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A Struma Ovarii with Increased Serum Basement Membrane Components: A Case Report

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Abstract. We report a case of struma ovarii with hyperthyroidism and elevated serum concentrations of type IV collagen and laminin. Circulating levels of type IV collagen and laminin were measured using specific radioimmunoassays (RIAs) for 7S collagen and the P-1 fragment of laminin, and the basement membrane components in the tumor were investigated by immunohistochemical analysis. Strong immunohistochemical staining specific for type IV collagen and for laminin was observed to be localized in the follicular walls. The serum levels of these antigens, as determined by RIA, were very high before removal of the tumor but decreased rapidly postoperatively. The present findings suggest that struma ovarii produces large amounts of type IV collagen and laminin. In addition, elevated levels of thyroid hormones might enhance the turnover of the basement membrane in various tissues.

Key words: Struma ovarii, Type IV collagen, Laminin, Radioimmunoassay, Immunohistochemistry

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STRUMA ovarii is a monodermal teratoma composed totally or overwhelmingly of thyroid tissue [1], and accounts for 1% to 3% of benign teratoma of the ovary. Components of the basement membrane, such as type IV collagen and laminin, are localized in the follicular walls of the normal thyroid gland [2, 3]. Type IV collagen and laminin has been shown to promote cell growth, adhesion, differentiation, and signaling [4–8]. To our knowledge, there have been no reports on serum levels of basement membrane components, such as type IV collagen and laminin, in patients with struma ovarii. In the present study, we measured the circulating levels of type IV collagen and laminin using specific radioimmunoassays for 7S collagen and the P-1 fragment of laminin, and we also investigated the basement membrane components in the tumor by immunohistochemical analysis.

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Case Report

In 1995, a 83-year-old postmenopausal woman visited the Department of Obstetrics and Gynecology at Wakayama Medical College, complaining of discomfort in the lower abdomen. Electrocardiogram showed atrial fibrillation, and serum levels of CA125, an ovarian tumor marker, was 210 U/ml. Serum thyroid-stimulating hormone (TSH) and thyroid hormones, such as free T_3 and free T_4, were measured by radioimmunoassay (Table 1). Ultrasonography revealed a cystic mass 30 cm in diameter with inhomogeneous echogenic solid lesion in the pelvic region. Computed tomography (CT) confirmed the presence of an inhomogeneous cystic tumor with a solid lesion in the pelvis (Fig. 1). No metastases were detected by various examinations. Surgical exploration revealed an encapsulated ovarian tumor, which was removed after careful dissection from the surrounding tissue. The tumor was confined to the ovary. It had a smooth surface covered by a capsule and was nearly spherical, measuring $35 \times 27 \times 22$ cm and weighing 3500 g. The cut surfaces of solid lesion in the solid tumor revealed yellow multiple cysts with

Table 1. Serum levels of basement membrane components, TSH and thyroid hormones in our patient before and after surgical removal of the struma ovarii.

Days after operation	−5 days	1 day	7 days
TSH (0.25–5.0 μU/ml)	<0.25		0.9
Free T_3 (2.73–4.33 pg/ml)	7.91		2.44
Free T_4 (1.28–2.14 ng/dl)	9.30		1.60
7S collagen (ng/ml)	32.2	18.9	4.0
laminin P-1 (U/ml)	7.0	3.8	1.2

Normal ranges are shown in parentheses.

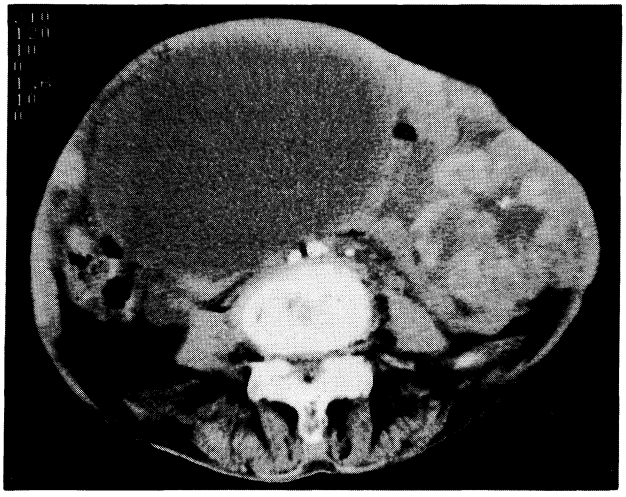

Fig. 1. Axial CT revealed a giant inhomogenous mass in the pelvic space.

