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CASE REPORT

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Heterotopic thyroid tissue at the porta hepatis in a fetus with trisomy 18

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Abstract Heterotopic thyroid tissue at the porta hepatis in a fetus with trisomy 18 is described. The fetus had an eutopic thyroid gland without any abnormalities. The heterotopic thyroid was found at the porta hepatis and showed histological features similar to the eutopic thyroid. Immunohistochemically, the heterotopic follicles were positive for thyroglobulin, but no calcitonin-positive cells were found. Intra-abdominal heterotopic thyroid is exceedingly rare in locations other than the ovary, and to our knowledge, this is the first report of a fetal case. The present case provides clear evidence that abdominal heterotopic thyroid can occur as a congenital anomaly. Migration abnormality of the median anlage of the thyroid is the most likely histogenesis of heterotopic thyroid at the porta hepatis.

Key words Heterotopic thyroid · Porta hepatis · Trisomy 18 · Fetus

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Introduction

Heterotopic thyroid of the tongue and mediastinum is well documented, and is considered to be caused by migration abnormality [1, 12]. In the subdiaphragmic region, heterotopic thyroid appears mostly as struma ovarii or a constituent of mature cystic teratoma of the ovary. Heterotopic thyroid in the subdiaphragmic region located in tissue other than ovarian is extremely rare, and it is sometimes difficult to exclude the possibility of metastatic thyroid carcinoma with minute atypia in adult cases. We present a case of heterotopic thyroid in a trisomy 18 fetus. To our knowledge, this is the first report of a fetal abdominal heterotopic thyroid. This case may provide some clues for understanding the mechanism responsible for heterotopic thyroid at the porta hepatis.

Clinical history

The patient, a male, was the second child of healthy parents. His elder 3-year-old brother was in good health with no remarkable clinical history. After 27 weeks of gestation, ultrasonographic examination revealed omphalocele and polyhydramnios. Chromosomal analysis of fetal cells obtained by amniocentesis showed an abnormal karyotype, 47,XY,+18. The parents were counseled and elected to terminate the pregnancy. At 30 weeks of gestation, the mother gave birth to a stillborn infant weighing 1040 g. Multiple malformations consistent with the features of trisomy 18 were observed. These included low-set ears, preauricular tags, micrognathia, low hairline, a large omphalocele, a narrow pelvis, overlapping fingers, bilateral thumb aplasia, bilateral radial aplasia, and rocker-bottom feet.

Materials and methods

Post-mortem samples were fixed with 10% formalin and embedded in paraffin. Sections were stained with haematoxylin and eosin.

