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De novo thyroid cancer after liver transplantation.

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Abstract

Introduction: The occurrence of de novo thyroid cancer following liver transplantation was rare. We reported our case to explore the clinical features, risk factors and preventive measures against the incidence of de novo thyroid carcinoma after hepatic transplantation.

Case report: This was a single case report. One female patient, aged 55 years old, undergoing allogeneic piggyback liver transplantation in combination with venacavaplasty and had de novo thyroid cancer subsequent. A palpable solid tumor with clear margins approximately 2 cm × 1 cm × 1 cm in size was detectable in the right neck. She underwent radical thyroidectomy, cervical lymph node dissection combined with exploratory operation. After receiving combined surgeries, she displayed stable vital signs and normal cardiopulmonary function, had no signs of hoarseness, difficulty in drinking or hand/ mouth numbness, etc. The patient was well recovered after postoperative 2-month follow-up.

Conclusion: The clinical and histopathological data were collected to analyse the clinical features, risk factors and preventive measures against the incidence of de novo thyroid carcinoma after hepatic transplantation.

Keywords: De novo, Thyroid cancer, Liver transplantation.

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Introduction

Cancer is a severe complication after organ transplantation with an increasing incidence. These patients have a higher risk of developing cancer than the general population. Skin cancer is the most common malignancy post-transplantation. Multiple factors contribute to the high risk of cutaneous carcinoma in immunosuppressed organ-transplant recipients [1]. For most common tumors, e.g. colon, lung, prostate, stomach, oesophagus, pancreas, ovary and breast, cancer rates were roughly twofold higher after kidney transplantation. Melanoma, leukemia, hepatobiliary tumors, cervical and vulvovaginal tumors were approximately fivefold more common. Kaposi's sarcoma, non-Hogkin's lymphomas, and non-melanoma skin cancers were more than 20-fold increased than in the general population [2]. The increasing length of survival of organ transplant recipients necessitates careful attention to the potential neoplastic complications of life-long immunosuppression's [3]. However, the occurrence of de novo thyroid cancer following liver transplantation has been rarely reported [4]. In this study, we reported one female patient with de novo thyroid cancer following liver transplantation on 31 March, 2014. Clinical and histopathological data were collected to analyse the clinical features, risk factors and preventive measures against the incidence of de novo thyroid carcinoma after hepatic transplantation.

Clinical Data

This study is approved by the General Hospital of Chinese People's Liberation Army and it is also obtained the signed informed consent from the patient. A female patient, aged 55 years, suffered from severe chronic virus B hepatitis for 10 years, which aggravated into posthepatitic cirrhosis at decompensatory phase. She underwent allogeneic piggyback liver transplantation plus venacavaplasty under general anesthesia on 31 December, 2011 at our hospital. Postoperative pathological examination revealed no signs of cancer cells in accordance with pathological manifestations of chronic posthepatitic cirrhosis.

Postoperative immunosuppression plan was determined as below: use of Tac plus Mycophenolate Mofetil (MMF) plus glucocorticoid was delivered at the beginning. At 3 months after surgery, she was orally administered with Cellcept, two tablets daily and Baraclude 1 tablet daily.

In June of 2012, a mass approximately 1 cm in size was identified in the right neck. She felt pain whereas had no hoarseness, dysphagia, hand quivering or shaking. She was accompanied with insomnia, bulimia and increased faecal frequency. No signs of fever were observed. Physical examination revealed a palpable solid tumor with clear margins approximately 2 cm × 1 cm × 1 cm in size in the right neck. No tenderness was detected. The tumor moved up and down along with swallowing. No vascular bruit was detected. A lymph node mass measuring 0.8 cm × 0.8 cm was detected at the

inferior margin of the right neck sternocleidomastoid muscle lymph node. The tumor was of solid substance and poor movement. Ultrasound examination revealed that cystic-solid node was identified in the right lobe of the thyroid and cystic node was detected in the left lobe, considered to be benign tumors. In addition, low-echo node was identified in the middle of thyroid left lobe and calcified node was detected on the dorsal side of the right lobe.

After the diagnosis was confirmed, she underwent radical thyroidectomy, cervical lymph node dissection plus exploratory operation. Postoperative pathological biopsy revealed papillary thyroid carcinoma in the right lobe and isthmus of the thyroid. Postoperatively, she presented with stable vital signs and normal cardiopulmonary function. She had no signs of hoarseness, difficulty in drinking or hand/ mouth numbness, etc. The levels of blood calcium and parathormone were normal. She started to use immunosuppressive drugs on the day of surgery and well recovered during 2-month follow-up.

