High frequency ultrasound features and pathological characteristics of medullary thyroid carcinoma

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Abstract: To study high-frequency ultrasound features and pathological characteristics of medullary thyroid carcinoma (medullary thyroid carcinoma, MTC) with the purpose to improve the diagnostic accuracy of this disease. The clinical data of 20 cases of patients with MTC confirmed by the clinical surgery were retrospectively analyzed. And the high-frequency ultrasound features were analyzed and compared with the pathological characteristics. There were 16 cases with tumor invasion into one side of the thyroid gland; 17 cases with tumor in the middle-upper pole of the thyroid gland. And 8 cases was detected with uneven echo of high frequency ultrasound appearance and pathological manifestations of cystic degeneration to necrosis seen under the light microscope or normal thyroid tissue within part of the lump. 16 cases was tested with even echo of high frequency ultrasound appearance, and tumor cells were formed in the solid and block-like shape under the light microscope. And 18 cases were manifested with low echo, with proliferation of fibrous tissue within the intercellular substance under the light microscope. 18 cases could be seen the calcification points and often amyloid-like content deposited in the intercellular substance seen under the light microscope. In addition, the pathological manifestations of the 8 cases combined with lymph node metastasis were the "lash tumor" of the metastatic lymph nodes and primary tumor. MTC was commonly located in the middle-upper region of the thyroid gland and in one leaf of the thyroid gland, combined with lymph node metastasis. The high frequency ultrasound appearance was the even low-echo tumor in round or quasi-circular shape, with obscure boundary and often combined with rough calcification. High frequency ultrasound could be used as the prior physical diagnostic method for medullary thyroid carcinoma.

Keywords: High frequency ultrasound, Tumor, Medullary thyroid carcinoma, pathology.

INTRODUCTION

Medullary thyroid carcinoma (medullary thyroid carcinoma, MTC) is a kind of medium-degree malignant tumor, originating from para follicular cells of the thyroid gland (also called C cells), which can secrete calcitonin (Chen Y *et al*, 2011), which is rare. And the form of organization is complicated under the light microscopy often combined with metastasis, and the malignant degree is higher than the most common thyroid papillary carcinoma and follicular carcinoma. It has been found in the detection of genetics in recent years, MTC is often induced by gene mutation of RET (Wang XL *et al*., 2009). 20 cases with complete clinical information and confirmed the MTC pathologically were selected, and the high frequency ultrasound test was compared with the pathology after operation. And the correlation between high frequency ultrasound features and pathological characteristics was analyzed to improve the diagnostic accuracy of medullary thyroid carcinoma.

MATERIAL AND METHODS

General information

20 cases received surgery form July 2008 to September 2015 and confirmed MTC pathologically were retrospectively analyzed, and all accepted high frequency ultrasound test. Among them, 4 cases were found in the physical examination, 15 cases in the treatment for the lump in the neck, and 1 case in the treatment for the hoarseness. And there were 6 male cases and 14 female cases with the ratio of 3:7, indicating that it was more common in women. In addition, the age were among 12 years to 65 years, with the average year of 43.6 years old.

Methods

The color ultrasonic diagnostic instrument of iu-22 in Philips Company and Logiq 9 in GE company were used to test, with the probe in line formation, the frequency of 7.5-10.0 MHz, and the condition was adjusted to suit for thyroid conditions. Patients took the supine position, with the shoulder padded higher, the head back-forward as best as possible to make the inspection area of the neck expose completely. The lesion location, size, echo, shape, edge, calcification, cervical lymph nodes were recorded. The primary lesion and the high frequency ultrasound features and pathological characteristics of the metastasis lymph node were compared and analyzed.

