Endokrynologia Polska/Polish Journal of Endocrinology
Tom/Volume 63; Numer Number 5/2012
ISSN 0423–104X

Mixed germ cells tumour primarily located in the thyroid — a case report

Mieszany guz zarodkowy pierwotnie zlokalizowany w tarczycy — opis przypadku

Joanna Wierzbicka-Chmiel[1], Małgorzata Chrószcz[2], Grzegorz Słomian[2], Dariusz Kajdaniuk[1, 3], Wojciech Zajęcki[4], Halina Borgiel-Marek[5], Bogdan Marek[1, 3]

[1]*Department of Endocrinology and Diabetology, Voivodeship Specialistic Hospital No 3, Rybnik, Poland*
[2]*Department of Oncology, Voivodeship Specialistic Hospital No 3, Rybnik, Poland*
[3]*Division of Pathophysiology, Department of Pathophysiology and Endocrinology, Medical University of Silesia, Zabrze, Poland*
[4]*Department of Pathomorphology, Medical University of Silesia, Zabrze, Poland*
[5]*Department and Clinic of Maxillofacial Surgery, Medical University of Silesia, Katowice, Poland*

Abstract

Germ cells tumours most frequently occur in the gonads. Extragonadal localisation is rare and concerns mainly the mediastinum, retroperitoneum and pineal.

We present the first description of a patient with a mixed germ cells tumour located primarily in the thyroid. A 35-year-old man in a good clinical condition was admitted to diagnose metastasis revealed in an X-ray of his lungs. Abnormal laboratory tests showed high concentrations of beta-HCG and LDH. Ultrasound examination revealed: hypoechogenic area 8 × 4 × 5 mm in the left testicle, and enlarged left thyroid lobe with echogenically heterogenous mass. In cytological examination of the thyroid, carcinomatous cells were found, which suggested metastasis. A diagnosis of cancerous spread of testicular cancer to the lungs and thyroid was made. The left testicle, with spermatic cord, was removed, yet in the histopathological examination no carcinomatous cells were found. Rescue chemotherapy, according to the BEP scheme (bleomycin, etoposide, cisplatin) was started, but during its course the patient died. Histopathology disclosed primary mixed germ cells tumour in the thyroid, predominantly with *carcinoma embryonale* and focuses of *choriocarcinoma*. Extragonadal germ cells tumours rarely occur in the thyroid. In medical literature, some cases of teratomas and a single case of *yolk sac tumour* in the thyroid have been described. The presence of *choriocarcinoma* was responsible for the high serum concentration of beta-HCG. Surgery of germ cells tumours proves insufficient. The conventional chemotherapy is based on cisplatin. In conclusion, extragonadal germ cells tumours are rare, but should be considered while co-existing with elevated markers such as: AFP, beta-HCG and lack of abnormalities in the gonads. **(Endokrynol Pol 2012; 63 (5): 388–390)**

Key words: *mixed germ cells tumour, thyroid*

Streszczenie

Pierwotne nowotwory z komórek zarodkowych zwykle są umiejscowione w gonadach. Rzadka jest pierwotna lokalizacja pozagonadalna i najczęściej dotyczy śródpiersia, przestrzeni zaotrzewnowej czy szyszynki.

Przedstawiono pierwszy opis pacjenta z mieszanym nowotworem zarodkowym o pierwotnej lokalizacji w tarczycy. Mężczyzna w wieku 35 lat, w dobrym stanie ogólnym, przyjęty w celu przeprowadzenia diagnostyki stwierdzonych w rutynowym RTG klatki piersiowej licznych ognisk przerzutowych w płucach. W badaniach biochemicznych spośród odchyleń od normy stwierdzono wysokie stężenia beta-HCG i LDH. W badaniu ultrasonograficznym w lewym jądrze zobrazowano obszar hipoechogeniczny o wymiarach 8 × 4 × 5 mm oraz znacznie powiększony lewy płat tarczycy z niejednorodną echogenicznie zmianą. Badanie cytologiczne zmiany w tarczycy wykazało komórki nowotworowe sugerujące zmianę o charakterze przerzutowym. Postawiono diagnozę rozsiewu raka jądra do płuc i tarczycy. Resekowano lewe jądro wraz z powrózkiem nasiennym, jednak w badaniu histopatologicznym materiału operacyjnego nie stwierdzono utkania nowotworowego. Rozpoczęto ratunkową chemioterapię według schematu BEP (bleomycyna, etopozyd, cisplatyna), w trakcie której nastąpił zgon chorego. Badanie autopsyjne wykazało ognisko pierwotne nowotworu w tarczycy — mieszany guz zarodkowy z przewagą w guzie utkania *carcinoma embryonale*, ogniskowo pola o morfologii *choriocarcinoma*. Pozagonadalne guzy zarodkowe bardzo rzadko lokalizują się w tarczycy. W dostępnym piśmiennictwie opisywano przypadki występowania w gruczole tarczowym potworniaków oraz jeden przypadek *yolk sac tumour*. Obecność utkania *choriocarcinoma* była powodem dużego stężenia beta-HCG w surowicy. Leczenie chirurgiczne nowotworów zarodkowych jako jedyne nie wystarcza. Standardem pozostaje chemioterapia oparta na cisplatynie. Pozagonadalna lokalizacja nowotworów zarodkowych jest rzadkością, jednak zawsze należy rozważać taką możliwość w przypadku współistnienia podwyższonych markerów AFP i beta-HCG oraz braku patologii w gonadach. **(Endokrynol Pol 2012; 63 (5): 388–390)**

