Metastatic Malignant Struma Ovarii

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Struma ovarii is a monodermal ovarian teratoma, composed mainly of differentiated thyroid tissue. It is a rare condition, representing less than 1% of all ovarian tumors. Almost always benign, malignant features present in only 5–10% of cases. We report the case of an adolescent with metastatic malignant struma ovarii with aggressive biologic behavior.

PATIENT DESCRIPTION

A 15 year old girl was admitted with the complaint of pain in the lower abdomen and pelvic discomfort. Abdominal ultrasonography showed a huge mass arising from the right ovary. A right oophorectomy was performed and macroscopic pathological examination revealed a tumor measuring 7 x 11.5 x 16.5 cm. Microscopic examination confirmed struma ovarii, a monodermal teratoma with positive thyroglobulin staining but without lymphovascular or capsular invasion.

Three months later, the patient complained of pain in the right hip and a lump in her posterior scalp. Brain computed tomography demonstrated a subcutaneous mass with destruction of the occipital bone and the appearance of intracranial expansion. The mass was excised and pathological examination confirmed follicular carcinoma of the thyroid with positive staining for thyroid transcription factor-1 and thyroglobulin. Neck ultrasonography was normal. The patient was clinically euthyroid.

Positron emission tomography-fluodeoxyglucose F 18 scan showed diffuse pathological uptake in the bones (right acetabulum, left clavicle, left scapula), spleen, lymph nodes (cervical, supraclavicular, mediastinal, axillary, retroperitoneal, pelvic and inguinal), and subcutaneous nodules in the left occipital region and right neck [Figure A].

Total thyroidectomy was performed and the pathological report showed normal thyroid tissue. During the 4 weeks without levothyroxine after the surgery, while waiting for thyroid-stimulating hormone levels to rise, the patient received palliative radiotherapy of 40 Gy to the right acetabulum and the left scapula, with marked clinical improvement. The postoperative I-131 scan showed 1% uptake after 2 and 24 hours, followed by I-131 treatment with 150 mCi. The post-treatment I-131 whole-body scan showed pathological uptake in bone metastases, paratracheal lymph nodes, upper neck and left parotid [Figure B]. Our plan was to continue treatment with I-131 and consider biological treatment in the near future.

COMMENT

The first description of follicular thyroid tissue in the ovaries was made in 1889 by Boettlin. A differential diagnosis of malignant struma ovarii from a benign ovarian teratoma is difficult to make. It requires lymphovascular tumor invasion, recurrence or metastases, or the typical cytopathological features of papillary thyroid cancer. The follicular variant of papillary thyroid carcinoma in struma ovarii exhibits the same morphological and immunohistochemical profile as the follicular variant in the thyroid.

Our case is different from those reported in the literature for several reasons: Firstly, struma ovarii usually presents during the reproductive years, in the fifth decade on average [1]. It rarely appears before puberty. Only a few cases of struma ovarii in patients between age 14 and 16 have been described [2,3]. Secondly, metastatic spread by local invasion, peritoneal, lymphatic pathways, and hematogenic dissemination to brain and lungs have been reported, but only 11 cases of bone metastases from malignant stuma ovarii have been described in the
literature [4]. Thirdly, several studies in the literature have reported high sensitivity (up to 98%) and specificity (up to 95%) of PET-FDG in metastatic differentiated thyroid carcinoma [5]. Little is known about the value of PET-FDG in malignant struma ovarii. In our case, PET/CT was performed and showed diffuse pathological uptake, which indicates aggressive disease. PET/CT showed additional uptakes that were not apparent on the post-treatment 1-131 scan, leading us to think of different approaches to the disease, not relying solely on radio-iodine treatment but including additional treatment such as biological therapy.

**References**


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**Capsule**

**Tagging a protein and stabilizing glycosylation**

Adding a glycan tag to a protein at a basic residue can be useful in therapeutic applications, because such tags can increase serum half-life, decrease aggregation propensity, or shield immunogenic epitopes of the protein. However, adding such tags to proteins that are not normally glycosylated (naïve proteins) can decrease their stability. Culyba et al. added a glycan tag to several naïve proteins at an Asn residue in a reverse turn that has a nearby Phe group. The interaction of the aromatic side chains and the glycan allowed energetic stabilization of the proteins.

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**Capsule**

**Starvation leads to autophagy**

Autophagy is a process by which eukaryotic cells engulf and break down cellular components to provide new substrates for metabolism. Egan et al. report a biochemical mechanism by which low energy stores in a cell can be linked to autophagy. The authors searched for targets of the adenosine monophosphate-activated protein kinase (AMPK), which is activated when cellular concentrations of adenosine triphosphate are depleted. AMPK was found to regulate another protein kinase, ULK1, which functions in regulation of autophagy. Cells engineered so that ULK1 could not be phosphorylated by AMPK failed to respond properly to starvation, had decreased autophagy, and were prone to starvation-induced cell death.

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**Capsule**

**DICER1 defect induces Alu RNA toxicity in age-related macular degeneration**

Geographic atrophy, an untreatable advanced form of age-related macular degeneration, results from retinal pigmented epithelium (RPE) cell degeneration. Kaneko et al. show that the microRNA (miRNA)-processing enzyme DICER1 is reduced in the RPE of humans with geographic atrophy, and that conditional ablation of Dicer1, but not seven other miRNA-processing enzymes, induces RPE degeneration in mice. DICER1 knockdown induces accumulation of Alu RNA in human RPE cells and Alu-like B1 and B2 RNAs in mouse RPE. Alu RNA is increased in the RPE of humans with geographic atrophy, and this pathogenic RNA induces human RPE cytotoxicity and RPE degeneration in mice. Antisense oligonucleotides targeting Alu/B1/B2 RNAs prevent DICER1 depletion-induced RPE degeneration despite global miRNA down-regulation. DICER1 degrades Alu RNA, and this digested Alu RNA cannot induce RPE degeneration in mice. These findings reveal a miRNA-independent cell survival function for DICER1 involving retrotransposon transcript degradation, show that Alu RNA can directly cause human pathology, and identify new targets for a major cause of blindness.

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