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RESULTS

20 cases were with 24 lesions, including bilateral lesions in 4 cases, unilateral lesions in 16 cases, lesions involving the isthmus in 4 cases, 14 cases with simplex medullary carcinoma. In addition, there were 6 cases combined with other lesions, including 4 cases combined with nodular goiter, 1 case combined with parathyroid hyperplasia, 1 case combined with sub acute thyroiditis. Among them, the maximum tumor diameters were 0.3-7.0cm. And there were 17 cases with lesions located in the two-thirds of thyroid gland, 18 cases with echo reduction (fig. 1A), 16 cases with even echo, 8 cases with uneven echo, 5 cases combined with cystic degeneration in various degree (fig. 1B), 18 cases with obscure boundary, 18 cases with calcification in the lesions, including 12 cases with rough calcification (diameter ≥1 mm) (fig. 1C), 6 cases with fine calcification (diameter <1 mm). And there were 8 cases combined with cervical lymph node metastasis, with the maximum diameter 0.3-4.0cm, 6 cases with low echo appearance (fig. 1D), 2 cases with equal echo, 6 patients with calcification (bulky calcification in 4 cases, small calcification in 2 cases) and the other 2 cases without calcification. The corresponding pathology: It could be seen the hyperplasia of fibrous tissue at various degree within the mesenchyme in the patients with echo reduction; and there were two pathological characteristics in the patients with uneven echo: one was combined with cystic necrosis (5 cases), the other was with normal thyroid tissue inside the tumor tissues (3 cases); 16 cases with even echo could be seen microscopically the tumor tissues in solid form, well-distributed and with less mesenchyme in which could be not seen the cystic degeneration necrotic tissue and normal thyroid tissue (fig. 2); and the tumor cells grew with invasion and the membrane been widely invaded in 18 cases with obscure boundary; the hilus structure containing collagen element disappeared within the mesenchyme and the tumor tissue similar to the primary lesion or amyloid substances could be seen in 18 cases combined with calcification. And the patients combined with the metastasis lymph nodes could be seen the formation of the calcification of lymph node, in which the blood vessels were very abundant.

Oncocytes in tumor were in the shape of fusiform and small round, arranged solidly and closely, unnormal nucleus in some cells, easy to be divided, surrounding with rich blood vessels.

DISCUSSION

MTC is rare in the pathological types of the thyroid carcinoma, but an independent clinical pathological type. It was first put forward by Hazard in 1959 (Kann PH *et al*., 2006), consisted of 5%-10% of the whole thyroid carcinoma (BallDW, 2007). MTC can secret calcitonin (CT), carcino-embryonic antigen (CEA) and other polypeptide hormones. Therefore, it is called neuroendocrine system tumor, or APUD tumor by pathologists. It is divided into the genotype and sporadic type clinically (Kloos RT *et al*., 2009). And the sporadic type makes up of the major (80%). MTC is mainly in the middle-age and elders with the age of 45years - 50 years the most and the lesion focus mainly the solitary nodule (Roman S *et al*, 2006). The group average age was 43.6 years, 14 cases with solitary nodule (58%), close to the report. There were no confirmed familial disease which might because the small samples and not detailed history asking.

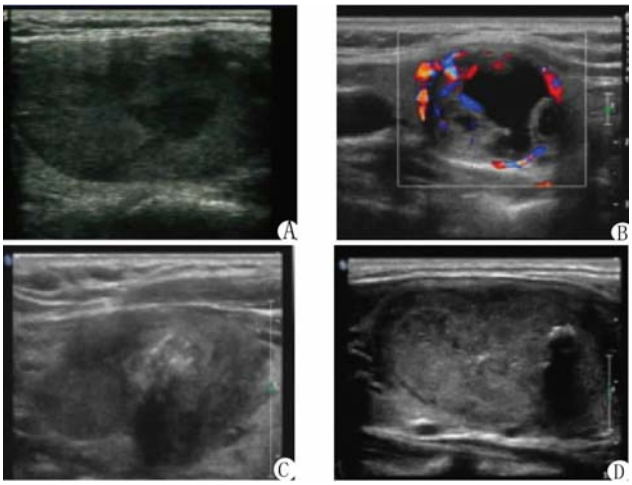

Fig. 1: Ultra sonogram of MTC
A: Echo reduction and uneven echo within nodules;
B: Cystic degeneration and necrosis within nodules, abundant color blood flow signal surrounding and within the nodes;
C: Bulky calcification combined with sound shadow within the nodes;
D: Lymph node metastasis of medullary thyroid carcinoma, echo reduction within the lymph node and disappear of hilus and obscure bundary of skin medulla, similar to the ultrasonogram of the primary MTC lesion, bulky calcification With acoustic shadow locally.

