Mediastinum Chordoma: A Case Report

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Chordoma is a slow-growing yet locally aggressive malignant neoplasm of the bone derived from remnants of the embryonic notochord. Thoracic chordoma is even rarer. It may occur at the skull base (35%), at the cervical, thoracic and lumbar spine (2.3-15%), and at the sacral regions (50%). We present a 21 year-old girl who had a slow-growing left-side mediastinal tumor for 14 years. The chest X-ray film showed a benign-looking, small-sized, well-circumscribed tumor with calcification; the benign appearance on the chest X-ray delayed her prompt diagnosis and treatment.

The patient began to experience left hand dryness 2 years previously, and a recent onset of back pain. Echo-guided aspiration revealed cords and lobules of large tumor cells in the chondroid stroma. Immunohistochemical staining was positive for S-100 protein, cytokeratin and vimentin. These observations indicated a malignant chordoma. She received a total surgical resection of the tumor, together with a partial osteotomy of C7 and T1-T3. The area of bone substance loss was filled with cement. Adjunctive stereotactic radiotherapy with 50 Gy was given. No local recurrence was seen after 5 months. *(Thorac Med 2009; 24: 54-59)*

Key words: mediastinum chordoma

Introduction

Chordoma is a rarely reported and slow-growing malignant neoplasm presumed to be derived from the remnants of the embryonic notochord along the length of the neuraxis at developmentally active sites, such as the end of the neuraxis and the vertebral bodies [1-3]. Despite current evidence indicating that such tumors contain immuno-phenotypic and ultra-structural markers of epithelial differentiation, they are generally classed among bone tumors because of their frequent association with extensive destruction of bony structures. Chordoma typically presents in adults 40 years of age or older and males are affected more often than females. Symptoms are localized and result from the mass effect of the tumor. The natural history is local recurrence with persistent tumor growth and eventual death from local diseases, or less frequently metastases [4].

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Case Report

We present a 21-year-old girl who had a slow-growing left-side mediastinal tumor for 14 years. She was regularly followed up by a family physician. Because the small-sized, well-circumscribed tumor with focal calcifications exhibited slow growth in the yearly chest X-ray follow-up, no further testing was done. She began to experience left hand dryness 2 years previously. There was no significant abnormal sensation in her left hand, and neither edematous change, nor abnormal skin color was noted. There was also no chest pain, cough, dysphagia or dyspnea noted in the past 2 years. She was referred to Chung Shan Medical School Hospital for further treatment because of the recent onset of back pain in the interscapular area and worsening anhidrosis. A chest X-ray showed widening of the mediastinum (Figure 1). A chest computed tomography (CT) scan revealed a well-defined hypodense mass with calcifications occupying the left posterior mediastinum, measuring 7.5 × 5.3 cm from the spinal level of T1 to T5, extending to the right posterior mediastinum at about 3.59 × 1.63 cm in size at the spinal level of T1 to T3, causing vertebral body erosion from T1 to T3 (Figure 2). There was no definite enhancement of the mass after IV contrast infusion. A bone scan revealed no metastatic lesions.

Echo-guided aspiration was performed after consent was obtained. Histopathologically, the lesion showed lobules and cords of large tumor cells embedded in a chondroid stroma (Figure 3A). Some cells showed nuclear atypia. Almost all of the tumor cells were physaliphorous with some intracellular vacuoles in their cytoplasm (Figure 3B). Neither necrosis nor mitotic features could be identified. The immunohistochemical study showed positive staining of the tumor cells with broad-spectrum keratin (AE1/3) (Figure 3C), S-100 protein and vimentin (Figure 3D). Histopathology and immunohistochemistry were both conclusive to the diagnosis of chondroid chordoma.

The patient received a thoracotomy incision, which extended posterior and superior to the spinous process of C7, and she underwent a total resection of the tumor together with a partial osteotomy of C7 and T1-T3, with the areas of bone substance loss being filled with cement.

After the operation, local adjuvant stereotactic radiotherapy with 50 Gy was performed. Five months later, there was no local recurrence, but the residual symptom of hand anhidrosis persisted. She will have regular follow-ups at 6-month intervals.
Chordoma is a rare, slow-growing, locally aggressive neoplasm of the bone. Thoracic chordoma is rarely seen. Its benign appearance on a chest X-ray may delay the en bloc resection of the tumor. A differential diagnosis should be made with chondrosarcoma, mucinous adenocarcinoma, myxopapillary ependymoma, and epithelioid hemangiendothelioma, according to the specific S-100 protein expression, vimentin and cytokeratin stains.

