

## BENIGN SUPRACLAVICULAR TUMOROUS LYMPHANGIECTASIA — A NEW DISEASE?

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### ABSTRACT

*We describe an isolated recurrent non-inflammatory tumorous swelling of the supraclavicular fossa in four premenopausal women. Ultrasonography, magnetic resonance imaging and computer tomography of the neck each suggested an inhomogeneous mass consistent with "lymphangioma." In each patient the clinical course and histopathologic findings suggested that the swellings were due to chronic localized lymph stasis with subsequent lymphangiectasia, possibly initiated by intermittent obstruction of the juncture of the thoracic or right lymph duct with the internal jugular vein. Enlargement may have been hormonally triggered by estrogens as each woman was taking oral contraceptive pills at the onset of the disease. To characterize this unique entity, we have termed the disorder benign supraclavicular tumorous lymphangiectasia.*

Four premenopausal women (ages 22-48 years) were seen in one year because of chronic recurrent swelling of the supraclavicular space. Lymphoma, lipoma, bronchogenic cyst or lymphangioma were initially suspected because of the clinical appearance of the mass and its localization in the supraclavicular fossa. However, histopathology of the surgically removed mass revealed only lymphangiectasia. Several cases

of primary lymphangiectasia of the intestine (1,2), the pelvis (3) and the thorax (4-6) have been described but not thus far in the neck. Although the disorder may have been initiated by a failure of communication between the jugular lymph sac and the venous system, its enlargement may have been stimulated by exogenous estrogen.

### CLINICAL EXPERIENCE

#### Case Reports

##### Case 1

A 36-year-old woman (165 cm, 52 kg) complained of recurrent swelling of the left supraclavicular fossa for 2 to 3 months. The swelling was not painful but was cosmetically disturbing and caused a feeling of constant pressure. The patient was in good general health; there was no history of cervical inflammation or trauma. Her only medication was clomiphene citrate for infertility; previously she had taken oral contraceptives. Palpation of the neck revealed a hard, non-tender mass in the left supraclavicular fossa. Chest x-ray, abdominal sonography and gastroesophagoscopy were unremarkable. Ultrasonography of the neck revealed an inhomogeneous mass in direct contact and posterior to the internal jugular vein. Magnetic resonance imaging (MRI) showed a



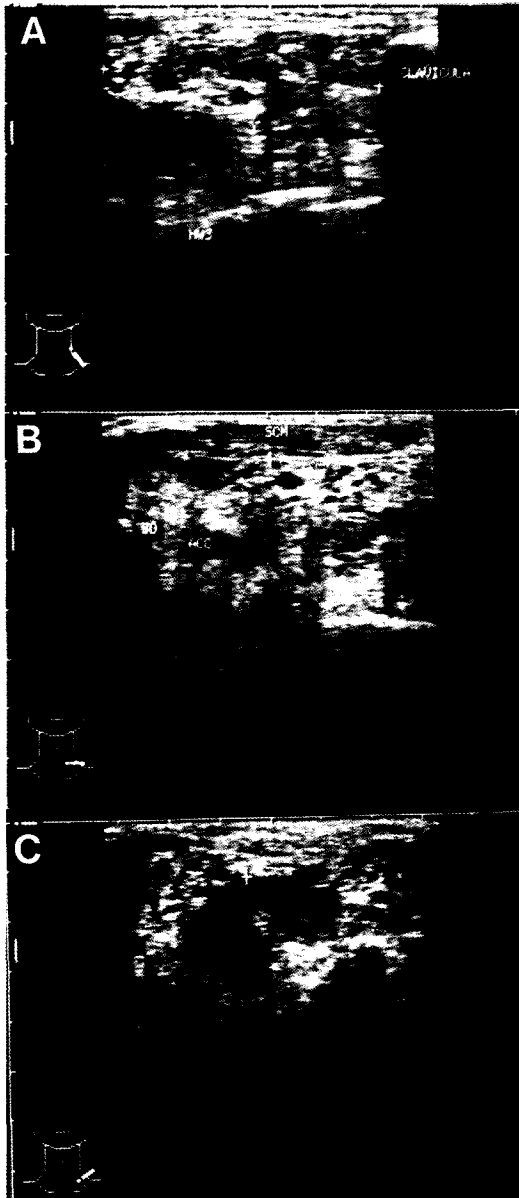
*Fig. 1. Lymphangiectasia (arrow) posterior and lateral to the internal jugular vein (star). Ectatic lymph vessels were removed with the surrounding fatty and connective tissue via a horizontal supraclavicular incision following the relaxed skin tension lines (case 1). The thoracic duct was sutured behind the clavicle.*

