Results of the Treatment of Cystic Hygroma with Intrallesional Bleomycin Injection: An Experience in 70 Patients

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Abstract

Background/Aim: Cystic hygroma is a congenital malformation of lymphatic system. Surgical excision is the treatment of choice and sclerosing agent injection into the cysts is an alternative one. The aim of this study was to review results of the treatment of cystic hygroma with intrallesional bleomycin injection in a 16-year period at a tertiary hospital for pediatric patients in Thailand.

Materials and Methods: Medical records of the patients with cystic hygroma treated by intrallesional bleomycin injection between 1992 to 2007 were reviewed. Bleomycin dosage of 0.3 – 0.6 mg/kg was injected into the cysts and repeated injections were performed at the interval of 2 – 6 weeks. Clinical outcomes were reviewed and analyzed.

Results: Seventy patients, 42 males and 28 females with age between one month to 14 years old, were treated with intrallesional bleomycin injections. An excellent response (complete clinical resolution) was obtained in 33 cases (47.1%). A good response (partial reduction > 50 % of the mass) was achieved in 25 cases (35.8 %). A poor result (no clinical response or mass reduction < 50 %) was noted in (17.1 %). Adverse reactions including fever, local swelling, redness and pain at the sites of injection were found in 30 cases (42.9 %). These reactions persisted only a few days. Three cases died due to pneumonia, respiratory failure and septicemia after bleomycin injection and partial surgical removal in 2 girls of the poor-result group. The third one in the excellent – result group developed thyroid carcinoma with metastasis at the opposite site of the first cystic hygroma. She died at another hospital because of intraoperative carotid artery injury with uncontrolled bleeding during left radical neck dissection.

Conclusions: Intrallesional bleomycin Injection is useful for treatment of cystic hygroma. It should be used in the patients with large cystic masses and extensive invasion in order to reduce the risk of vital organ injuries.

Key words
• lymphangioma
• cystic hygroma
• bleomycin

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Introduction

Lymphangioma or cystic hygroma is a congenital malformation of the lymphatic system that mostly presents at birth. The head and neck regions are the most frequently affected site, but lymphangiomas can occur throughout the body [1]. They are composed of lymph – containing endothelium – lined spaces which vary in size from channels of capillary dimension to cysts several centimeters in diameter [2]. Although histologically benign, these lesions can invade the surrounding organs and sometimes cause serious complications such as respiratory tract obstruction, nerve compression and intracystic hemorrhage [1-4]. Lymphangioma was first described by Redenbacher in 1825 [1]. Landing and Farber [5] classified lymphangioma into 3 groups: (1) lymphangioma simplex, composed of small capillary - sized, thin – walled lymphatic channels; (2) cavernous lymphangioma, comprising dilated lymphatic channels, often with adventitious covering; and (3) cystic lymphangioma or cystic hygroma, consisting of multiple cystic cavities filled with straw – colored fluid. Stal et al [6] divided lymphangioma into 4 groups including, capillary, cavernous, cystic and hemolymphangioma. Most of lymphangioma which occurs in children is cystic hygroma. The terms “cystic hygroma” and “lymphangioma” are often used interchangeably, and described a spectrum of benign cystic tumors of the lymphatic system [6]. Surgical excision is the treatment of choice but it is very difficult in some cases because of infiltrative nature of the multiple cysts to the surrounding organs. Complete excision can not always be accomplished and recurrences commonly occur after surgery [2,4,7]. Risks of surgical removal of lymphangioma include vital organ injuries, bleeding, infection and scar formation. Alternative treatments such as radiation therapy and injection of sclerosing agents had been tried but the results were not satisfactory [8-10]. Recent over years, two sclerosing agents, bleomycin and OK – 432, have been favored by some surgeons for the treatment of cystic hygroma [11-14]. Yura [11] was the first clinician to use bleomycin solution as a sclerosing agent for treatment of cystic hygroma. The results were effective in some cases but not so in some types of lymphangioma. A retrospective study was conducted to evaluate the effectiveness of bleomycin injection for the treatment of cystic hygroma or lymphangioma from a tertiary hospital for pediatric patients in Thailand.

