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Combination percutaneous cryotherapy and iodine-125 seed implantation for unresectable malignant thymoma: Experience in 19 patients ☆

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ABSTRACT

Thymomas are the most common tumors of the mediastinum. These tumors often compress vital mediastinal organs and severely impact the quality of life of thymoma patients. To avoid the side effects of chemoradiotherapy, some patients with unresectable malignant thymomas have opted to undergo cryotherapy in our hospital. We reviewed the cryosurgery, nursing and follow-up records of our hospital for the past 8 years, and evaluated the safety and efficiency of cryotherapy in 19 patients with unresectable malignant thymomas. No severe complications involving the vital organs surrounding the tumor occurred during or after cryosurgery. The most common side effect was pleural effusion, which occurred in 11 patients and healed after drainage within 1 week. Cough, mediastinal and pericardial effusions, pneumothorax, mild fever and chest tightness also occurred and resolved 1 week after symptomatic treatment. Since our patients had high KPS scores and mild myasthenia gravis symptoms before the treatment, myasthenia gravis did not occur after the treatment. The progression-free survival of the patients was 14–29 months (median, 18 months), and did not differ between patients with large tumors and those with small tumors ($P = 0.6753$). In conclusion, cryotherapy is a safe and efficient method for the treatment of unresectable malignant thymoma.

Introduction

Thymomas are the most common tumors of the mediastinum; they originate from the epithelial parts of the thymus and account for 0.2–1.5% of all malignancies [10]. In patients with thymoma, complete surgical resection with or without radiation therapy is the gold standard treatment for both early – [15,23] and late-stage [9] disease, with a 5-year survival rate of 60% for benign thymoma and 20% for malignant thymoma. Even if a complete resection cannot be achieved, the prognosis of patients with partially resected thymoma is still significantly better than that of unoperated patients [15]. To ablate the tumor in situ, several tumor-ablation techniques have been applied in the clinical treatment of solid tumors, such as radiofrequency ablation, microwave ablation and cryoablation. Of these, cryoablation has some advantages such as good visibility of the ice ball under computed tomography (CT) scanning and close approximation between the ice ball coverage area and the complete necrosis area [18,28]. To preserve the collagenous architecture [19] and the integrity of the large vessels and airways [22], percutaneous cryoablation has been widely used in the palliative treatment of several common cancers and for the simultaneous ablation of primary and metastatic lesions [3,4,26]. In 2012, a case report showed that percutaneous cryoablation may be used as a component of a multimodality treatment for the palliative control of locally advanced, treatment-refractory mediastinal tumors [33]. In this study, we retrospectively reviewed the records of 19 patients who underwent combination percutaneous cryoablation and iodine-125 seed therapy for thymoma in our hospital and were followed up for 8 years. The treatment efficacy and safety were analyzed.

Materials and methods

Ethics

The study protocol was approved by the regional ethics committee of Guangzhou Fuda Cancer Hospital. Written informed

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consent was obtained from each participant in accordance with the Declaration of Helsinki.

Patient selection

Between March 2004 and January 2012, 45 patients with malignant thymoma were treated in our hospital and only 19 patients met our inclusion criteria and were enrolled in this study. Surgery, radiation and chemotherapy were deemed unsuitable in case of any of the following conditions: multifocal disease, unresectable thymoma, refusal to undergo radiation and chemotherapy, seeking of further treatment after failure of a previous treatment and advanced age. Ideal patients for thymus cryoablation were those with a Karnofsky performance status (KPS) score $\geqslant 70$; no obvious signs of myasthenia gravis (MG); platelet count, $\geqslant 80 \times 109/l$; white blood cell count, $\geqslant 3 \times 109/l$; neutrophil count, $\geqslant 2 \times 109/l$; hemoglobin level, $\geqslant 90$ g/l; prothrombin time international normalized ratio, $\geqslant 1.5$; absence of level 3 hypertension, severe coronary disease, myelosuppression, respiratory disease and acute and chronic infection; and normal heart and lung function.

In all 19 patients, malignant thymoma was diagnosed by radiological imaging and fine-needle aspiration biopsy. Enhanced CT and positron-emission tomography-CT can often distinguish thymomas from benign mediastinal lesions or lymphomas in patients with multiple mediastinal abnormalities [21]. In all, 13 patients were in stage I, and 6 patients were in stages II (3 patients), III (1 patient, with neck lymph node metastasis) or IV (2 patients, with clavicle, chest and liver metastases). Nine patients had mild symptoms of MG, and all of these patients were in stage I. There were a total of 24 masses in the patients, and all patients received their final treatments in our hospital within 8 years of follow-up.