normal configuration of the supraclavicular region. At operation, the fatty and connective tissue near the junction of the thoracic duct with the internal jugular vein was characterized by ectatic lymphatic vessels over an area of 5 x 3 cm (*Fig. 1*). The abnormal tissue was adherent to the deep cervical fascia and extended to the midline behind the internal jugular vein inferiorly to the lung apex. A complete excision was performed and the thoracic duct was ligated behind the clavicle to prevent lymphorrhea.

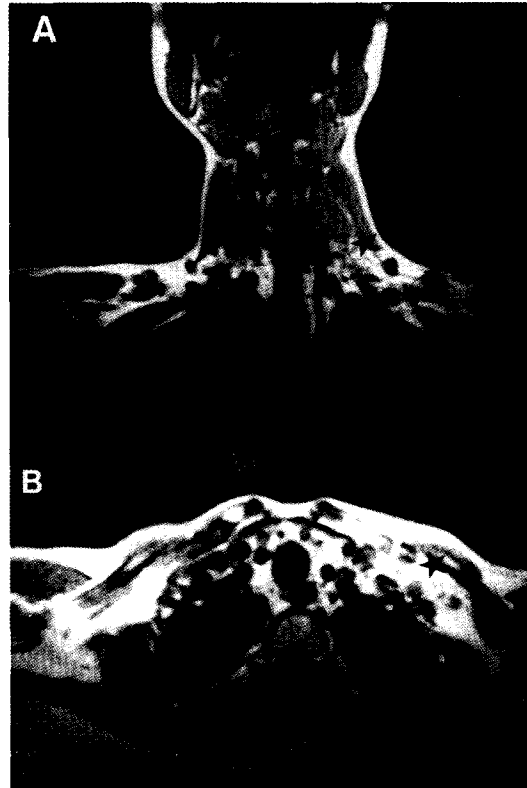
#### *Case 2*

A 37-year-old female (164 cm, 56 kg) had a 7-month history of recurrent swelling of the

left supraclavicular fossa which sometimes was the size of a tennis ball. She was otherwise in good general health. There was no previous operation, inflammation or trauma in the neck. Her only medication was "birth control pills." Palpation revealed a soft, non-tender, poorly delineated mass in the left supraclavicular fossa. On ultrasonography of the neck, the mass appeared as an inhomogeneous "tumor" with ill-defined margins. It was primarily hypoechogenic with thick internal septae, and extended behind the clavicle (*Fig. 2*). In appearance it resembled a cystic lymphangioma. Small lymph nodes and enlarged lymph vessels were detected by MRI with diffuse swelling of the subcutaneous tissue on the left side of the neck (*Fig. 3*). The



*Fig. 2. Ultrasonography of the left side the neck. (A) Sagittal scan, (B) transverse scan, and (C) oblique scan of the supraclavicular fossa of case 2. Note the inhomogeneous, poorly marginated pattern, an appearance typical of primary lymphangiectasia of the supraclavicular fossa. The mass extended behind the clavicle (A) and was located posterior to the sternocleidomastoid muscle (B). The tumor was 6 x 4 cm (C).*



*Fig. 3. Coronal (A) and axial (B) T2-weighted MR scan of the neck (case 2). The left supraclavicular fossa is marked by a star. The MR scan shows multiple small lymph nodes (<1cm) and ectatic lymph vessels. A diffuse thickening of subcutaneous tissue is seen compared with the contralateral side.*

intraoperative finding showed the supraclavicular fatty and connective tissue close to the internal jugular vein to be characterized by abundant ectatic lymph vessels at the junction of the thoracic duct. These tissues were removed en toto. The thoracic duct, which entered the mass, was ligated to minimize lymphorrhea. Four months after the operation, she complained of similar symptoms on the opposite side of the neck. Palpation revealed a non-tender mass situated in the right supraclavicular fossa. Ultrasonography showed a 2.5 x 2 cm mass with ill-defined margins behind the sternomastoid muscle. The sonographic

pattern was inhomogeneous. She described that the swelling increased with use of the right arm. Because symptoms were similar to those previously in the left side of the neck, it was elected to follow the benign tumor expectantly by ultrasonography at regular intervals.

