoperative frozen section showed no malignancy, and those tumors were finally diagnosed with biliary hamartoma and hemangioma, respectively. The largest tumor was prominence from the liver surface with high tense, which appeared to rupture with ease. At this time, we diagnosed every small tumor as benign, which were not need to be resected; on the other hand, we considered the largest tumor should be resected whether they were benign or not for fear of tumor rupture.

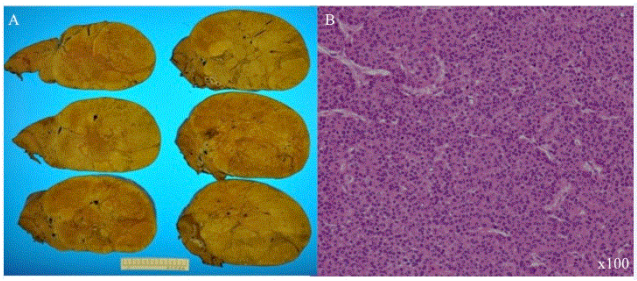

Figure 3: (A) Macroscopic appearance: 72 × 70 × 25 mm in size, single nodular type, (B) Hematoxylin and Eosin stain: Single nodular type in macroscopic appearance, well to moderately differentiated HCC with fibrous capsule formation. Neither vascular invasion nor microscopic tumor dissemination around tumor was seen. Underlying liver had mild fatty change (20%), dilation of portal area partly coexisting with fibrosis bridging and mild lymphocyte and plasma cell infiltration.

The curative segment eight resections were performed. Her postoperative course was uneventful. In the result of the histopathological examination, the largest tumor was diagnosed as single nodular type, well to moderately differentiated HCC with fibrous capsule formation without vascular invasion and microscopic tumor dissemination (Figure 3). Background liver had mild fatty change without chronic inflammation. Three years after the operation, the recurrence of HCC from residual tumors was detected through follow-up abdominal ultrasonography.

Discussion

We presented young HCC with medication history of CPA during childhood, which arose from normal background liver without virus infections and other causes of liver dysfunction. The patient had multiple tumors in the liver, and only the largest one was diagnosed as HCC.

HCC under 40 years of age individuals is relatively rare, and its occurrence rate is reported as 0.6% in overall patients with HCC [1]. The characteristics of young HCC patients are significantly higher rate of hepatitis B-related disease, better Child-Pugh status and more advanced disease at diagnosis [2]. For our patient, it is significantly rare that HCC arose from normal liver at this age. Although the patient does not seem to have a specific cause of HCC, possible pathogenesis of HCC in this patient is CPA, which is considered as a carcinogenic agent. CPA is a synthetic progestagen to suppress gonadotropin secretion and blocks androgen action as a competitive inhibitor of androgen receptors. CPA has been used in the treatment of hypersexuality, deviationism, and prostatic carcinoma [3]. In Japan, CPA had been introduced in 1983 to treat precocious puberty. However, its selling had been forbidden in 2001 because CPA administration had been considered as a potential carcinogen of liver cancer [4]. In an experimental study, CPA clearly induced a variety of genotoxic effects. Topkinka et al. firstly confirmed DNA adducts formation, which was a piece of DNA covalently bonded to a cancer-causing chemical and this process was considered as the start of a cancerous cell [5]. Also, Werner et al. confirmed DNA adduct formation were detected in CPA-treated human hepatocytes of two male and four female donors, and it happens dose-dependently [6].

In the review of the literature, 5 cases of HCC in the patients with CPA administration are reported. 4 CPAs are administered for growth retardation induced by endocrinological diseases such as Russell-Silver syndrome, Turner syndrome, McCune-Albright syndrome and adrenal hyperplasia. Especially, Watanabe et al. reported five cases of HCC whose cumulated doses are more than 500-1500 g. HCCs were confirmed from 12-22 years old [4]. However, the association between HCC and CPA is still controversial. Heinemann et al. concluded in a retrospective study with 2506 patients that correlation between hepatocarcinogenesis and CPA administration could not be established [7].

In this case, there were some augments about our decision leading to hepatectomy. Before the operation, we didn't perform trans-percutaneous biopsy not to disseminate tumor into the peritoneal cavity. During surgery, although excisional biopsies of two tumors were benign, we only resected the largest tumor for fear of rupture. However, we could not say whether all small tumors are benign or not and our operation would have been sufficient. As long as three years following up, the patient doesn't have growing tumors from residual ones. We need to keep close follow-up.

Considering those who received CPA in childhood get more than 30 years old in these days and the number of the patient who receives CPA for prostate cancer gets the increase, although the relationship between HCC and CPA is still controversial, clinician should bear in mind the importance of reviewing medication history and routine check-up of the liver.

Conclusion

We present a case of HCC with medication history of CPA, which can be a potential irritant of HCC. These days, it's time to reconfirm the importance of reviewing medication history and routine check-up of the liver among CPA users because those who received CPA in childhood get more than 30 years old and the number of the patient who receives CPA for prostate cancer gets the increase.

Conflicts of Interest

No conflict of interest to declare.

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