areas of hemorrhage and necrosis. The pathologic diagnosis was struma ovarii (Fig. 2a). Atrial fibrillation was improved on day 4 after operation and patient was discharged from hospital 18 days postoperatively in excellent condition.

A specific mouse monoclonal antibody [9] for human type IV collagen was generated in our laboratory and a specific polyclonal antibody raised in rabbits against human laminin was purchased from Fuji Chemical Co. (Toyama, Japan). We investigated the localization of type IV collagen and laminin in the tumor tissues using the indirect immunofluorescence method. We also incubated sections with normal rabbit serum as a control.

Specific immunofluorescence for type IV collagen and for laminin was strong in the tumor. Type IV collagen (Fig. 2c) and laminin (Fig. 2d) appeared to be localized in the thyroid follicular wall in the tumor. Staining for type IV collagen was similar to that for laminin. Control specimens treated with normal rabbit serum showed no fluorescence (Fig. 2b).

Serum levels of type IV collagen and laminin were measured with RIA kits for 7S collagen (Hoechst AG, Frankfurt, Germany) and for the P-1 fragment of laminin (Nippon ODC Co., Tokyo, Japan), respectively. The control subjects were 32 female volunteers aged from 8 to 63 years without liver dysfunction or any other diseases. Serum was obtained from the patient 1 day before, 1 day after, and 7 days after the operation. All serum samples were tested in duplicate, as previously described [10–14]. The serum concentrations of 7S collagen and the P-1 fragment of laminin in the control subjects were 3.5 ± 0.7 ng/ml and 1.12 ± 0.18 U/ml (mean ± SEM), respectively. Serum levels of basement membrane components, TSH and thyroid hormones in our struma ovarii patient are shown in Table 1. The concentrations of 7S collagen and laminin were 32.2 ng/ml and 7.0 U/ml, respectively before the operation, and these levels were markedly elevated compared with those in the control group. After extirpation of the tumor, the concentrations of 7S collagen and laminin decreased rapidly and were within the normal range by day 7.

Discussion

In the present patient, circulating levels of type IV collagen and laminin were markedly elevated and declined rapidly after surgical removal of the tumor. In addition, strong immunostaining for both type IV collagen and laminin was observed in the tumor, and these basement membrane components were localized in the follicle walls. The tumor also showed massive necrotic change and degeneration. These findings suggest that the increased serum levels of type IV collagen and laminin might have been due to either increased synthesis or degradation of these components in the struma ovarii. In addition, it is possible that increased synthesis and degradation of basement membrane components occurred simultaneously in the patient.

Serum levels of type IV collagen and laminin are also reported to be high in patients with various malignant tumors [10–12]. Brocks *et al.* [10]

