Case Report

OCT4 Expression on a Case of Poorly Differentiated (Insular) Carcinoma of the Thyroid Gland and Minireview

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Poorly differentiated (insular) carcinoma of the thyroid gland is rare and defined as follicular-cell neoplasms that show limited evidence of structural follicular cell differentiation and occupy both morphologically and behaviourally an intermediate position between differentiated (follicular and papillary carcinomas) and undifferentiated (anaplastic) carcinomas. The authors report a case of a 37-year-old Thai woman who presented with a prolonged left thyroid nodule. Final pathological diagnoses of her mass were poorly differentiated (insular) carcinoma with lymphovascular invasion and nodular goiter. The tumor cell arrangements were nest (insular) and trabecular patterns with some follicular formations. Immunohistochemistry of the tumor cells revealed negative immunostaining for OCT4. Expression of OCT4 gene is involved in the regulation and maintenance of pluripotency of embryonic stem cells, germ cells, and in tumor cells. The authors believe that poorly differentiated (insular) carcinoma of the thyroid gland probably develops from the remnant of thyroid stem cells and is not associated with dedifferentiation (anaplasia or loss of cellular differentiation) from nodular goiter or cells of other thyroid carcinomas. Although there was negative immunostain for OCT4 in the presented case, the authors assumed that the tumor cells behave with an intermediate position between thyroid stem cells and prothyrocytes Also they do not behave with thyroblasts. Additionally, the tumor may be associated with new cellular dedifferentiation. However, there is only one case of immunohistochemistry of OCT4 in poorly differentiated (insular) carcinoma of the thyroid gland. Thus, prognosis of the presented still is mainly correlated with clinical and histological findings. Further research on expression of OCT4 gene on thyroid cancers and other malignant tumors relating to tumorigenic cancer cells (cancer stem cells) may be useful to prognostic evaluation and administration of a new chemotherapy and/or radiotherapy that is specific for tumor-initiating cells.

Keywords: *OCT4, Thyroid stem cells, Poorly differentiated carcinoma, Insular carcinoma, Thyroid gland*

J Med Assoc Thai 2005; 88(Suppl 3): S281-9
Full text. e-Journal: *http://www.medassocthai.org/journal*

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The incidence of thyroid cancer in Thailand is highest in females in the Northeast. According to the representative population-based cancer

registry in Khon Kaen for the Northeast, follicular carcinoma is more frequent than papillary carcinoma, which may be related to a low iodine intake in the Northeast where, 10-50% of children were found to have thyroid goiters. However, papillary carcinoma is the most common type of thyroid cancer in other parts of Thailand[1]. Poorly differentiated (insular) carcinoma of the thyroid gland is rare[2] and remains a controversial entity. It is therefore difficult to evaluate whether the different prevalence rates among different geographic regions reflect true etiological differences or mere variations in diagnostic criteria[3].

In the present article, the authors report a case of poorly differentiated (insular) carcinoma of the thyroid gland with histopathological, aspiration cytological, and immunohistochemical findings with our review of the literatures. In addition to the traditional immunohistochemistry, the authors also first demonstrate immunohistochemical staining for detecting OCT4 expression on this tumor relating to tumorigenic cancer cells. OCT4 expression should be useful to prognostic evaluation and administration of a new chemotherapy and/or radiotherapy that is specific for tumor-initiating cells.

Case Report

A 37-year-old Thai woman presented with a painless palpable mass in the anterior midline of the neck for 7 years prior to admission to the hospital. She received anhydrous thyroxine Na (Eltroxin®) for 3 years. Her neck mass had rapidly increased in size since 4 months ago. There was no history of radiation exposure. Physical examination revealed a non-tender palpable nodule in the left lobe of the thyroid gland. An ultrasonography showed a solid mass in the left lobe of the thyroid gland, measuring 3.6x3.4 cm in size. Fine-needle aspiration cytology elicited high cellularity consisting of numerous isolated and syncytial sheets of follicular cells containing enlarged and overlapping nuclei, rare nucleoli, and abundant cytoplasm. Few flare cells (follicular cells with pink material in their apical cytoplasm), thin colloid material and fibrous stroma were noted. The left thyroid nodule was diagnosed as a benign thyroid nodule that was suggestive of adenomatous goiter with focal hyperplastic change. Left lobectomy of the thyroid gland was done.

