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Jean-Michel Maury, Gabrielle Drevet, Stéphane Collaud, Renaud Grima, Isabelle Pavlakovic, et al.. Cytoreductive Pleurectomy and Intrathoracic Chemohyperthermia for Pleural Relapse of Thymomas. *Annals of Thoracic Surgery*, 2019, 107, pp.e157 - e160. 10.1016/j.athoracsur.2018.07.058 . hal-03486691

HAL Id: hal-03486691

<https://hal.science/hal-03486691>

Submitted on 20 Dec 2021

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Cytoreductive Pleurectomy and Intra Thoracic Chemo Hyperthermia for Pleural Relapse of Thymomas

Running Head: Intra Thoracic Chemo Hyperthermia

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Abstract

Several surgical procedures, from debulking to extra pleural pneumonectomy, may be applied for stage IVa Masaoka thymomas but their efficiency is still controversial. Case studies favored R₀ resection as the cornerstone of multimodal therapy for loco-regional metastatic extension. We report our standardized procedure associating cytoreductive surgery and intra thoracic chemo hyperthermia on a 46-years old patient presenting B2 thymoma and synchronous unilateral pleural metastasis.

Thymomas are rare thymic epithelial tumors that may be aggressive and difficult to treat. Complete R₀ surgical resection is the cornerstone of a multimodal treatment and the most significant prognostic factor¹. Patients (7-10% of cases) develop upfront or delayed pleural metastasis, and pleural surgery improve survival rate². However, there is a lack of consensus on the surgical resection extent, especially in the context of bulky pleural invasion. Pleural involvement may be considered as a metastatic disease, with a limited chance of complete resection. We previously showed the benefit of subtotal cytoreductive pleurectomy associated with Intra Thoracic Chemo Hyperthermia (ITCH)³. We here report on the complete procedure on 46 years-old women, with B2 thymoma.

Technique

All patients with advanced, recurrent thymic tumors were discussed within the RYTHMIC⁴ expert tumor board network to consensually decide for the patient care. Selected patients for ITCH procedure must be <75 years-old and presented with *de novo* pleural extension or pleural relapse of previously surgically resected thymomas. Thymic carcinomas were excluded. Patients undergone 18-FDG PET-Scan to confirm diagnosis of isolated pleural relapse. Cardiopulmonary functions were evaluated before surgery.

Case description

We here report the procedure performed on a 46 years-old women, presenting with bulbar myasthenia gravis requiring plasma replacement and treated with human immunoglobulin (Tegeline[®]). The 18-FDG PET-scan evidenced a mass of the anterior mediastinum with superior vena invasion and multiple right pleural nodes (Figure 1A, 1B). A CT-scan guided biopsy confirmed the diagnosis of B2 thymoma. The patient received neo-adjuvant chemotherapy⁵ with a partial response and undergone a two-step surgery one month after the end of the treatment. For the first step, we realized enlarged thymectomy (pericardium and superior vena cava with prosthetic replacement upon median sternotomy).

The second surgical step has been performed after one month with subtotal pleurectomy associated with ITCH.

ITCH procedure

Epidural catheter was inserted before induction and the patient was monitored (central venous and radial arterial catheters). Body temperature was carefully monitored through thermal probes positioned in the esophagus and the bladder. Complete anesthesia was performed, and double lumen bronchial tube was inserted. The patient was positioned in lateral decubitus and a fifth space postero-lateral thoracotomy without muscle sparing was performed avoiding areas of separation to limit the risk of parietal toxicity during the ITCH procedure (Figure 1C). The surgery was performed on excluded lung with extra pleural dissection without opening the pleural cavity (Figure 1D). It is of importance to completely remove the pleura in contact to the phrenic muscle; the muscle fibers must be perfectly visible (Figure 1E)³. After the complete removal of the parietal pleura (Figure 2A), we performed the gross examination of the lung parenchyma (Figure 1F) and remove all lung implants using wedge resections and all lymphatic nodes. Rigorous hemostasis was performed with argon beam to avoid clot formation that may obstruct the ITCH device (CAVITHERM[®], SOFRAMEDICAL).

Chest tubes were inserted: a curved 28-30F tube medially inserted to the posterior cardio-phrenic angle (outflow) and a 28-30F tube laterally inserted to the apex (inflow) (Figure 1C). Two thermal probes were inserted next to the chest tubes to monitor local temperature. Thoracotomy was hermetically closed after restoration of the bilateral lung ventilation. Tubes and thermal probes were connected to the ICTH device. At this point, the ambient temperature of the surgical room must be set up to 18°C up to the end of the procedure. Patient was then positioned in dorsal decubitus and ice was placed around the neck to avoid cerebral hyperthermia and next to the femoral arteries. The saline isotonic solution supplemented with 5% glucose was pre-warmed to 42° C. The healthy lung was ventilated at 4 to 5 ml/kg while the lung to be treated was semi-inflated to increase the surface in contact

to the ITCH solution. The chest cavity was filled with 1.4 l/m² of solution with a continuous monitoring of the central venous pressure and of the cardiac flow to avoid hemodynamic failure secondary to intra thoracic hyper pressure. The ITCH solution flow was stabilized around 500-700 ml/min up to inflow/outflow temperature equilibrium to 41-42 °C (Figure 2B and 2C); 25 mg/m² mitomycin (max 60 mg) and 50 mg/m² cisplatin (max 100 mg) were finally injected in the sterile circuit⁶ for a 90 minutes procedure. Then, the solution was eliminated and the chest tubes were connected to pleur-evac® at -20 mm Hg.