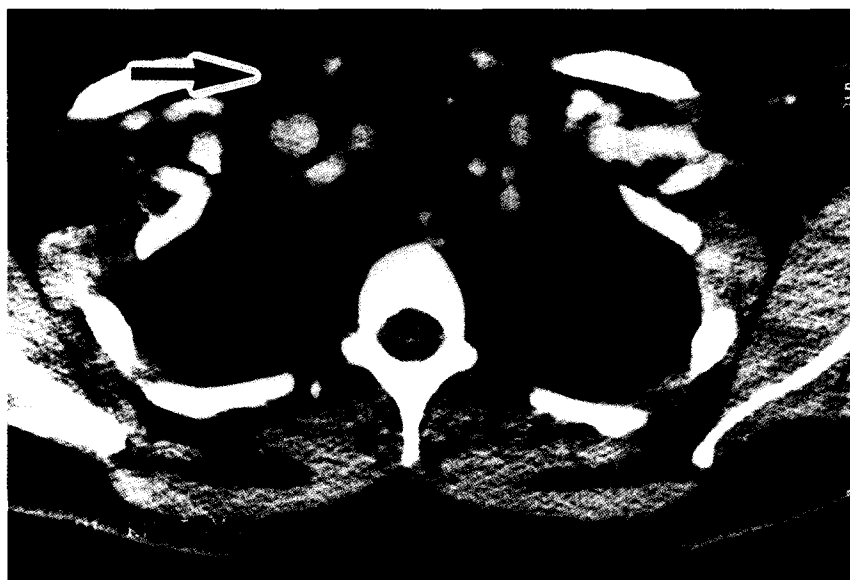
### Case 3

A 48-year-old female (164 cm, 65 kg) described a 10-year history of recurrent swelling of the right supraclavicular fossa which increased in size with strenuous effort. She had undergone cholecystectomy 27 years earlier and she had a cervical disc prolapse (C2). She was taking estradiol valerate for menopausal symptoms and had taken oral contraceptives for the previous decade. She smoked 10 cigarettes per day. Palpation of the neck revealed a small, hard mass in the supraclavicular fossa beneath the sternomastoid muscle at its clavicular attachment. Ultrasonography of the neck showed a well-circumscribed, cystic mass of 2 cm diameter lateral to and in direct contact with the internal jugular vein in the supraclavicular fossa. Computer tomogram (CT scan) revealed a well-defined, round, low density

tumor of 9 mm diameter which resembled a lipoma (*Fig. 4*). At neck exploration, there was induration of the fat and connective tissue lateral to the internal jugular vein with the right lymphatic duct entering the tumor mass. The right lymphatic duct was opened and subsequently ligated behind the clavicle to prevent continued lymphorrhea.

### Case 4

A 22-year-old female (167 cm, 59 kg) developed swelling of the left supraclavicular fossa over several weeks. Her only regular medication were oral contraceptive pills. There was no previous neck operation, trauma, or inflammation. Other than seasonal allergic rhinitis, she was in good general health. A hard, non-tender mass was initially palpable posterior to the sternomastoid muscle in the supraclavicular fossa. Ultrasonography of the neck revealed a 4x4 cm well-margined, compressible cystic structure lateral to the carotid artery, posterior to the sternomastoid muscle with a hyperechogenic area in the center. Initially the swelling resolved but a CT scan 10 days later when the mass had redeveloped showed edema of the



*Fig. 4. Axial post contrast CT scan of the neck at the level of the supraclavicular fossa (case 3). A round, well-defined, low density lipoma-like tumor of 9 mm diameter is seen just above the clavicle (arrow). Cranial to this lipoma-like structure was a nodular thickening of the skin and subcutaneous fatty tissue, reminiscent of postinfectious scar tissue.*

supraclavicular fossa consistent with an inflammatory process. A week thereafter the neck swelling had progressed. Repeat ultrasonography reconfirmed a cystic structure lateral to the carotid artery. At operation, the mass was a flat cystic structure adherent to but without infiltration of the posterior aspect of the sternomastoid muscle. The cyst communicated with the thoracic duct by a connection which passed between the sternal and clavicular portions of the sternomastoid muscle. Cyst and duct were entirely removed together with the surrounding fat and connective tissue. The thoracic duct was ligated behind the clavicle.

