Electrochemical therapy of tumors

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Abstract

Application of electric current for the tumor-destruction has a long time history. The theory of the direct galvanic current (galvano-therapy, GT) is worked out by B.Nordenstrom in the frame of biologically closed electric circuits (BCEC). Later GT was extended by chemical considerations (EChT) and starting with pioneering work of Professor Xin YouLing, a wide, intensive application had been developed in China. My objective is showing the principles and practice of the EChT treatment modality for multiple advanced lesions.

1. Introduction

The efficacy of electrochemical therapy (EChT) in mice with implanted Jensen sarcoma tumors was reported in 1953 by Reis and Henniger [1]. However, the clinical application of this modality was initiated by the Swedish radiologist, Bjorn Nordenstrom. In 1983, he published a book in which he described his theory of biologically closed electrical circuits (BCEC) and the results of two decades of research on EChT treatment of malignancies in animals based on this [2]. He also reported the results of EChT in 20 lung cancer patients with 26 tumors in which he used the "skinny needle" he had developed for biopsy purposes as an electrode.

Follow-up after 2 to 5 years revealed that 12 tumors had either disappeared or were markedly reduced in size. This study stimulated interest in utilizing EChT for treating lung malignancies, and Japanese researchers subsequently confirmed Nordenstrom's results in animals and in several patients [3-7]. Anyway, the real application of the technique widely has begun in China (China-Japan Friendship Hospital as the center of this application) after it was introduced to the country in 1987. Electrodes which special produced by platinum were inserted into tumor and connecting its with an apparatus, the current arouse strong chemical reactions around electrodes and lead degeneration and necrosis of tumor cells. It is a new type method to treat tumor without surgical resection. The final result is caused by current inducing chemical reactions, so we call it EChT.

The advantages of EChT are that it is much safer, easier to administer, and less costly than surgical procedures and can be just as effective in certain instances. In addition, it provides an opportunity to treat tumors in those patients in whom surgery, radiation, and/or chemotherapy has not been successful or may be contraindicated.

2. Experimental studies on mechanism of EChT

It has been well established that tumor cells are more sensitive to certain changes in the environment than adjacent normal cells. Various treatment approaches, including radiation, chemotherapy, hyperthermia, microwave, laser, and antiangiogenesis strategies, are based on these differences.

Multiple pathological changes occur in the tumor tissue during EChT such as pyknosis of nuclei, disruption of cell membranes, disappearance of mitochondria, as well as coagulation and necrosis of nuclear proteins [2]

In animal experiments, histopathological studies have demonstrated that the killing effect of EChT on tumor tissue in the anode area differs from that around the cathode area. Tumor tissue at the anode shows coagulation necrosis with destroyed cellular structure, pyknosis of cells, and denaturation. Tumor tissue around the cathode has a different pattern, it is characterized by necrosis due to liquefaction, complete disruption of cell structures and accumulation of water molecules due to the presence of positively charged sodium ions, large protein molecules. Although the features of damage are different in anode and cathode areas, the extent of tissue destruction is about the same [8].

On the basis of large amount of animal experiments and clinical pathological examination, the mechanism of killing action of EChT is electrolysis by direct electric current induces pH changes in the environment.

The killing action of DC per se is limited only around the surface of electrode. To expand the killing effect are the substances resulted from electrolysis of water and electrolytes, NAOH and HC1 that disseminate a certain distance from the electrode. Na+ formed after electrolysis will move toward the cathode and combine with OH ions to form NaOH which yields a strong alkaline environment (pH 12-14). Chloride ions accumulate around the anode and combine with H + to form HC1, which is strongly acidic (pH 1-2). The strong alkalinity and acidity are the main destructive mechanisms of EChT. During the application of

electrochemical therapy, large amount of foam ooze out from the surface of the electrode releasing Cl2 and H2O2 [9]. There are, however, additional mechanisms of action which are operative during EChT of tumors.

These can be summarized as follows:

The application of electric current increases the permeability of the cell membrane of tumor cells that allows ions to migrate inside cells and exert antitumor effects. Activity of enzymes in plasma can be released; proteins will be denatured and coagulated and precipitated whereby necrosis may be induced. Electrolysis changes the distribution of ions, which results in necrosis around the anode and edema around the cathode. That in turn, results in biological effects. Coagulation and extensive embolism may occur in blood vessels in the anode area, whereas significant edema in cathode area results in blockage of the microcirculation, and the blood supply to tumor cells is interrupted.

White blood cells and T lymphocytes accumulate in the anode area that may also have antineoplastic effects. At the same time, the negatively charged tumor cells are attracted to the anode so that metastasis of tumor cells may be hindered or prevented. Fragments of damaged tumor cells resulting from direct electric current application could serve as antigens and stimulate the body's immune system defences [4-7, 10].



The strong alkalinity and acidity are the main killing factors of EChT.



The figure of cancer cells disappeared and a mass of air bubbles came forth 10 minutes after beginning EChT.



The anode made tumor tissues dehydrated & carbonized, protein coagulated & necrosis.



Cancer cells were dissolved & breakdown, congestion & edema of tissue were representaed in the area of cathode.

3. Clinical application of EChT

The clinical applications of EChT to treat cancer began in 1983. In that time Nordenström reported 20 cases of lung cancer (26 tumors in number) which he treated with EChT. There were only 10 cases (12 tumors in number) disappeared or obviously reduced.

From 1987, the China—Japan Friendship Hospital in Beijing took the lead to using EChT, and they have finished more than thousands therapy for many kinds of malignant and benign tumors.