Słowa kluczowe: *mieszany guz zarodkowy, tarczyca*

Introduction

Germ cells tumours are generally rare, but among men aged 15–35 they constitute the commonest tumours. Usually, they are located in the gonads (ovary and testis). Extragonadal localisation is uncommon, i.e. 1–5%, and concerns predominantly the mediastinum, retroperitoneum and pineal. Some rare cases of germ

Joanna Wierzbicka-Chmiel Ph.D., Department of Endocrinology and Diabetology, Voivodeship Specialistic Hospital No 3, Energetyków St. 46, 44–200 Rybnik, Poland, tel.: +48 32 429 15 63, fax: +48 32 422 24 58, e-mail: jwierzbickachmiel@wp.pl

cell tumours have been described in the liver, pancreas, lungs, and soft tissues of the head and neck (paranasal sinuses, orbital and nasal cavity) [1, 2].

Case report

A 35-year-old man in good clinical condition was admitted to the Internal Ward due to metastasis revealed during a routine X-ray of his lungs. The patient's history did not disclose any important data, and he had not previously suffered from any chronic diseases. On admission, physical examination did not display any abnormalities. Laboratory tests showed elevated concentrations of beta-human chorionic gonadotropin (beta-HCG) 4323.0 mIU/mL (n. 0–1 mIU/mL), lactate dehydrogenase (LDH) 379.8 IU/L (n. 135–250 IU/L), C-reactive protein (CRP) 11.41 mg/L (n. 0–5), and aspartate transaminase (Aspat) 69.2 IU/L (n. < 37 IU/L). Other values, along with cancerous markers, were within normal limits. Ultrasound examination revealed a hypoechogenic area measuring 8 × 4 × 5 mm in the left testicle and an enlarged left lobe (31 mm × 43 mm × 80 mm) with a pathological, echogenically heterogeneous mass 29 × 36 × 44 mm in the thyroid gland. As a result of the cytological examination of the thyroid's tumour, carcinomatous cells were found, which suggested metastasis. Computed tomography of the thorax and abdomen (100 mL of Iomeron was administered) revealed many metastases 2 cm in diameter in the lung, and isolated lymph nodes along the aorta approximately 12 mm in diameter. Additional examinations such as oesophagogastroduodenoscopy and colonoscopy showed no abnormalities. We suspected cancerous spread of the testicular cancer to the lungs and thyroid. The patient was transferred to the Urological Ward where the left testicle and spermatic cord were removed without any complications. Yet as a result of the histopathological examination of the excised organs, no cancerous cells were detected. The patient was discharged in a good clinical condition with an order to continue his treatment under the supervision of an oncologist.

After nine days, the patient was readmitted to the Internal Ward because of increasing dyspnoea and progressive weakness.

The laboratory findings revealed augmenting concentration of D-dimer 4.9 ug/mL (n. < 0.5 ug/mL) to 18.4 ug/mL and a significant increase of beta-HCG to 33 132 mIU/mL. The angio-CT excluded pulmonary thrombosis and the patient was transferred to the Department of Oncology. Taking into consideration the high concentration of beta-HCG (> 40,000 mIU/mL), clinical state, radiological findings and considerable dynamics of the disease, extragonadal germ cells tumour (ExGCT) was assumed as the primary focus of cancer. Rescue chemotherapy was begun according to the BEP scheme (bleomycin, etoposide, cisplatin) which is the therapy of choice in such tumours. On the third day of the cycle, considerable worsening of the physical condition was observed, cardiovascular and pulmonary insufficiency developed. Despite intensive medical care, the patient died. Since there was no clear diagnosis, an autopsy was performed. Histopathological examination disclosed diffuse metastasis with necrosis in the lungs (Fig. 1), metastatic lymph nodes, and in the thyroid (Fig. 2) — mixed germ cells tumour with substantial areas of carcinoma embryonale and focuses of choriocarcinoma, whereas the testis and brain proved normal.

Discussion

GCTs are rarely situated in the thyroid. Cases of teratomas, predominantly in children, and accidentally in adults, where they are generally found to be malignant, have been reported in medical literature. There has also been a single case of yolk sac tumour detected in a child [3–7]. There is no information in the medical databases about mixed germ cells tumour primarily located in the thyroid. Extragonadal localisation generally concerns men. The most frequently formulated hypothesis of the occurrence of ExGCTs has assumed that they are the result of abnormal germ cells migration during embryogenesis [8–10]. Surgery alone of GCTs proves insufficient as radical treatment, even in the initial phase of the disease. These tumours are sensitive to chemotherapy in which cisplatin is the drug of choice. The most popular scheme includes bleomycin, etoposide and cisplatin. Radiotherapy is effective, supplementary to surgery and the chemotherapy method, in the treatment of seminomas [11, 12].