Cryoablation procedure

Percutaneous cryotherapy was performed in all patients, and obvious intra- and extrathymic masses were completely cryoablated. Cryosurgeries were performed using an argon gas-based cryosurgical unit (Endocare, Irvine, CA) and cryoprobes with a diameter of 3 mm (Endocare). Two to eight cryoprobes were inserted into the mass via the intercostal space under CT guidance. Two freeze/thaw cycles were performed, and in each cycle, the temperature at the tip of the probe reached −180 °C. The freezing time depended on the achievement of an "ice ball," visible as a low-density area on CT images. Generally, the tumor was frozen for a maximum of 15 min and thawed for 5 min, and this cycle was repeated. A circumferential margin of at least 0.5 cm of normal tissue was frozen around the thymoma. For masses with a diameter of 5–9 cm, three or four cryoprobes were used to ensure freezing of the entire tumor; for masses with a diameter >9 cm, five to eight cryoprobes were required to ensure adequate cryolesions (Fig. 1). In addition to the primary tumor, lymph node or distant metastases were also ablated in the same operation. To avoid injuries to the trachea, thoracic aorta, nervus vagus, esophagus and myocardium (later referred to as "high-risk regions"), care was taken to avoid creating ice balls that reached these organs. Instead of cryoablation, we preferentially implanted iodine-125 seeds (Syncor Pharmaceuticals, Shanghai, China) in these regions (using a percutaneous transhepatic cholangiography [PTC] needle and a 3D treatment-planning system; usually <20 seeds) to control tumor growth. The cryoablation tract was sealed off with fibrin glue immediately after the removal of the cryoprobe to ensure hemostasis.

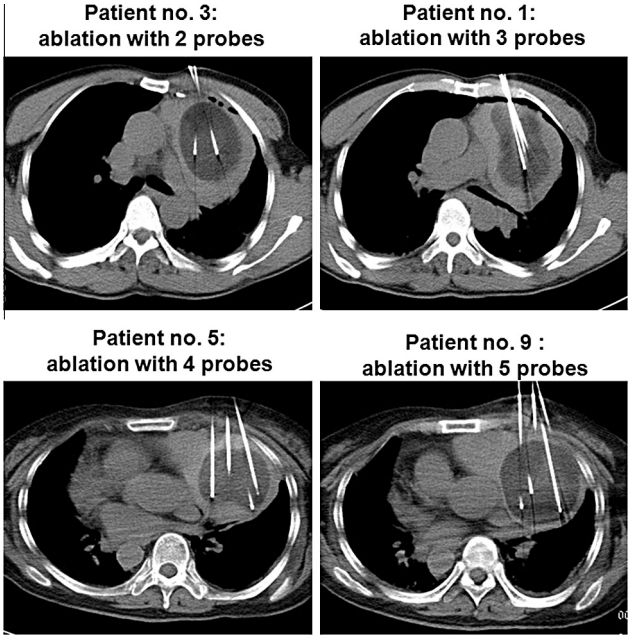

Fig. 1. Computed tomography images of four patients who underwent cryosurgery for thymoma. The white lines in the pictures are cryoprobes; the dark areas around the cryoprobes are the location of the thymoma and the ice ball.

Evaluation and statistical analysis

Complications were recorded and classified in accordance with the Common Terminology Criteria of Adverse Events v4.0. Radiographic local tumor control was assessed using image-guided tumor ablation criteria [13]. Thoracic ultrasonography was performed both 1 day and 1 week after the minimally invasive treatment of primary and metastatic tumors. Follow-up dynamic CT was performed at 1 month and then at 3–4 month intervals. The revised Response Evaluation Criteria in Solid Tumors v1.1 were used to assess the response of the thymomas [7]. Three diagnostic radiologists reviewed the CT scans of every patient to determine whether progression or recurrence had occurred. The serum levels of anti-acetylcholine receptor (anti-AChR) antibodies and anti-muscle-specific tyrosine kinase (anti-MuSK) antibodies were determined to confirm the diagnosis of MG, especially if the clinical symptoms were atypical [2,25]. Progression-free survival (PFS) was calculated from the date after the cryosurgery and compared using Kaplan–Meier analysis with the log-rank test. Statistical differences were indicated by $P < 0.05$. All analyses were conducted using the GraphPad software (San Diego, CA).

Results

Clinical data

In total, 7 men and 12 women underwent cryoablation of malignant thymomas. Their ages ranged from 23 to 71 years, with a mean age of 53 years. Seven patients were diagnosed with MG after the measurement of their anti-AchR and anti-MuSK levels. Informed consent was obtained from all patients (Table 1). Twelve patients were from China, and seven patients were from Southeast Asia. All patients had been diagnosed with unresectable malignant thymoma in other centers, and they came to our hospital for cryosurgery. The thymomas were situated in the anterior compartment of the mediastinum in 14 patients, in the frontal and upper mediastinum in 3 patients and in the upper mediastinum in 2 patients.