Discussion

Incidence and type of de novo cancers after liver transplantation

The predilection sites, types and incidence of de novo malignant tumors following hepatic transplantation significantly vary among individuals from Asia, Europe and the United States. The incidence of de novo malignant tumors after liver transplantation in Europe ranged from 2.6% to 21.9% [5]. Zhu et al. reported a significantly lower incidence of 0.3% to 09% in China [6].

Li et al. [7] found that the most common types of de novo malignancy after hepatic transplantation included digestive system carcinoma, blood system cancer, urinary system malignant tumors and respiratory system cancer. Skin cancer is the most common de novo malignancy arising in the post-transplantation setting with an incidence 70 times higher compared with general population. Armin et al. suggested oropharyngeal tumors as the second most common type of cancer after liver transplantation due to high alcohol intake and smoking habit. Approximately 0-0.6% of liver transplantation recipients were diagnosed with colon cancer following liver transplantation. The incidence of liver cancer in patients with alcoholic liver disease was significantly ascended [2]. The high incidence of de novo malignancy has been proven to be associated with smoking, gender, increasing age, post-transplantation immunosuppression, increased risk of opportunistic infection, and transplantation-associated medical problems [8].

Pathogenesis and clinical manifestations of de novo thyroid cancer after liver transplantation

Recently, thyroid cancer is becoming the most rapidly increasing malignancy and the incidence of thyroid cancer ranks the 10th among all types of carcinoma with an age-adjusted incidence of 4.21 per 100 000 individuals in China [9]. However, the incidence of de novo thyroid cancer following liver transplantation has been rarely reported at home and abroad. A variety of risk factors collectively contribute to the incidence of de novo thyroid cancer post-transplantation, such as the interaction among post-transplantation immunosuppression, increased risk of opportunistic infection, inheritance susceptibility and external environmental factors [10].

Graves' disease is an autoimmune disease and most commonly enlarges the size of thyroid by twice or more, with related hyperthyroid symptoms such as increased heartbeat, muscle weakness, disturbed sleep and irritability, which is considered as a risk factor inducing thyroid cancer. The incidence of thyroid cancer in patients with thyroid node disease was significantly higher compared with normal counterparts [11]. Thyroid lymphoma arises from Hashimoto's Thyroiditis (HT), probably because antigen chronic irritation causes the malignant hyperplasia of lymph follicle centrocytes. Larso et al. suggested that HT patients had a 3 times higher incidence of thyroid cancer as compared to the general population. After liver transplantation, the usage of immunosuppressive agents further reduced the immune surveillance function of the host, impaired the immunity supervising mechanism, promoted the proliferation and differentiation of cancer cells and led to the de novo tumorigenesis. Moreover, certain immunosuppressive drugs may have intrinsic oncogenic properties. As a result, liver transplant recipients have an increased risk of de novo neoplasia. In a recently published randomized trial, patients with alcoholic cirrhosis had a higher risk of non-hepatic neoplasia if they were transplanted than those receiving standard care (5-year risk of neoplasia: 37% *vs.* 6%) [12].

Li et al. demonstrated that EBV infection was detected in the thyroid cancer tissues, hinting that EBV infection was significantly correlated with the incidence of thyroid carcinoma. EB virus was associated with the incidence of post-transplantation lymphoproliferative disorders. Postoperative use of immunosuppressive agents provides favorable conditions for the activation and proliferation of EB virus. Hence, EB virus probably plays a pivotal role in the incidence of development of de novo thyroid cancer following hepatic transplantation.

Preventive measures and early diagnosis of de novo thyroid cancer after liver transplantation

The first recommendation is to perform surgical therapy combined with alternative comprehensive treatment for patients with thyroid cancer. It prolongs patients' long-term survival, reduces the recurrence rate of thyroid cancer and enhances quality of life.

Papillary thyroid carcinoma is the most common type of thyroid cancer, whereas the surgical method remains debated. However, most physicians agreed on the following two aspects. First, perform surgery was not recommended if less than one thyroid lobe of would be excised. Second, total and

subtotal thyroidectomy could be applied in patients with high-risk factors, bilateral tumors or serious tumor invasion. However, the resection area for low-risk patients with unilateral cancer is uncertain. Whether lymph node dissection should be applied for lymph node-negative patients? Which dissection pattern should be selected?