The prognosis even in advanced GCTs is comparatively promising. It depends on the histological type (seminomas prognosticate better than non-seminomatous GCTs), primary localization (gonadal tumours prognosticate better than extragonadal ones) and the stage of the progress of the disease [11–15]. In the autopsy of the performed case, an extremely rare tumour consisting of more than one histological type and primarily located in the thyroid, was depicted. The presence of *choriocarcinoma* was the reason for the high concentration of beta-HCG in the patient's serum. An initial incorrect diagnosis of metastasis to the thyroid was proposed on the basis of the result of fine-needle biopsy. Metastasis to the thyroid gland is detected in 1.4–3% of the total number of patients operated on because of suspicions of malignancies. The primary focuses are the kidneys (48%), large intestine (10%),

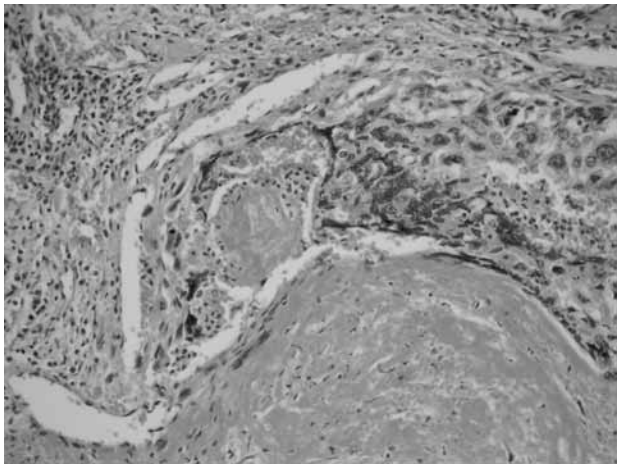

Figure 1. *Histologic specimen of metastatic tumour to the lungs (stained with haematoxylin and eosin). Fragments of carcinoma embryonale and syncytiotrophoblast cells*

Rycina 1. *Wycinek histopatologiczny guza przerzutowego do płuc (barwienie hematoksyliną i eozyną). Fragmenty carcinoma embryonale oraz komórki syncytiotrofoblastu*

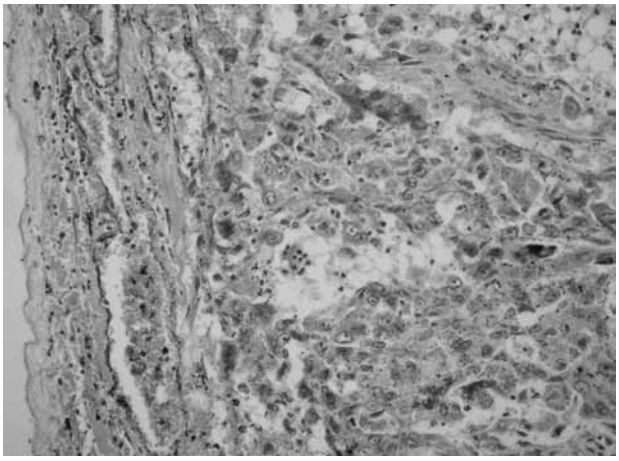

Figure 2. *Fragment of thyroid tumour with carcinoma embryonale and choriocarcinoma components (stained with haematoxylin and eosin)*

Rycina 2. *Fragment guza w tarczycy zawierający elementy carcinoma embryonale i choriocarcinoma (barwione hematoksyliną i eozyną)*

lungs (8%), breast cancer (8%), *sarcoma* (4%) and hardly ever gonads. More frequently, these kinds of metastasis are reported in women than in men [16], as has been described by Polish authors. They presented female patients with advanced breast cancer and thyroid metastasis [17].

The case of a man with the thyroid as the target of seminoma's metastasis has been reported. Metastasis in the thyroid occurred six years after the first diagnosis and associated treatment of *seminoma* [18]. Metastasis from unknown sites sustains 5–10% of non-cutaneous neoplasms and the prognosis is pessimistic. One exception to this rule is GTC.

Conclusions

Extragonadal localisation of germ cells tumours is quite rare, but should be always considered in a case of elevated concentration of beta-HCG, AFP and a lack of pathology in the gonads. The primary focus should be then intensively investigated.

Having suffered therapeutic defeat, every doctor should ask her/himself what could have been done better. In our case, undoubtedly, suspicious findings in the testicle during ultrasound examination and ambiguous cytological results misled the initial diagnostic management, thus delaying accurate diagnosis. At the same time, co-existing with rapid progression of the disease, chemotherapy was initiated when a diagnosis of spread cancerous disease with unknown primary focus was formulated.

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