Results

In the present example, chest tubes were removed at day six, the patient was discharged to a rehabilitation center at day 12 without post-operative complications. Pathologist examination revealed 23 pleural nodes (1 mm to 15 cm). Six months after surgery the patient was free of tumoral disease.

Comment

We report our ITCH procedure to treat a patient with pleural involvement of B2 thymoma. We previously reported the feasibility of ITCH, without significant morbidity³. This surgical procedure is useful in the context of pleural metastasis of thymoma; the main benefit for the patient is to limit mortality, morbidity and functional consequences associated with extensive surgery such as extra-pleural pneumonectomy^{7,8}. Nevertheless, ITCH may be associated with thoracic surgery-related complications or drug-related systemic complication such as reversible acute renal insufficiency (prevented by pre and post-operative hyper-hydration) and reversible bone marrow aplasia, as reported in < 5% of treated patients³.

From a treatment strategy standpoint, ITCH is feasible as multimodal therapy associating pre-operative systemic chemotherapy. From a technical standpoint, challenges include the pleura removal within the phrenic-rib angle secondary to the depth of the operating field which may require an additional lower thoracotomy possibly associated with phrenic muscle resection.

In our report, and based on our expertise (26 patients), we report the key steps to be followed for successfully performed the ICTH procedure. A multi-centric, controlled, randomized study is needed to assess the benefit of ICTH in treating relapse of thymomas, but is hardly feasible due to the rarity of this cancer.