Grossly, the left lobe of the thyroid gland measured 7x3x3 cm and weighed 32 gm. The external surface was smooth. Serial sectioning revealed two firm masses, measuring 3.5x2.7x2.3 cm and 2.2x2x1.5 cm. The first one was an ill-defined white mass and close to the thyroid surface for less than 0.1 cm. The second one was a well-circumscribed grayish tan mass. They had no cystic lesions and calcification. Microscopic appearance of the first mass (Fig. 1, A-D) showed well-defined solid round or oval nest and trabecular patterns that were composed of uniform small cells with round to oval nuclei containing fine chromatin, inconspicuous nucleoli, and scant cytoplasm. Two patterns were separated from each other by thin fibrovascular tissue. There were some follicular formations that contained homogeneous pink material. Mitoses were rare. No areas of necrosis, calcification, and papillary arrangement were present. The tumor invaded lymphovascular vessels and situated less than 0.1 cm from the perithyroidal tissue.

Microscopic appearance of the second mass (Fig. 2) showed follicles morphologically similar to those in the surrounding thyroid tissue that contained colloid. The follicular epithelial-lining cells were uniform cuboidal to low columnar, and had non-atypical basophilic nuclei, inconspicuous nucleoli, and eosinophilic cytoplasm. There was no fibrous encapsulation and calcification.

Congo-red staining for amyloid was negative. Immunohistochemistry of the tumor cells (Fig. 3, A-F) revealed immunoreactivity for carcinoembryonic antigen (CEA), thyroid

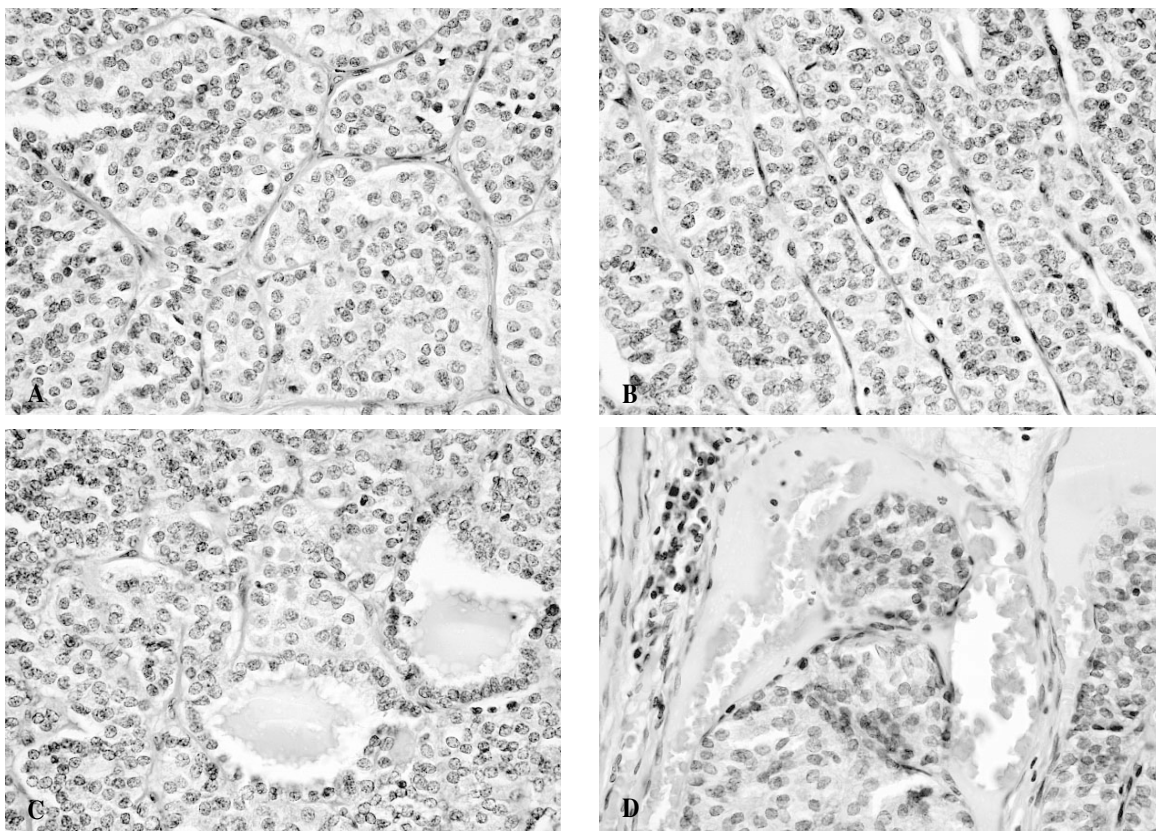


Fig. 1 Poorly differentiated (insular) carcinoma of the thyroid gland. A, Tumor cell nests (Insular pattern); B, Trabecular pattern; C, Follicular formation; and D, Lymphovascular invasion (H&E, x400)