Each patient had an uneventful recovery without local recurrence except for patient #2 who displayed a similar lesion on the opposite side of the neck.

### *Histopathology*

Removed tissue was fixed in 10% formaldehyde and embedded in paraffin. Sections were stained with hematoxylin-eosin and Giemsa and by the Periodic acid Schiff reaction. The naphthol-ASD-chloracetate-esterase reaction was used to visualize myeloid cells. Iron-positive pigment was stained by Berlin-blue. The following antibodies (Dakopatts, Hamburg, FRG) were used for immunohistochemistry: L26 (CD20), UCHL1 (CD45R0), KP1 (CD68), anti-lysozyme and anti-SM-actin.

Histopathology of the excised tissue revealed a fairly uniform pattern. In three patients, small and medium-sized, lymph nodes were embedded in fat and connective tissue, which was rich in loosely packed collagen fibers. The lymph nodes were surrounded by ectatic afferent and efferent lymphatic vessels. In the fourth patient, there were ectatic lymphatic vessels unassociated with lymph nodes. Immunohistochemistry showed that the lymph vessels contained numerous smooth muscle cells (*Fig. 5a*) and focally increased amount of interstitial collagen fibers (*Fig. 5b*). The lymph nodes

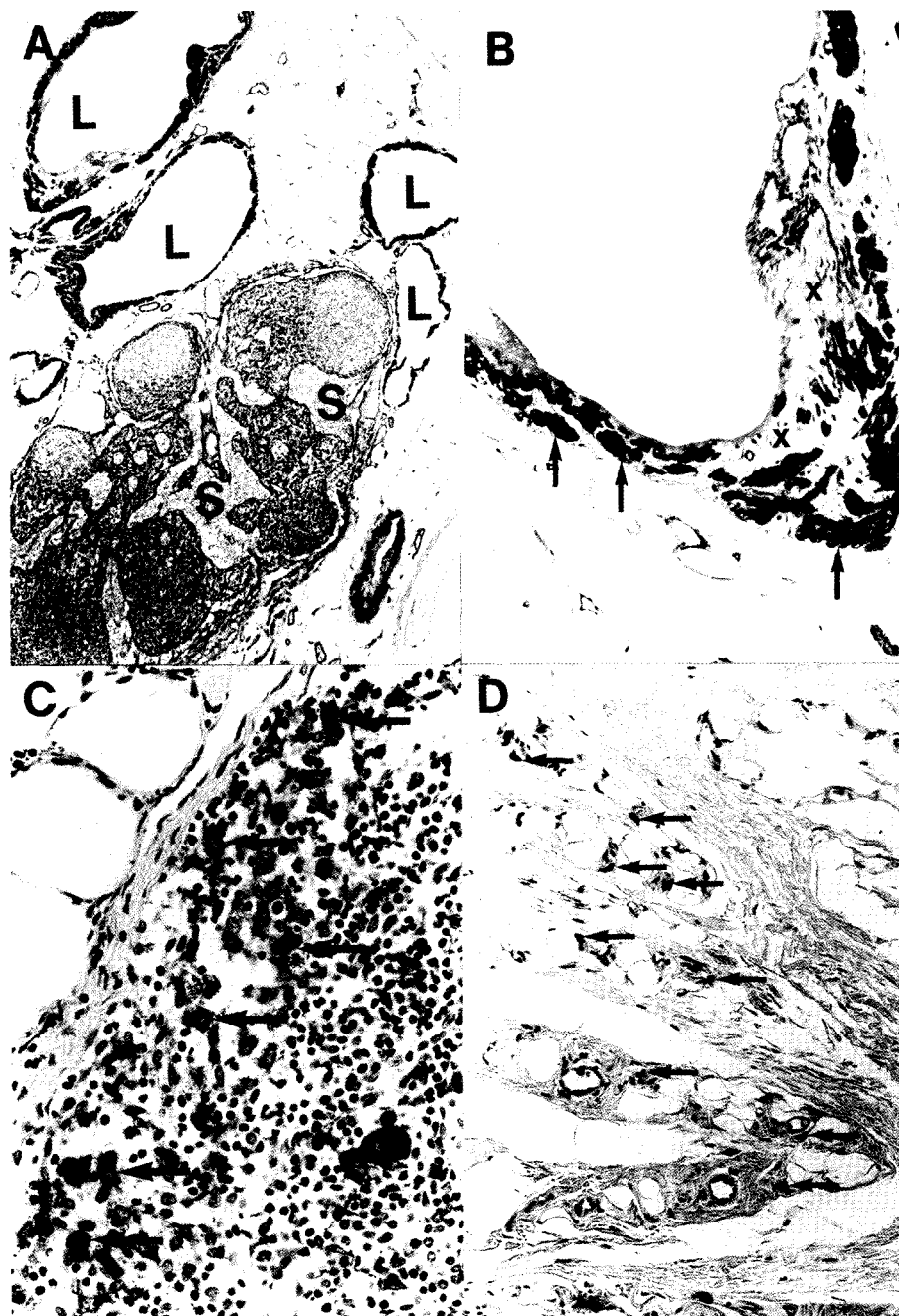
were characterized by enlarged sinuses which contained KP1-positive (*Fig. 5c*) and lysozyme-marked macrophages. In one patient, there were also tissue mast cells. The lymphatic tissue was highly organized into T- and B-cell specialized regions. The germinal centers were small. The T-cell region contained predominantly small lymphocytes and only a small number of immunoblasts. In two patients, there was a discrete focal lymphocytic infiltrate, both in the lymph node capsule and in the trabeculae which seemed sporadically slightly enlarged. In addition to mature fat, in two patients, there was also brown fat without further cytological characteristics. A focal increase of fibrous tissue was noted in two patients in whom focal areas contained a large number of mast cells with typical cholesterase-positive staining characteristics (*Fig. 5d*). The number of macrophages was not increased outside the lymph nodes.