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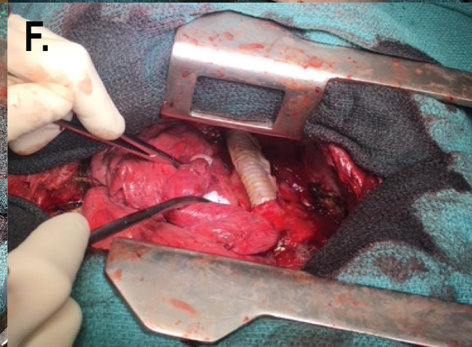
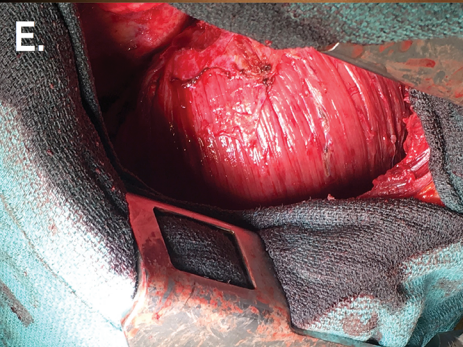
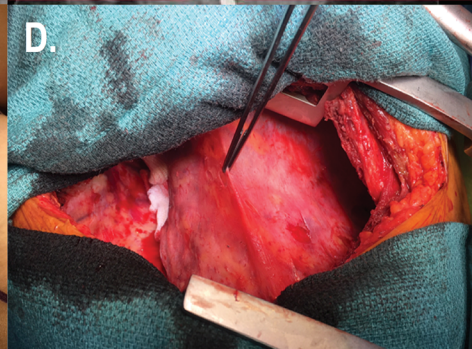
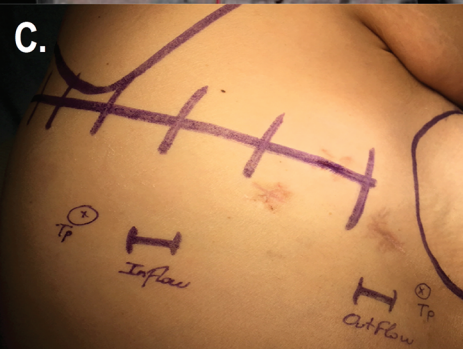
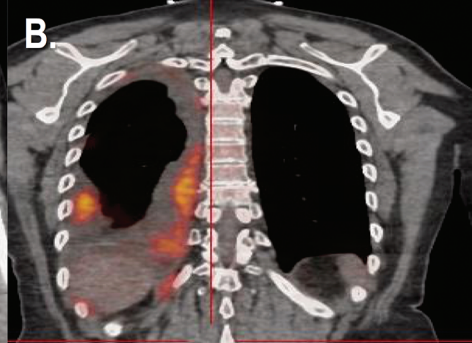
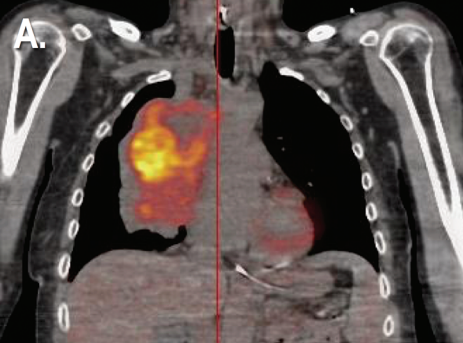
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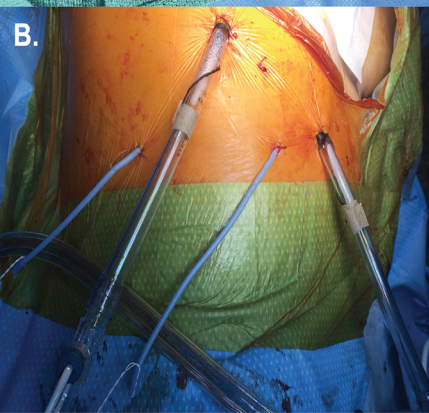
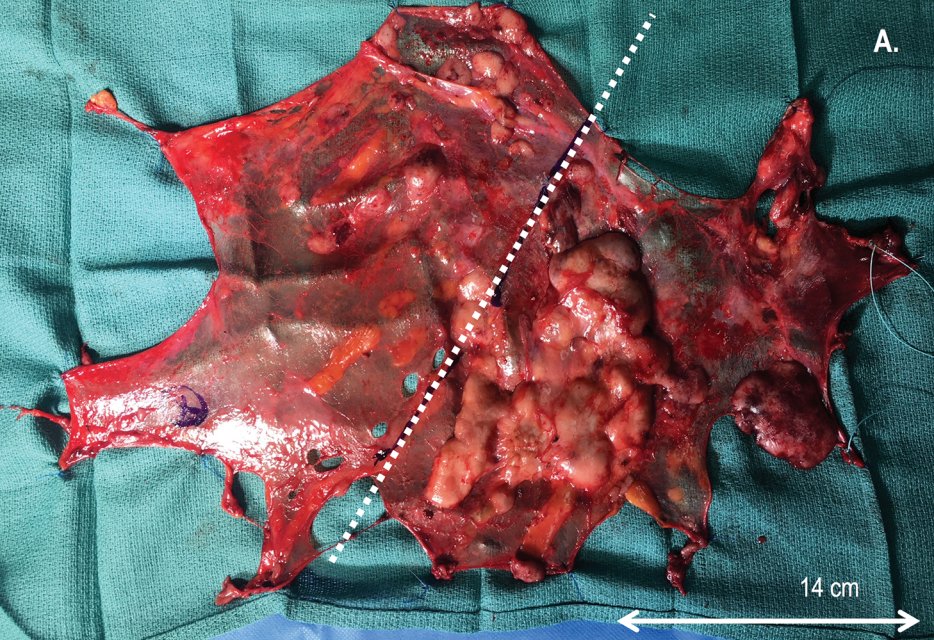
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Figure Legends

Figure 1. Pre-operative 18 FDG Ct-Scan: thymoma invading the superior vena cava (A) pleural localizations (B). Procedure for ITCH: (C) skin mapping of incision. (D) extra-pleural dissection of the lung. (E) Phrenic muscle after complete pleurectomy. (F) Gross examination of lung parenchyma.

Figure 2. (A) post-operative view of the resected parietal pleura; discontinuous white line separates upper and lower half. (B) Position of thermic probes and chest drain on the chest. (C) Monitoring screen during chemo-hyperthermia, *blue*: temperature inflow, outflow and patient; *orange*: patient solution's volume. *Purple*: solution flow.





C.

Cœur
 Ramassage circuit
 Extra ramassage circuit
 Préchauffage

CHAUFFEMENT
 Ramassage patient
 Hyperthermie (chauffé)
 Hyperthermie (non chauffé)
 Ventose (chauffé)
 Ventose (non chauffé)
 Ventose circuit
 Ventilation
 Arrêt fonction

Chauffage circuit patient
 Entrée
 Arrêt
 Marche
 Ventose

Œsophagienne (°C) (m)	41,5	Thoracique (°C) (m)	41,2
Intème 3	Non disponible	Sortie patient (°C)	41,2
Entrée patient 1 (°C) (m)	42,8	Entrée patient 2	Non disponible
Sortie chauffage (°C)	41,7	Entrée réservée	Non disponible
Pression (mm Hg)	31	DEBIT (l/min)	0,68
Durée (min)	2	Volume (l)	2,5

CONSIGNES

Température (°C)	46,0
Durée (min)	90
Volume (l)	2,5

ALARMES

Température max (°C)	50,0
Pression max (mmHg)	150
Temps max (min)	2,00
Volume max (l)	0,30

Cœur: Arrêt Marche Arrêt
 Type ID: CHD
 Capteur Pression: Cassés
 Filtrer: Collationneuse

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