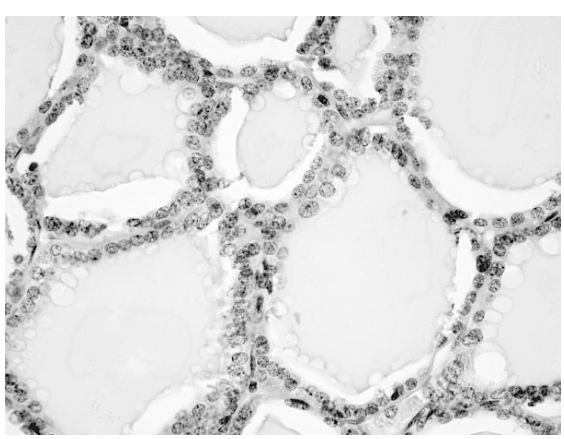


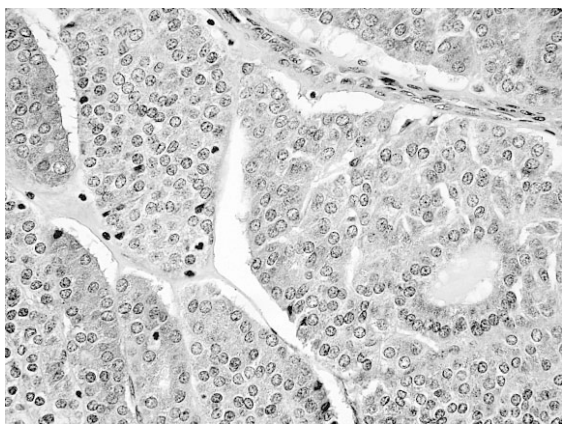
Fig. 2 Nodular goiter of the second thyroid mass. The follicles are various sizes and lined by flat to cuboidal epithelium (H&E, x400)

transcription factor-1 (TTF-1), thyroglobulin, calcitonin, p53, and Bcl-2. There were negative immunostaining for epithelial marker (AE1/AE3), neuron specific enolase (NSE), chromogranin A, synaptophysin, and OCT4.

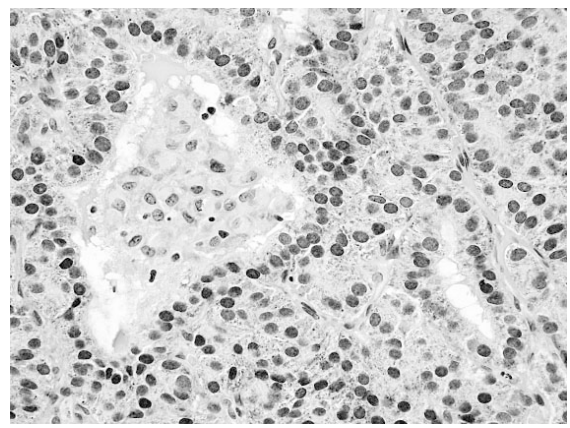
Final pathological diagnoses were poorly differentiated (insular) carcinoma and nodular goiter for the first and second thyroid nodule, respectively.

Discussion

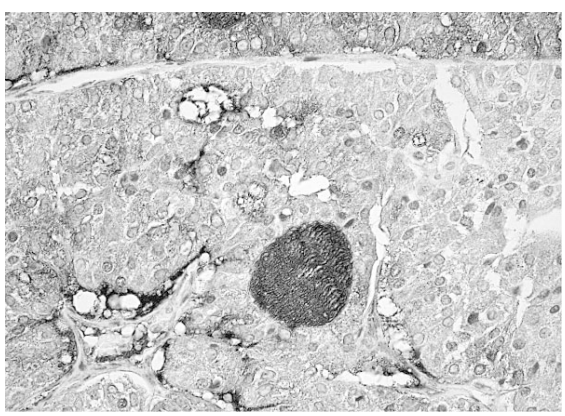
In the traditional scheme of thyroid neoplasia, malignant tumors of follicular cells are divided into a well-differentiated type, composed of papillary and follicular carcinoma, and an undifferentiated or anaplastic type[4]. Poorly differentiated (insular) carcinoma of the thyroid gland is defined as follicular-cell neoplasms that show limited evidence of structural follicular cell differentiation and occupy both morphologically and behaviourally an intermediate position between differentiated (follicular and papillary carcinomas) and undifferentiated (anaplastic) carcinomas[3].