### *DISCUSSION*

Four women underwent resection of a supraclavicular tumor-mass under general anesthesia. The primary aims were to obtain a histopathologic diagnosis, to relieve pressure symptoms interfering with free movement of the shoulder and to remove a cosmetically disturbing growth. Each patient underwent cervical ultrasonography whereas two patients were examined by magnetic resonance imaging (MRI) and two patients by computer tomography (CT) scan of the neck.

### *Clinical Presentation*

The presentation of four comparatively young women within a short period of time with an unusual supraclavicular mass is both surprising and disturbing. One characteristic that each patient had in common was the ingestion of estrogen-containing medication at the onset of neck mass enlargement. Otherwise, all were in good general health. The clinical course was similar with three



*Fig. 5. A) Lymph node with intact basic structure and slightly enlarged sinuses (S) (case 2). The lymph node is surrounded by ectatic lymph vessels (L). Smooth muscle fibers in the wall of lymph vessels are marked black by muscle-specific antigen (see also B). 45x magnification, anti-SM-actin labeling. B) Lymph vessel from A at 180x magnification. The lymph vessel is characterized by prominent smooth muscle fibers (arrows) and loosely packed, fiber-rich interstitial connective tissue (X). Anti-SM-actin labeling. C) Marginal sinus of a lymph node with scattered, KPI-positive macrophages (marked black, arrows). Magnification 360x, KPI (CD68). D) Fiber-rich connective tissue with an increased content of scattered tissue mast-cells (arrows). Magnification 180x, Naphthol-ASD-Chloracetatesterase-stain.*

women having recurrent swelling in the *left* supraclavicular fossa. One later developed a similar mass on the opposite side. The final patient had a mass in the *right* supraclavicular fossa. The tumor-mass presentation varied from several weeks to ten years. The swellings were typically non-inflammatory and sometimes subsided overnight. This finding suggests intermittent obstruction of lymph flow. Histopathology supports this hypothesis with ectasia of otherwise benign lymph vessels in tissues surrounding the junction of the thoracic or right lymphatic duct with the internal jugular vein. A chronic process involving the supraclavicular region is suggested by partial sclerosis of the wall of the lymph vessels, discrete and localized infiltration of the lymph node capsule, slight increase of lymph node macrophages and localized fibrosis of the interstitial connective tissue with increased mast cells. The clinical course together with the histopathology favors that enlargement was initiated by temporary, perhaps spastic, obstruction of the thoracic duct or right lymphatic duct junction with subsequent lymph stasis in the supraclavicular space. Based on the operative findings, it seems unlikely that lymph vessels in the mediastinum or abdomen were also involved.