In this report, she presented with de novo thyroid cancer after liver transplantation, belonging to the high-risk population. Radical thyroidectomy, cervical lymph node dissection and exploratory operation were adopted. The scope of excision and lymph node dissection was determined based upon tumor invasion depth and alternative high-risk factors.

Intraoperative application of recurrent laryngeal nerve monitor

Thyroid cancer operation may cause intraoperative nerve injury. Nerve monitor could protect the nerve from injury and enhance surgical safety. In this case, recurrent laryngeal nerve monitor was applied to precisely pinpoint and effectively protect recurrent laryngeal nerve. However, the scope of this technique is still limited due to the challenges related to technology, devices, price and safety.

Proper use of immunosuppressive agents after liver transplantation

Another recommendation is to avoid over immunosuppression, as intense regimens of immunosuppression are associated with a higher frequency of malignancy [13]. The use of mTOR inhibitors could be associated with a lower incidence of neoplasia, but this benefit was proven merely in renal transplant patients [14]. In this report, the intensity and dose of immunosuppressive agents yield a relatively high efficacy and safety.

Conclusion

This study also has several limitations. Due to relatively short follow-up duration, long-term role of immunosuppressive protocols remains to be further investigated. Preventive measures for early diagnosis of thyroid neoplasia cannot be widely recommended until the evidence of their usefulness become more convincing. The occurrence of de novo thyroid cancer following liver transplantation was rare. We collected the clinical and histopathological data to analyse the clinical features, risk factors and preventive measures against the incidence of de novo thyroid carcinoma after hepatic transplantation.

References

1. Otley CC, Pittelkow MR. Skin cancer in liver transplant recipients. Liver Transpl 2000; 6: 253-262.
2. Wong WW, Bain VG. Update in liver transplantation. Can Fam Physician 1999; 45: 1241-1249.
3. Frezza EE, Fung JJ, van Thiel DH. Non-lymphoid cancer after liver transplantation. Hepatogastroenterology 1997; 44: 1172-1181.
4. Akdur A, Kırnap M, Yildırım S, Altundag O, Moray G. Posttransplant malignancies in liver transplant recipients. Exp Clin Transplant 2014; 12: 162-165.
5. Vallejo GH, Romero CJ, de Vicente JC. Incidence and risk factors for cancer after liver transplantation. Crit Rev Oncol Hematol 2005; 56: 87-99.
6. Zhu ZJ, Li L, Zhang YM. Diagnosis and treatment of de novo malignancy after liver transplantation. Zhonghua Zhong Liu Za Zhi 2007; 29: 237-238.
7. Li XY, Zhu JY, Li GM. De novo neoplasms after liver transplantation: a clinical study. Chin J Hepatobil Surg 2013; 19: 102-104.
8. Herrero JI. De novo malignancies following liver transplantation: impact and recommendations. Liver Transpl 2009; 2: 90-94.
9. Yang L, Sun TT, Yuan YN, Wang N. Time trends and pathological characteristics of thyroid cancer in urban Beijing, 1995-2010. Chin J Prevent Med 2013; 47: 109-112.
10. Zhang XZ, Wang WT, Yang J. Attach great importance to the occurrence and prevention of the de novo malignancy after liver transplantation with 5 cases in a single center. Pract J Clin Med 2011; 8: 46-51.
11. Boone RT, Fan CY, Hanna EY. Well-differentiated carcinoma of the thyroid. Otolaryngol Clin North Am 2003; 36: 73-90.
12. Vanlemmens C, Di Martino V, Milan C, Messner M, Minello A, Duvoux C, Poynard T, Perarnau JM, Piquet MA, Pageaux GP, Dharancy S, Silvain C, Hillaire S, Thiefin G, Vinel JP, Hillon P, Collin E, Mantion G, Miguet JP. Immediate listing for liver transplantation versus standard care for Child-Pugh stage B alcoholic cirrhosis. A randomized trial. Ann Intern Med 2009; 150: 153-161.
13. Benlloch S, Berenguer M, Prieto M, Moreno R, San Juan F, Rayn M, Mir J, Segura A, Berenguer J. De novo internal neoplasms after liver transplantation: increased risk and aggressive behavior in recent years? Am J Transplant 2004; 4: 596-604.
14. Monaco AP. The role of mTOR inhibitors in the management of post-transplant malignancy. Transplantation 2009; 87: 157-163.

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