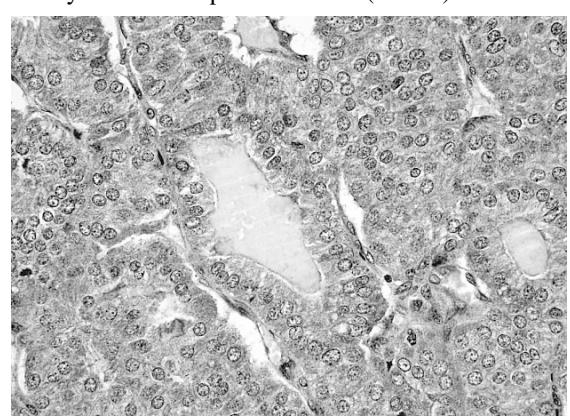
A Carcinoembryonic antigen (CEA)



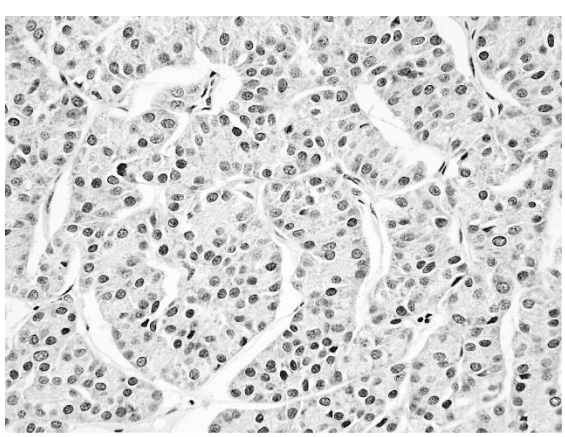
B Thyroid transcription factor-1 (TTF-1)



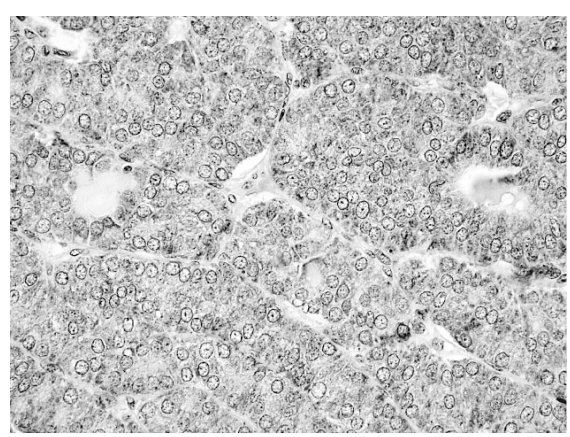
C Thyroglobulin



D Calcitonin



E p53



E Bcl-2

Fig. 3 Immunohistochemistry of poorly differentiated (insular) carcinoma of the thyroid gland. A, Positive immunostain for carcinoembryonic antigen (CEA) is evidenced by mild diffuse reaction within cytoplasm of tumor cells.; B, Positive immunostain for thyroid transcription factor-1 (TTF-1) is evidenced by moderate focal reaction within nucleus of tumor cells.; C, Positive immunostain for thyroglobulin is evidenced by moderate focal reaction within cytoplasm of tumor cells. It is also stained on colloidal material in the follicular arrangement of the tumor cells.; D, Positive immunostain for calcitonin is evidenced by moderate diffuse reaction within cytoplasm of tumor cells. There is no immunoreactivity on colloidal material in the follicular arrangement of the tumor cells.; E, Positive immunostain for p53 is evidenced by mild diffuse reaction within nucleus of tumor cells; and F, Positive immunostain for Bcl-2 is evidenced by mild diffuse reaction within cytoplasm of tumor cells (Paraffin sections, x400)