The immunohistochemical staining of chondrosarcoma shows positive for S-100 protein and CD99, and negative for vimentin and cytokeratin stains. Mucinous adenocarcinoma reveals positive staining for vimentin and cytokeratin, but is negative for S-100 protein. Myxopapillary ependymoma is positive for S-100 protein, glial fibrillary acidic protein and CD99, and negative for vimentin and cytokeratin stains. Epithelioid hemangiendothelioma appears

Fig. 2. Chest tomography showing a left posterior mediastinum calcified mass with T1-T3 vertebral body erosion.

Fig. 3A. Low-powered view of clusters of tumor cells in the chondroid stroma (hematoxyline & eosin stain, X200).

Fig. 3B. Low-powered view of physaliphorous tumor cells with vacuolated cytoplasm (hematoxyline & eosin stain, X400).
positive for factor VIII-related antigen and vimentin and negative for S-100 protein expression and cytokeratin stains. Immunohistochemical studies of benign chondroma have been reported to have positive staining for CAM 5.2, broad-spectrum keratin, epithelial membrane antigen (EMA) and vimentin, and to a lesser extent, S-100 protein [5]. In addition, stains for muscle actin, carcinoembryonic antigen (CEA), and desmin have been negative.

The clinical presentation depends upon the site of origin and extension of growth. Magnetic resonance imaging (MRI) is the best technique for assessing the extent of tumor, but CT is important for demonstrating local bone destruction.

In less than 10% of cases, chordomas contain sarcomatous or malignant spindle cell features. These undifferentiated chordomas tend to be even more aggressive with early distant metastases [2]. There are no reports of elevated beta-hCG in patients with chordomas, but it is possible that an undifferentiated chordoma with sarcomatous features may produce beta-hCG [2].

Chordoma is 1 of the most challenging of mesenchymal tumors to treat effectively, despite the relatively slow growth rate. The standard therapy is radical resection. High-dose radiation is increasingly used in combination with surgery (for close or positive tumor margins) or alone for nonresectable lesions, especially S1-2 lesions. Local regrowth or metastatic disease may develop after 15 years; in other words, there is a possible disease-free survival rate of 15 years, but not necessarily a cure. Chordoma has a low sensitivity to chemotherapy; aggressive initial therapy improves the overall outcome. Surgery is performed to obtain diagnostic tissue and reduce the tumor burden, which increases the effectiveness of radiotherapy. Conventional photon irradiation appears to result in poor local control in patients with macroscopic residual disease following surgery. The local control rate is dependent upon the volume of residual disease following surgery. Park reported a high local control rate with surgical and radiation treatment of primary lesions (12 of 14), compared to recurrent lesions (1 of 7). Therefore, high-dose proton/photon therapy offers an effective treatment option for primary lesions [6].
Several factors may help predict the survival rate following proton beam irradiation, that is, female sex, skull base chordoma, and larger tumor volume (≥70 ml) may decrease the survival rate. Surgical resection plus post-surgical radiotherapy seems to be the standard treatment for chordoma, but the prognosis for this kind of tumor is unpredictable because of the high recurrence rate (50%). The slow growth, benign appearance, and nearly symptom-free nature lead physicians to ignore the continuing growth and eventual local invasion into the contra-lateral vertebral body. Although our patient received a total resection of the mediastinal chordoma, the symptom of hand anhidrosis remained. Her prognosis would have been much better if a radical resection had been arranged years before. This case study of a rare thoracic chordoma allows us to recommend maintaining an aggressive attitude toward a mediastinal tumor, because a calcified and well-defined tumor could be a malignant chordoma.

References

縱隔腔脊索瘤──病例報告

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脊索瘤是一種緩慢生長，起源於殘餘胚性背索的腫瘤，但是對局部組織破壞性很強，可發生於顱骨底（35%）、顱，胸，腰脊椎（2.3-15%），和薦椎（50%）。胸廓的脊索瘤同樣罕見。在此一病例報告中，我們報告一個21歲女性病患，有一個緩慢生長達14年的左側縱隔腔腫瘤。其X光表現像良性的腫瘤，即邊緣清楚，鈣化及生長緩慢，而延遲病患的及時診斷和治療。

她兩年前開始出現左手乾燥的症狀。最近出現胸後背部痛。超音波指引抽吸術病理檢查報告為小葉和圈狀的大腫瘤細胞於軟骨樣基質。特殊免疫染色呈現對S-100蛋白，細胞角蛋白（cytokeratin），波形蛋白（vimentin）陽性。這些檢查證實為惡性脊索瘤，病患隨後接受此縱隔腔腫瘤的完全切除，同時進行C7, T1-T3的局部切骨術及填充骨泥。病患術後接受50Gy局部立體放射線治療，至今5個月也沒有局部復發。

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關鍵詞：縱隔腔脊索瘤