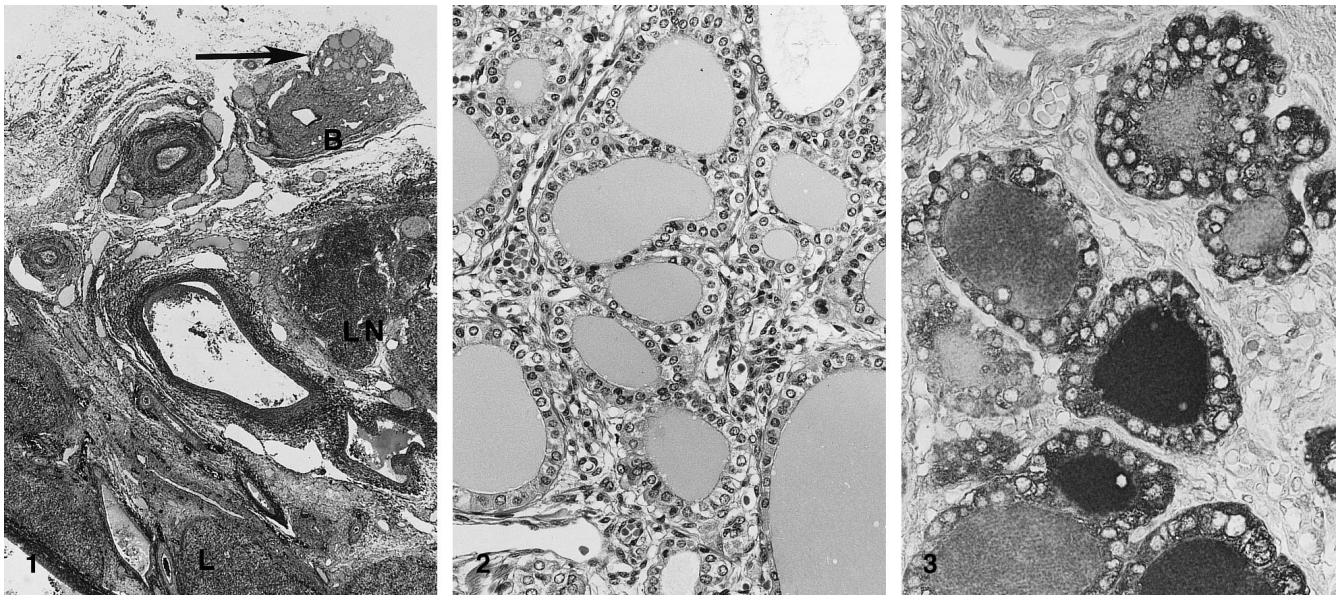

Fig. 1 Heterotopic thyroid tissue (arrow) at the porta hepatis beside the bile duct. B; Bile duct. L; Liver. LN; Lymph node. Haematoxylin-eosin. ×10

Fig. 2 Heterotopic thyroid tissue composed of variably sized follicles lined by cuboidal epithelium and containing colloidal material. Haematoxylin-eosin. ×120

Fig. 3 The heterotopic thyroid tissue is immunoreactive with anti-thyroglobulin antibody. Both epithelial cells and colloidal material are strongly positive. Avidin-biotin complex method. ×180

Immunohistochemical staining to confirm the presence of thyroid tissue in the heterotopic thyroid and the normal thyroid gland was performed on formalin-fixed, paraffin-embedded sections by the avidin-biotin complex method. The primary antibodies used were anti-thyroglobulin antibody (Nichirei, Tokyo, polyclonal) and anti-calcitonin antibody (Nichirei, Tokyo, polyclonal).

Pathologic findings

Autopsy was performed about 20 h after delivery. The omphalocele contained approximately half of the liver. Ventricular septal defect was noted.

The eutopic thyroid gland measured 14×12×5 mm and appeared normal in location, size, and shape. The histological findings were consistent with the histology of normal 30-week fetal thyroid tissue. The heterotopic thyroid, which was 2 mm in diameter, was found incidentally at the porta hepatis, at the anterior side of the gall bladder (Fig. 1). The heterotopic thyroid was composed of round follicles containing colloidal substance (Fig. 2). The epithelial cells were cuboidal and possessed uniform, round nuclei. The heterotopic thyroid was histologically similar to the eutopic thyroid gland.

Immunohistochemically, the follicular epithelial cells and colloidal substance in the follicles were strongly positive for thyroglobulin, in both the eutopic thyroid gland and the heterotopic thyroid (Fig. 3). Calcitonin-positive cells were dispersed singly or as small clusters in the interfollicular areas of the middle portion of the lateral lobes of the eutopic thyroid gland. However the heterotopic thyroid was not positive for calcitonin.

Other organs examined showed normal histological development for a fetus of 30 weeks gestation.

Discussion

There are various possible causes of accessory heterotopic thyroid tissue: (1) teratoma, (2) epithelial metaplasia, (3) abnormal migration in embryogenesis, (4) implantation due to trauma or operation, and (5) metastasis of thyroid carcinoma with minimal atypia. Because the present case is a fetal one, the latter two causes are unlikely.

Struma ovarii, a tumour that is not uncommon, is considered to be due to one-sided development of a teratoma. This explanation is supported by the fact that thyroid tissue is found in 5–15% of mature cystic teratomas [2]. If heterotopic thyroid tissue at the porta hepatis is monodermal teratoma aetiologically similar to struma ovarii, there should be more reports of teratoma at the porta hepatis. However, we could find no examples of mature cystic teratoma at the porta hepatis in the literature. In the present case, and in the five reported cases of heterotopic thyroid at the porta hepatis and gallbladder, there were no other teratoma components associated with the heterotopic thyroid [4, 6, 9, 13, 16]. In the subdiaphragmatic region, one case of heterotopic thyroid associated with parathyroid gland in the vaginal wall, and two of struma salpingis have been reported [7, 8, 9]. From their location, teratoma is thought to be responsible for their pathogenesis.