Most patients with poorly differentiated (insular) carcinoma of the thyroid gland present with a solitary, large thyroid mass, cold by scintigraphy[3], with or without concurrent enlarged regional lymph nodes[3,5]. The tumor has a predominance in women, presentation in the sixth decade of life[4,6,7], and association with the antecedent of long-standing uninodular or multinodular goiter (>10 years)[3, 6, 7]. It is possible that this tumor might represent a dedifferentiation (anaplasia or loss of differentiation of cells) of benign thyroid neoplasm[7]. Conversely, the tumor may occasionally present as rapidly growing masses[3]. The tumor has a high local recurrence[7]. Distant metastases are seen in 32% of patients with poorly differentiated (insular) carcinoma of the thyroid gland. In addition to nodal metastases, lung and bone metastases are also relatively frequent at the time of diagnosis[3,5,6].

The most distinctive microscopic feature of the tumor is the presence of well-defined solid nests [insulae (L. 'island')] of round or oval shape, composed of a monotonous population of small cells with round to oval nuclei and scant cytoplasm. The predominant pattern of growth is solid, but microfollicles are also commonly encountered, some of which contain dense colloid. Mitoses are always present but in variable number[4,5]. The pattern of growth is characteristically infiltrative, and blood vessel invasion is common[5]. Foci of necrosis are frequent[4,5]. Focal papillary area can be encountered in this tumor[2].

Poorly differentiated (insular) carcinoma of the thyroid gland has no amyloid deposits[2]. The tumor cells show immunoreactivity for keratin[5], thyroid transcription factor-1 (TTF-1)[3,4], and thyroglobulin[2-5]. They have negative immunostaining for calcitonin[4,5]. However, Ljungberg O et al described that intermediate type of differentiated thyroid carcinoma has immunohistochemical evidence for the production of thyroglobulin, somatostatin, and calcitonin. They suggested that differentiated thyroid carcinoma can be regarded as a continuous spectrum of tumor types, with pure follicular carcinomas and classic medullary carcinoma representing the two extremes and the tumors with biphasic features representing a broad intermediate group[8]. No p53 immunoreactivity is in poorly differentiated (insular) carcinoma of the thyroid gland[6,9]. Overexpression of the p53 tumor suppressor gene might have a role in dedifferentiation from poorly differentiated (insular) carcinoma to anaplastic carcinoma[6]. Bcl-2 expression probably plays a role in loss of differentiation of cells of thyroid carcinomas[9].

In the presented case, all clinical history, aspiration cytologic, histologic, and immunohistochemical findings were compatible with those of poorly differentiated (insular) carcinoma of the thyroid gland. For fine-needle aspiration cytology diagnosis, her thyroid nodule was suggestive of adenomatous goiter with focal hyperplastic change. The authors supposed that the aspirated cells were derived from follicular pattern of the tumor or the mass with nodular goiter. All thyroid carcinomas are usually positive for thyroid transcription factor-1 (TTF-1). The presented thyroid tumor had a combination of immunoreactivity for follicular carcinoma including thyroglobulin and Bcl-2, and medullary carcinoma including carcinoembryonic antigen (CEA), calcitonin, and Bcl-2. Thus, it has both morphologically and behaviourally an intermediate position between follicular and medullary carcinomas.

The prognosis of patients with poorly differentiated (insular) carcinoma of the thyroid gland depends primarily on the TNM staging, completeness of surgery and responsiveness to radioactive iodine therapy[3]. Santoro M et al reported that poor survival in poorly differentiated (insular) carcinoma of the thyroid gland is associated with old age, male sex, invasion of extrathyroidal

soft tissues, coexistence in the same tumor of oncocytic features with insular growth pattern, and distant metastases but not RET oncogene activation[10]. The presented patient possibly has poor prognosis because her thyroid carcinoma had lymphovascular invasion.

Takano proposed a new model of thyroid carcinogenesis, which he termed the "fetal cell carcinogenesis" model. In this model, thyroid carcinomas are derived from the remnants of fetal thyroid cells which, unlike normal thyroid follicular cells (thyrocytes), have the ability to migrate to surrounding tissues. During the normal course of development, these characteristics of fetal thyroid cells are shown only in limited situations, whereas once fetal cells are transformed into cancer cells, they are no longer kept under control[11].