#### *Pathophysiology*

The pathophysiology of these supraclavicular lymphangiectasias is obscure. Conspicuously, each patient was a woman in her reproductive years and each was taking a form of estrogen therapy at time of onset of neck swelling. At time of presentation, patient #3 was on clomiphene citrate, a nonsteroidal stimulator of ovulation with weak estrogenic activity. Moreover, she had been on oral contraceptives at the onset of neck swelling and had taken clomiphene only for a short period of time. These data suggest that benign supraclavicular tumorous lymphangiectasia may be hormone (estrogen)-aggravated. Pulmonary lymphangiomyomatosis is a well-recognized disorder that also primarily affects

women during their reproductive years (7-9) and seems to be a proliferative lesion of smooth muscle within lymphatic vessels. These latter patients typically develop progressive pulmonary dysfunction and die without lung transplantation within ten years of diagnosis. One patient with remission has been described after bilateral oophorectomy (9) but these occurrences are most unusual. In support of hormonal dependence of supraclavicular lymphangiectasia are experimental findings in ewes where acute *in vivo* administration of estrogen decreases the pumping ability of the thoracic duct, increases whole-body capillary filtration and lowers the outflow pressure at which lymph flow decreases (10). Whereas it is unlikely to cause lymphangiectasia, estrogen ingestion may have contributed to endothelial-smooth muscle proliferation and enlargement or possibly temporary "spasm" of lymph vessels with lymph stasis and subsequent lymphangiectasia. Preliminary results from experiments in the pig have shown increased spontaneous and noradrenalin-induced *in vitro* contractions of the mesenteric lymph vessels after estradiol administration (personal observations).

#### *Differential Diagnosis*

Uniformly lymph drains directly or indirectly to the supraclavicular areas. Prescalene lymph nodes near to where the thoracic duct or the right lymphatic duct drain into the venous system are often involved in tumors of the head and neck but also may be involved from metastases from tumors of the thorax and abdomen. Accordingly, masses of the supraclavicular region require histopathologic diagnosis to exclude malignant disease. Differential diagnosis includes lymphadenopathy from metastatic carcinoma or malignant lymphoma or infectious etiologies. Other possibilities in this region are lipoma, cystic hygroma, lymphangioma, and bronchogenic cyst (11). In the four female patients presented,

ultrasonography of the neck was the most helpful of the imaging techniques. The masses appeared as inhomogeneous, cystic, and poorly margined. In one patient, lymphangioma was suspected from the ultrasonographic image, a finding that conformed to lymphangiectasia as seen at operation. In each of the four patients, operation revealed ectatic lymph vessels embedded in the fat and connective tissue surrounding the junction of the thoracic duct or right lymph duct with the internal jugular vein. In one patient, the ectatic lymphatics communicated with the thoracic duct. MRI and CT scan did not provide notable information beyond that of ultrasonography and the final diagnosis was only established by microscopy after excision. Supraclavicular lymphangiectasia is similar to the histopathologic appearance of lymphangiectasia at other sites such as the intestine or mediastinum (1-6). Lymphangiomyomatosis, lymphadenitis, malignant lymphoma, metastatic carcinoma, and mesenchymal tumor were excluded by histopathology.

### CONCLUSION

Benign tumorous lymphangiectasia of the supraclavicular space is a hitherto undescribed disorder. It seems to occur exclusively in "fertile" women and its enlargement may be attributable to estrogen stimulation as it occurred with the taking of oral contraceptive pills. Due to its supraclavicular location, it needs to be distinguished from other malignant and benign tumors. A typical history of recurrent swelling in the anterior triangle of the neck in a woman on oral contraceptives, in conjunction with palpation of an ill-defined non-tender mass in the supraclavicular fossa, which on ultrasonography resembles a lymphangioma should suggest the diagnosis of benign supraclavicular tumorous lymphangiectasia. Because the lesion is benign, excision is necessary only for histologic confirmation or if the mass is cosmetically disturbing or symptomatic.

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