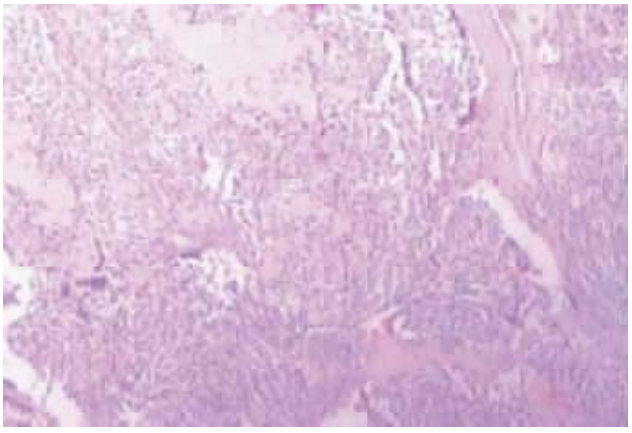

Fig. 2: Pathological section of MTC

The ultra sonography of the 24 cases of the group were manifested in round shape or oval, 16 cases with multi-

invasion and one-leaf (16/24), 18 cases with low echo block mass (18/24), 16 cases with even echo (16/24), 18 cases with obscure boundary (18/24), 18 cases with calcification (18/24). Corresponding pathology: A large number of collagen fiber organization and less ground substance and rich blood vessel could be seen in the patients with low echo. And it was not easy to occur necrosis within the tumor, which might because the very abundant blood vessel, and also being one of the reasons that caused even echo. The tumor cells growing with invasion and widely invasion of the capsula could be seen in 18 cases with obscure boundary. And it could be seen the diolame in the ultra sonogram in 6 cases, indicating that the normal thyroid tissue were oppressed to form the pseudo capsule. There were 18 cases combined with calcification, including 12 cases of rough calcification (12 /18), which was different from the combination with the calcification of papillary thyroid carcinoma (papillary thyroid carcinoma, PTC), the calcification of PTC was rather small and loose, induced by the psammoma bodies while the formation of MTC calcification was that the local calcium salt was enveloped to deposit gradually (Jun P *et al*, 2005). Psammoma bodies under the light microscope were often manifested with the calcification body in round or concentric, with the smaller diameter of 10~100um. It was reported in the document that the psammoma bodies were often the deposition of calcium salt of the dead cells caused by the focal infarction in the nipple cutting-edge (Wang XY *et al*., 2004). Parts of the MTC manifestation were similar to adenoma, often with single quasi-circular lesion. But the difference was: MTC was in the middle-upper of the thyroid gland, with a high occurrence of calcification without diolame commonly and the thickness of acoustic halo was not even and incomplete while the diolame of the adenoma was complete and the acoustic halo of adenoma was even and with annular blood flow and regular blood vessel.

MTC generally grows slowly while lymph node metastasis may appear in the earlier period. There are cervical lymph node metastasis in more than 50% patients when they are diagnosed with MTC (Guo JJ *et al*., 2012). The maximum diameter of the cervical lymph node metastasis were 0.3-4cm in 8 cases (8/20), which was lower than the document. The reason might because that MTC was often transferred to the front of the mediastinal lymph node, which was often not detected by ultra sound inspection. There were 6 cases (6/8) with the echo reduction and disappearance of the lymph hilus within the metastasis of lymph nodes. And the obscure boundary was similar to the ultra sonogram of the MTC lesion, manifesting in “lash tumor”. It was reported in the document that the calcification could be seen in the 50%-60% of the metastatic lymph nodes of MTC (Shi W, 2011), which was also found in the data of the group, that the calcification was found in 6 cases (6/8). In addition, the condition of the calcification in the metastatic lymph nodes was also similar to that in the primary lesion. It could be seen the bulky calcification in the metastatic lymph nodes of MTC in 4 cases (4/6), which was different from the micro-calcification of the metastatic lymph nodes of PTC.

CONCLUSION

There are some certain features in the high-frequency ultrasound of MTC. MTC is mostly located in the middle-upper region of the thyroid gland with the even hypoechoic mass lesion in the shape of round or quasi-circularin and with high occurrence of calcification and obscure boundary. It is in one leaf of the thyroid gland, often combined with lymph node metastasis. High frequency ultrasound can be used as the first physical diagnostic method for medullary thyroid carcinoma.

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