The development of normal thyroid gland results from the differentiation of fetal thyroid cells including thyroid stem cells, thyroblasts, prothyrocytes, and thyrocytes in order. Thyroblasts do not form thyroid follicles. Prothyrocytes are more differentiated than thyroblasts and have the ability to form thyroid follicles. Thus, thyroid stem cells, thyroblasts, and some prothyrocytes posses cancerous characteristics, and as they proliferate, they act as cancers. Any event that prevents fetal thyroid cells from differentiation can be a cause of cancer. Fetal thyroid cells lose their cancerous characteristics as they differentiate into thyrocytes. Follicular tumors, papillary carcinomas, and anaplastic carcinomas of the thyroid gland are derived from the remnants of prothyrocytes, thyroblasts, and thyroid stem cells, respectively. Fetal cell carcinogenesis regards carcinogenesis as an abnormal development of fetal thyroid cells, but not dedifferentiation of normal or benign thyroid follicular cells[11]. For this theory, the authors assume that poorly differentiated (insular) carcinoma of the thyroid gland probably develops from the remnant of thyroid stem cells and the tumor is not dedifferentiated (anaplasia or loss of cellular differentiation) from nodular goiter or from follicular carcinoma and medullary carcinoma.

Tumors with a remnant of thyroid stem cells are likely to take an unfavorable clinical course, since even if a tumor is dissected surgically, it will grow back because of the cells' unlimited ability of proliferation. In contrast, the tumors that do not contain thyroid stem cells are likely to shrink after surgical dissection since they have limited proliferative potential[11]. When a tumor shrinks in size as a result of chemotherapy, it is believed that the patient is responding to treatment. However, tumors often initially shrink in response to treatment only to recur later on, suggesting that tumor shrinkage and patient response may not exactly be synonymous. It may be associated with cancer stem cells[12].

The identification of tumorigenic and nontumorigenic cancer cells also has important therapeutic implications[11,13]. Only a minority of cancer cells "cancer stem cells" within a tumor had the ability to form new tumors (tumorigenic) and thus responsible for driving tumor growth and metastasis. The majority of cancer cells within the tumor mass are non-tumorigenic[12,13], which are more susceptible to standard cancer treatments than the cancer stem cells[12]. But if a therapy effectively kills the thyroid stem cells, the tumors are rendered incapable of maintaining themselves or growing[11].

In the present article, the authors first established immunohistochemical expression of OCT4 gene in the paraffin-embedded thyroid tissue of the poorly differentiated (insular) carcinoma. There is, in addition, a demonstration of this gene expression relating to tumorigenic cancer cells should be useful to prognostic evaluation and administration of a new chemotherapy and/or radiotherapy that is specific for tumor-initiating cells. OCT4 is a nuclear transcription factor involved

in gene regulation; thus, only nuclear staining is considered a positive result[14]. From the above-mentioned fetal cell carcinogenesis model, poorly differentiated (insular) carcinoma of the thyroid gland probably develops from the remnant of thyroid stem cells and is not associated with dedifferentiation from nodular goiter or cells of other thyroid carcinomas. the authors believe that tumor cells behave with an intermediate position between thyroid stem cells relating to the development of undifferentiated (anaplastic) carcinoma and prothyrocytes relating to the development of follicular carcinoma. Also they do not behave with thyroblasts relating to the development of papillary carcinoma[3,11]. This is the possible reason for negative immunostain for OCT4 in the presented case. The tumor may be associated with new cellular dedifferentiation (anaplasia or loss of cellular differentiation) because it was positive immunostaining for Bcl-2 and p53 and negative immunostaining for epithelial marker (AE1/AE3). However, there is only one case of immunohistochemistry of OCT4 in poorly differentiated (insular) carcinoma of the thyroid gland. Thus, prognosis of the presented case still is mainly correlated with clinical and histological findings. The authors have to do further research in the use of OCT4 expression for histopathological prognostic marker for thyroid carcinomas and other malignant epithelial tumors.

The patients with poorly differentiated (insular) carcinoma of the thyroid gland have 61% of survival rates at 36 months[7] and 42% of the 10-year survival rates[6]. The majority of patients die in the first three years after diagnosis. Death is usually caused by regional and distant metastases rather than by local invasion[3].