Materials and Methods

Medical records of patients with cystic hygroma treated with intraliesional bleomycin injection at Queen Sirikit National Institute of Child Health between 1992 to 2007 were reviewed. The study was begun after the research proposal was approved by Institutional Review Board (Document No. 52 -030). Patient records were reviewed with respect to age at initial treatment, sites of the lesion and response of the treatment. Diagnosis of lymphangioma was made by physical examination and plain film x- rays in most cases. Ultrasonography and computerized tomography (CT) scan were done in some cases. Most of the patients (80%) were admitted as the in-patient service and some cases were managed at the out-patient unit. Complete
blood count and chest x-rays were examined before the procedure. Under general or local anesthesia depending on the patients’ age, cystic fluid was aspirated as much as possible. After aspiration, bleomycin solution (1 mg. in normal saline solution 1 ml) was injected into the cystic lesions with the dosage of 0.3 – 0.6 mg/kg and the maximum dose not more than 10 mg per injection [12]. Injections may be repeated at the interval of 2-6 weeks depending on the outcomes of achievement. Adverse reactions were observed within 24-48 hours. The patients were subsequently recalled for follow-up at 2 weeks to one month after injection. A chest x-ray was repeated at 6 months to one year. The criteria for clinical responses were based on the former reports [12,15,16]. An “excellent” response was considered if the masses disappeared completely or almost completely with slight induration. A “good” response was indicated if the masses diminished remarkably (over 50% reduction) with some residual lesions. A “poor” response was used in the cases in which the masses diminished slightly (under 50% reduction) or remained the same size.

Results

Seventy patients, 42 males and 28 females, with lymphangioma were treated with intrallesional bleomycin injections. Most of the cases (90%) were cystic hygroma. Age incidence varied from one month to 14 years (Table 1). Primary treatment with bleomycin injection was noted in 51 cases (72.9%) and the remaining 19 cases (27.1%) were treated by this method after recurrences from previous surgical excision. The most common site of lymphangioma was predominately in the neck with expansion into surrounding organs. The diameter of the mass was over 5 cm. in most cases. Bleomycin injection into the cystic lesions produced satisfactory results in 58 cases (82.9%) (Table 2). An excellent result (Fig. 1,2) was obtained in 33 cases (47.1%). Nine cases required only single injection. The cyst contents could be easily drawn from the cavities in large quantity in almost all of the 33 patients. Reduction of the masses was usually achieved by 2 weeks to 2 months. There was no recurrence during the follow-up period of over one year. A good result (Fig.3,4) was obtained in 25 cases (35.8%). In 5 of these 25 cases, the tumors recurred and subsequently required surgical excision. A poor response (Fig.5,6) was noted in 12 cases (17.1%). Seven of these 12 cases received 2-5 injections and were lost to follow-up without clinical response. The remaining 5 cases underwent surgery and only incomplete resection was accomplished. The details of clinical response correlation with various sites of the tumors were summarized in Table 2.

Minor side effects of bleomycin including local swelling, redness, pain and low-grade fever were noted in 30 cases (42.9%). They were noted within 24 – 48 hours after injection and mostly recovered within a few days. Marked swelling and inflammation of the tongue occurred in one case and persisted more than 2 weeks. Intracystic hemorrhage was found in 3 cases and was managed by aspiration with blood transfusion. Leucopenia was noted in 3 infants below one year of age and the white blood cells returned to normal limit within 2 weeks after drug administration. None of the patients developed pulmonary fibrosis during this study.
Three patients died within 1 month to 5 years after the last injection. Two cases of the poor-result group were female infants with 5 and 11 months of age. They had huge masses of the neck involving the upper respiratory tract with respiratory distress. They underwent tracheostomy and partial resection of cystic hygroma within one week after birth. The masses did not diminish and respiratory symptom persisted. The first girl received bleomycin injection 2 times at the age of 3 and 4 months. She died within one month after the second injection due to pneumonia, septicemia and respiratory failure. The second one received three bleomycin injections at the age of 7, 8 and 9 months. After the third injection, the mass became rapidly larger and repeated surgical removal was performed. She developed wound infection, pneumonia, septicemia and succumbed at the age of 11 months. The third girl was classified in the excellent-result group and died at 8 years old. She had a large right submandibular mass and received only one bleomycin injection at the age of 3 years. The mass disappeared within 2 months. Five years later, she developed follicular carcinoma of the thyroid gland with metastasis to the left cervical lymph nodes. Left radical neck dissection was performed at another hospital. Intraoperative carotid artery injury and uncontrolled bleeding resulted in postoperative mortality in this case.