Thyroidal metaplasia was suggested as the pathogenesis of a duodenal heterotopic thyroid that was intermingled with Brenner's gland [17]. In the present case, the heterotopic thyroid appeared to be an individual nodule,

Table 1 Review of literature of subdiaphragmic heterotopic thyroid outside the ovary

Reference	Age/Sex	Location	Pathologic description
[7]	44/F	Salpinx	40 mm in diameter
[13]	73/F	Adjacent to the bile duct	20×20×8 mm
[4]	19/F	Gallbladder	10 mm in diameter, associated with heterotopic gastric mucosa of the gall bladder
[10]	3/F	Vaginal wall	9×7×3 mm, associated with parathyroid gland
[17]	63/M	Duodenum	Microscopic, intermingled with Brunner's gland
[3]	63/F	Posterior to the spleen and pancreas	Lobular mass, 100×75×50 mm, adenomatous hyperplasia
[16]	58/F	Between the gallbladder and hepatoduodenal ligament	45 mm in diameter
[8]	44/F	Salpinx	2 mm in diameter associated with struma ovarii
[14]	69/F	Behind the head of the pancreas	70×50×30 mm
[18]	61/F	Adrenal	Cystic mass, 35 mm in diameter
[6]	35/F	Adjacent to the gallbladder	7 mm in diameter
[9]	58/F	Porta hepatis	75 mm in diameter, with hyperplastic change
[15]			
Case 1	50/F	Adrenal gland	Several cystic lesions
Case 2	50/M	Adrenal gland	Cystic lesion
Present case	30 weeks fetus/M	Porta hepatis	2 mm in diameter

and not directly related to the adjacent bile duct epithelium. Metaplasia occurs as a reaction to chronic stimulation such as that resulting from an inflammatory condition. Because the present case occurred in a fetus with no evidence of infection, this possibility is unlikely. More cases may be needed to verify the concept of thyroidal metaplasia.

In our review of literature (Table 1), we were able to find only fourteen cases of subdiaphragmic heterotopic thyroid other than struma ovarii [3, 4, 6–10, 13–18], which included three cases that were considered to be cases of monodermal teratoma as described above. In five of the remaining eleven cases, the heterotopic thyroid tissue was located at the porta hepatis or near the gallbladder [4, 6, 9, 13, 16]. This relative frequency might suggest the same underlying pathogenesis of heterotopic thyroid at the porta hepatis. It is well accepted that mediastinal heterotopic thyroid is caused by excessive migration associated with descent of the mediastinal organs [1, 12]. We consider that heterotopic thyroid at the porta hepatis is also caused by excessive migration before the diaphragm is completely formed. Based on this assumption, it is reasonable that the porta hepatis, the uppermost portion of the abdomen, is found to be the site where heterotopic thyroid occurs relatively frequently in the subdiaphragmatic region. Furthermore, the present case suggests that this thyroidal heterotopia is congenital.

The thyroid gland is formed from a median anlage that originates from the primitive pharynx, and two lateral anlagen that originate from the ultimobranchial bodies. C cells are derived from the neural crest and migrate to the ultimobranchial bodies before being incorporated into the thyroid gland. This suggests that, the median anlage does not contain C cells. Heterotopic thyroid related to the thyroglossal duct cyst arises during descent of the median anlage. In a study of 23 cases of thyroglossal duct cysts with adjacent thyroid tissue and one case of lingual thyroid, not a single C cell was found by immunohistochemical investigation [11]. Furthermore, there have been many reports of carcinoma arising in heterotopic thyroid in midline structures, whereas no case of medullary carcinoma has been reported. Thus, the absence of calcitonin-positive cells in the present case is consistent with the finding of heterotopic thyroid tissue caused by abnormal migration of part of the median anlage.

The aetiological relationship of the heterotopic thyroid to the chromosomal abnormality remains uncertain. Only hypoplasia has been described previously as a thyroidal abnormality in trisomy 18 and there have been no reports of an association with thyroidal heterotopia [5].

This case provides evidence that heterotopic thyroid tissue beneath the diaphragm can have a congenital etiology, and we consider that excessive migration is the most likely histogenetic cause of heterotopic thyroid tissue at the porta hepatis.

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