Conclusion

Poorly differentiated (insular) carcinoma of the thyroid gland is a rare malignant tumor. It is defined as follicular-cell neoplasms that show limited evidence of structural follicular cell differentiation and occupy both morphologically and behaviourally an intermediate position between differentiated (follicular and papillary carcinomas) and undifferentiated (anaplastic) carcinomas. At present, prognosis of the presented tumor is mainly associated with clinical and histological findings. The tumor probably developed from the remnant of thyroid stem cells and the tumor is not dedifferentiated from nodular goiter or cells of other thyroid carcinomas. Thus, the further research on expression of OCT4 gene on thyroid cancers and other malignant tumors relating to tumorigenic cancer cells (cancer stem cells) should be useful to prognostic evaluation and administration of a new chemotherapy or radiotherapy that is specific for tumor-initiating cells.

Acknowledgements

The authors wish to thank Colonel Udomsri Pojjaroenanant and her colleagues of the Immunohistochemistry Unit, Army Institute of Pathology, Bangkok, Thailand, for their kind cooperation in all immunostaining.

References

1. Vatanasapt V, Sriamporn S, Vatanasapt P. Cancer control in Thailand. Jpn J Clin Oncol 2002; 32 (Suppl 1): S82-S91.
2. Paik SS, Kim WS, Hong EK, Park MH, Lee JD. Poorly differentiated ("insular") carcinoma of the thyroid gland-two cases report. J Korean Med Sci 1997; 12: 70-4.
3. Sobrinho-Simões M, Albores-Saavedra J, Tallini G, Santoro M, Volante M, Pilotti S, et al. Poorly differentiated carcinoma. In: DeLellis RA, Lloyd RV, Heitz PU, Eng C, eds. Pathology and Genetics of Tumours of Endocrine Organs (World Health Organization Classification of Tumours). France: IARC Press, 2004: 73-6.

4. Rosai J. Poorly differentiated carcinoma. In: Rosai J, ed. Ackerman's Surgical Pathology. Vol 1. 9th ed. USA: Mosby, 2004: 549-52.
5. Rosai J, Carcangiu ML, Delellis RA. Poorly differentiated carcinoma. In: Atlas of Tumor Pathology: Tumors of The Thyroid Gland. 3rd series. Fascicle 5. USA: Armed Forces Institute of Pathology (AFIP), 1992: 123-33.
6. Lam KY, Lo CY, Chan KW, Wan KY. Insular and anaplastic carcinoma of the thyroid: a 45-year comparative study at a single institution and a review of the significance of p53 and p21. Ann Surg 2000; 231: 329-38.
7. Luna-Ortiz K, Hurtado-Lopez LM, Dominguez-Melagon H, Ramirez-Marin R, Zaldivar-Ramirez FR, Herrera-Gomez A, et al. Clinical course of insular thyroid carcinoma. Med Sci Monit 2004; 10: 108-11.
8. Ljungberg O, Bondeson L, Bondeson AG. Differentiated thyroid carcinoma, intermediate type: a new tumor entity with features of follicular and parafollicular cell carcinoma. Hum Pathol 1984; 15: 218-28.
9. Pestereli HE, Ogus M, Oren N, Karpuzoglu G, Kerpuzoglu T. Bcl-2 and p53 expression in insular and in well-differentiated thyroid carcinomas with an insular pattern. Endocr Pathol 2001; 12: 301-5.
10. Santoro M, Papotti M, Chiappetta G, Garcia-Rostan G, Volante M, Johnson C, et al. RET activation and clinicopathologic features in poorly differentiated thyroid tumors. J Clin Endocrinol Metab 2002; 87: 370-9.
11. Takano T. Fetal cell carcinogenesis of the thyroid: a hypothesis for better understanding of gene expression profile and genomic alternation in thyroid carcinoma. Endocr J 2004; 51: 509-15.
12. Webb T. Work on breast cancer stem cells raises questions about treatment strategies. J Natl Cancer Inst 2003; 95: 774-5.
13. Al-Hajj M, Wicha MS, Benito-Hernandez A, Morrison SJ, Clarke MF. Prospective identification of tumorigenic breast cancer cells. Proc Natl Acad Sci 2003; 100: 3983-8.
14. Jones TD, Ulbright TM, Eble JN, Baldridge LA, Cheng L. OCT4 staining in testicular tumors: a sensitive and specific marker for seminoma and embryonal carcinoma. Am J Surg Pathol 2004; 28: 935-40.