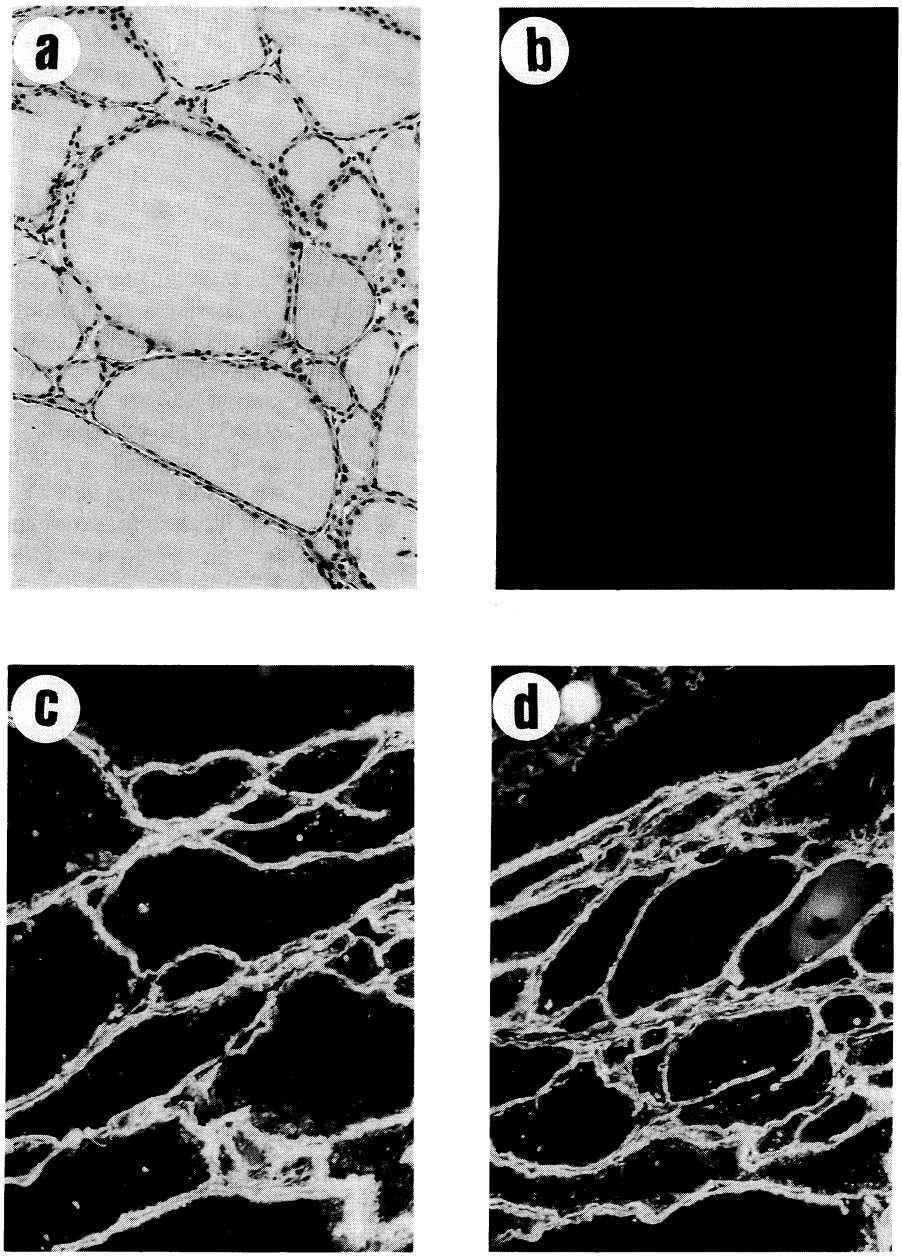

Fig. 2. Photomicrographs of the struma ovarii employing hematoxylin and eosin-staining and indirect immunofluorescence with antibodies against human type IV collagen and human laminin (× 125). a, Hematoxylin and eosin staining; b, Control; c, Immunostaining for type IV collagen; d, Immunostaining for laminin.

reported that serum laminin levels were increased in about 50% of cancer patients. This increase may be explained by destruction of the basement membrane due to tumor invasion and increased synthesis of fibrous components that surround the tumor. In our patient with hyperthyroidism, it is suggested that elevated thyroid hormone levels might enhance the turnover of basement membrane in many organs and tissues [13, 14]. In addition, it is also suggested that elevated serum laminin level in hyperthyroidism might be the result of interaction of cytokine activated lymphocytes with extracellular matrix and subsequent release of basement membrane proteins in the bloodstream, or enhanced synthesis during

generation of new blood vessels [14].

In patients with struma ovarii, serial measurement of the serum levels of basement membrane components, such as type IV collagen and laminin, in combination with other tumor markers, TSH and thyroid hormone, might be helpful for detecting the lesion, evaluating prognosis, and monitoring treatment.

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