Primary Ependymoma in the Posterior Mediastinum

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A 46-year-old woman was referred to our hospital because of back pain and an abnormality on chest imaging. Chest computed tomography showed a well-delineated tumor in the left paravertebral space. Histological analysis of the resected tumor revealed perivascular pseudorosettes, and immunoreactivity for glial fibrillary acidic protein established the diagnosis of ependymoma. A few cases have been reported in the ovary, broad ligament, sacrococcygeal region, lungs, and mediastinum, but the pathogenesis has not yet been clarified. Female predominance in these tumors and organogenesis of the sites may suggest a key to the pathogenesis.

Keywords: mediastinal tumor, ependymoma, female, embryology

Introduction

Ependymomas generally arise from ependymal cells of the central nervous system (CNS): the ventricular system, choroid plexus, and central canal of the spinal cord, and less often in the brain parenchyma as a result of migration of ependymal cells from periventricular areas during embryogenesis. They rarely arise in the extra-axial region, outside the CNS. A few cases have been reported in the ovary, broad ligament, sacrococcygeal region, lungs, and mediastinum; however, the exact origin of such extra-axial ependymomas has not been clarified.

We treated a patient with an ependymoma in the posterior mediastinum that had no association with the spine. Immunohistochemical analysis of the resected lesion revealed the unique characteristics of this tumor, particularly reactivity for female hormone receptors, which is reportedly common in extra-axial ependymomas.

Case Presentation

A 46-year-old female smoker was referred to our hospital because of back pain and an abnormality on chest imaging. She had been well until 6 months earlier, when she developed back pain and was seen by a family doctor without any improvement. Five months later, she had an annual chest screening test, in which an abnormal shadow in the left lung field was noticed on chest X-ray. She also reported weight loss of 3 kg in the previous 3 months.

On examination, vital signs and neurologic examination were unremarkable. Laboratory tests were within the reference range. Chest X-ray revealed a mass in the left middle lung field (Fig. 1), and chest computed tomography showed a well-delineated tumor with smooth contours in the left paravertebral space at the T7 to T9 level (Fig. 2A). The tumor contained calcification and was heterogeneously and weakly enhanced with intravenous contrast media (Fig. 2B). There was no evidence of invasion of the adjacent aortic wall, thoracic vertebrae, or ribs. Magnetic resonance imaging of the chest showed that, compared with the spinal cord, the tumor was iso-intense on T1-weighted images (Fig. 3A), and moderately intense with foci of signal heterogeneity on T2-weighted images (Fig. 3B). Gadolinium enhancement was moderate and inhomogeneous on T1-weighted images (Fig. 3C). Additional CT imaging with myelography indicated no
Fig. 1 Chest X-ray revealing a mass in the left middle lung field.

Fig. 2 A: Chest CT showing a well-delineated tumor in the left paraspinous space. B: The tumor contained calcification with heterogeneous and weak enhancement.

Fig. 3 A) MRI of the chest showing that, compared with the spinal cord, the tumor was iso-intense on T1-weighted images, and B) moderately intense with foci of signal heterogeneity on T2-weighted images. C) Gadolinium enhancement was moderate and inhomogeneous on T1-weighted images.

Involvement of the intervertebral foramens or spine. Via thoracotomy, the tumor was resected en-bloc with the 7th and 8th intercostal muscles and the thoracic sympathetic trunk passing over the tumor.

The resected tumor measured $57 \times 47 \times 33$ mm and weighed 50 g with a lobulated pale yellow cut surface and was encapsulated. Microscopically, the tumor demonstrated solid, trabecular, and cystic architecture and consisted of columnar tumor cells with apically located oval nuclei and elongated fibrillary cytoplasmic processes with moderate nuclear pleomorphism (Fig. 4A). Perivascular pseudorosettes and true rosettes were frequently
present (Fig. 4B). Immunohistochemical analysis showed positive reactivity for glial fibrillary acidic protein (GFAP) (Fig. 4C), cytokeratin 7 (CK7) (Fig. 4D), and epithelial membrane antigen; and negative reactivity for S-100, CD99, CAM5.2, and CK20. MIB-1 index was up to 15% through the tissue section, and marked immunoreactivity for estrogen and progesterone receptors (ER, PR) was present (Fig. 4E and 4F). Based on these findings, the tumor was diagnosed as primary mediastinal ependymoma, grade II according to the World Health Organization grading.

The postoperative course was uneventful, and the patient was discharged on postoperative day 15 without major complications. She remains well with no sign of recurrence 18 months after surgery.

Discussion

The posterior mediastinum is a common site for neurogenic tumors, such as neurofibromas and schwannomas, in adults. However, ependymomas at this site are extremely uncommon; to the best of our knowledge, there have been 9 cases reported in the literature including the present case (Table 1).6–11

Histological and immunohistochemical analysis has indicated differences between CNS and extra-axial ependymomas.5) Extra-axial ependymomas demonstrate more architectural varieties than their CNS counterparts. The most striking difference is that extra-axial ependymomas preferentially express CK7, CAM5.2, ER, and PR, but do not express CD99, to which CNS ependymomas are strongly immunopositive. Specimens of the present case showed various histological features, with perivascular pseudorosettes and true rosettes frequently observed. Immunohistochemical analysis demonstrated positive reactivity for GFAP, CK7, ER, and PR and negative reactivity for CD99, CAM5.2, and CK20. With the exception of CAM5.2, these features coincide with those mentioned in a previous report.5)

Immunoreactivity for CK7 and non-reactivity for CK20 generally indicate the site of origin of a given carcinoma, such as the lung, breast, ovary, endometrium, thyroid, or salivary gland.12) Immunoreactivity for both ER and PR is associated with target organs of female hormones. The present findings suggested a mediastinal metastasis of ovarian ependymoma; however, there was no evidence of such a primary tumor in our patient.

CNS ependymomas are equally distributed between the sexes.13) Sacrococcygeal ependymomas have the same distribution as CNS ependymomas.4) However, other

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**Fig. 4** Pathological findings of the resected specimens. A) Columnar tumor cells with apically located oval nuclei and elongated fibrillary cytoplasmic processes, B) perivascular pseudorosettes and true rosettes, C, D, E, and F) immunostaining of GFAP, CK7, ER, and PR. Original magnification is × 400 in B, and × 100 in A and C to F.
extra-axial ependymomas in the ovary, broad ligament, lung, and mediastinum appear only in women. Sacrococcygeal ependymomas reportedly originate from ependymal rests or coccygeal medullary vestiges. The difference in sex distribution between sacrococcygeal and other extra-axial ependymomas seems to suggest a difference in their pathogenesis.

Primordial germ cells originate from the yolk sac endoderm, and migrate through the cloaca, hindgut, and dorsal mesentery into the gonadal ridge, where the ovary, broad ligament, and sacrococcygeal region develop. Misdirected primordial germ cells have been found in the sacrococcygeal region and mediastinum, One interesting hypothesis is that ependymomas in the ovary, broad ligament, and mediastinum might originate from misdirected primordial germ cells under the influence of female hormones, and this could explain the female predominance of such tumors.

In summary, we have presented a case of primary mediastinal ependymoma. From the clinical, immunohistochemical, and developmental point of view, we suggest that mediastinal ependymomas may originate from misdirected primordial germ cells influenced by female hormones.

References