การแสดงออกของจีน OCT4 ในมะเร็งของต่อมไทรอยด์ชนิด poorly differentiated (insular) carcinoma จากผู้ป่วย 1 ราย

เจตนา เรืองประทีป, ชนิดา โลหชิตรานนท์, ธารา พูนประชา, ไพบูลย์ ปุญญฤทธิ์

มะเร็งของต่อมไทรอยด์ชนิด poorly differentiated (insular) carcinoma พบน้อยมากและเป็นเนื้องอกของ follicular cell ของต่อมไทรอยด์ที่ไม่ค่อยพบลักษณะของ follicular cell differentiation อีกทั้งยังมีรูปร่างและพฤติกรรมของเซลล์มะเร็งที่อยู่ระหว่างมะเร็งของต่อมไทรอยด์ชนิด differentiated (follicular และ papillary) carcinomas กับชนิด undifferentiated (anaplastic) carcinoma บทความนี้รายงานกรณีผู้ป่วยหญิงไทย 1 ราย อายุ 37 ปีที่มีก้อนที่ต่อมไทรอยด์ด้านซ้ายเป็นเวลานาน ซึ่งผลการวินิจฉัยทางพยาธิวิทยาของก้อนนี้คือ poorly differentiated (insular) carcinoma with lymphovascular invasion ร่วมกับ nodular goiter โดยการเรียงตัวของเซลล์ของเนื้องอกนี้เป็นแบบ nest (insula) และ trabecula ร่วมกับการสร้าง follicles ในบางส่วน เมื่อนำเนื้องอกนี้มาศึกษาโดยวิธี immunohistochemistry พบว่ามีการให้ผลลบต่อ OCT4 ซึ่งการแสดงออกของจีน OCT4 มีความเกี่ยวข้องกับการควบคุมการเปลี่ยนสถานภาพของ embryonic stem cells, germ cells และเซลล์ของเนื้องอก ดังนั้นบทความนี้จึงเสนอแนวความคิดว่ามะเร็งของต่อมไทรอยด์ชนิด poorly differentiated (insular) carcinoma มีความเป็นไปได้ที่พัฒนามาจากเซลล์ต้นกำเนิดของต่อมไทรอยด์ (thyroid stem cells) ที่ยังคงอยู่ในต่อมไทรอยด์นั้นและไม่มีความเกี่ยวข้องกับการเกิด dedifferentiation (anaplasia หรือการสูญเสีย differentiation ของเซลล์) จาก nodular goiter หรือเซลล์มะเร็งในมะเร็งของต่อมไทรอยด์ชนิดอื่น สำหรับสาเหตุของการเกิดผลลบในการศึกษาโดยวิธี immunohistochemistry ดังกล่าวข้างต้นนั้นอาจเกิดจาก 2 กรณีดังต่อไปนี้คือ กรณีแรกอาจจะเกิดจากการที่เซลล์ของเนื้องอกในผู้ป่วยรายนี้มีการแสดงพฤติกรรมที่อยู่ระหว่างเซลล์ต้นกำเนิดของต่อมไทรอยด์กับ prothyrocytes และเซลล์ของเนื้องอกในผู้ป่วยรายนี้ก็ไม่ได้มีการแสดงพฤติกรรมของ thyroblasts ส่วนกรณีที่ 2 นั้นอาจจะเกิดจากการที่เซลล์ของเนื้องอกในผู้ป่วยรายนี้มี dedifferentiation เกิดขึ้นใหม่อีกครั้งหนึ่ง อย่างไรก็ตามกรณีผู้ป่วยที่ปรากฏในบทความนี้เป็นเพียงรายเดียวเท่านั้น ดังนั้นการพยากรณ์โรคของผู้ป่วยรายนี้จึงขึ้นอยู่กับลักษณะทางคลินิกและทางพยาธิวิทยาเป็นหลัก การศึกษาและวิจัยเรื่องของการแสดงออกของจีน OCT4 ในเซลล์ต้นกำเนิดของมะเร็ง (tumorigenic cancer cells หรือ cancer stem cells) ในมะเร็งของต่อมไทรอยด์และมะเร็งชนิดอื่นนั้นน่าจะมีประโยชน์สำหรับการพยากรณ์โรคและการพิจารณาการให้ยาเคมีบำบัดและ/หรือรังสีรักษาที่มีความจำเพาะต่อเซลล์ต้นกำเนิดของมะเร็งชนิดนั้น ๆ ต่อไปในอนาคต