(1) Indication of EChT

When a cancer patient is not suitable for surgical operation, or radio-, chemotherapy are not effective, EChT may show its special effectiveness. The superficial tumors are well indication of EChT, such as cancer of head and face, breast cancer, parotid cancer, cancer of oral cavity, cancer of toque, cancer of superficial lymph node, melanoma, rhabdomyosarcoma, cancer of vulva, cancer of penis, etc.

Electrodes can be inserted accurately and arranged properly for those cases. Electric field for treatment can cover the whole cancer. Position and number of electrodes should be adjusted at anytime necessary. EChT could have satisfactory result if other treatment is ineffective.

Especially for late stage patients that have ulceration on the tumor (for example, local recurrence of operated breast cancer) which was not effectively treated in the past.

EChT can be a complementary method for surgical operation. For the cases which cannot be operated during thoracotomy (central type of lung cancer, mediastinal tumor), electrode could be inserted accurately to treat tumor.

It is the same for abdominal surgery and gynecological operation for cancers which could not be resected. (liver cancer, kidney cancer, pancreas cancer, ovarian cancer, etc.). Symptoms could be relieved and there is effectiveness to certain extent. [11-15]

The effectiveness of treating benign tumors is even admiring. In fact, EChT has been shown to be a unique therapeutic method and superior to surgery for treating venous malformation since there is no bleeding and no scar formation so that in addition to a good cosmetic result, function is maintained. [15, 16]

EChT was applied on breast hypotrophy and endometriosis in abdominal wall and satisfactory result has been achieved. [17]

Before EChT



13ms after ECht



During EChT



Male, 53ys. Suffered from a left thoractic & abdominal tumor, 14x8x4 cm. Both thoracic and abdominal cavity was opened but the tumor could not be resected. Pathologic diagnosis: neurofibroma. EChT was performed. The patient was followed up for 13 months and recovered well

(2) Complication of EChT and its management

EChT is relatively nontraumatic so that even fragile patients are able to tolerate the procedure without difficulty. A moderate rise in body temperature and in white blood cell (WBC) count may occur but a return to normal generally takes place after 3-5 days. DC is not harmful under 30 V, so EChT can be considered to be quite safe. During EChT a voltage much lower than 30 V is used but if the insulation around the cannula is not properly arranged, surrounding normal tissue and skin may be damaged. Such damage is usually limited and typically restricted to an area of about 0.5-1.0 cm in diameter around the electrode, and no treatment is needed since spontaneous healing takes place [12].

4. The procedure of electrochemical therapy

(1) Selection of Instrument and Electrodes

Instrument: Computer controlled ZAY-B multifunctional instrument is used. It has two outputs with data storage and print function. Electric current, voltage and electric quantity needed could be pre-set. Alarm system could be started when short circuit or disconnection occurs.

Electrode: Electrodes are made of platinum with a 0.7-mm diameter and 160 mm in length with high electrical conductivity and good anti-erosive properties. Needles are also coated with plastic catheter for insulation to protect normal tissue against electrical injury and strict sterilization is necessary.



Electrochemical therapeutic apparatus and electrodes: ZAY-B electrochemical therapeutic instrument and platinum electrodes. Made of China

(2) Manipulation

Cathodes are usually placed in the center of tumor and anodes in peripheral. However, both the cathodes and anodes could be placed one besides the other, alternately. Electrodes must be covered the whole tumor to avoid incomplete treatment. Insulating plastic tubes are used to protect normal tissue from injury due to electrolysis. Then electrodes are connected to the instrument to start treatment

Based on the data obtained from our experiments, the destruction radius of each electrode is about 1.0 cm. Since the distance between two electrodes should be less than 1.5 cm, the number of electrodes can be calculated according to tumor size. [9, 18]

When treating tumors in the lower part of the body, epidural anesthesia is recommended. When treating tumors in the other part of the body, general anesthesia is preferable.



No cancer cells remained when electrodes' distance is shorten than 2 cm.



The distance of electrodes is over 3 cm, Cancer cells can be found in the remaining area

There will be a rupture drop area of electric field between 2 electrodes when the distance of electrodes is over 2 cm. So 1.0~1.5cm will be the best choice of the distance between electrodes during EChT

(3) Requirement of electric current, voltage and electric quantity

Voltage usually used is 8—12 V and electric current is in a range of 80—180 mA. Electric quantity is determined by tumor size, usually 100 coulombs per 1.0 cm diameter of tumor mass.

(4) Duration of treatment

The concept of increasing electric current to high level in order to shorten treating time is wrong. That is because the action of EChT is electrolysis which needs time to perform the action. According to animal experiment, 4 V voltage and 20 mA is enough to have killing effect.

To improve the effectiveness of EChT for treating malignant tumors, following measures are recommended: [19,20]

(A) For patients with advanced tumor who can not be treated with other therapies, EChT might relieve their sufferings. And their life quality could be improved

(B) For large tumor mass, more electrodes should be needed. If short circuit does not occur, the distance between electrodes could be reduced to 1.0cm in order to increase killing effect

(C) EChT should be combined with radio-chemotherapy, because EChT could make tumor cells more sensitive to radio-chemotherapy. Positively charged antitumor agents, such as adriamycin and bleomycin, could be injected into the tumor, whereby the electric gradient will move the chemotherapeutic agent toward the cathodic area and destruct tumor cells. Systemic chemotherapy, interventional therapy, and immunotherapy could also be considered in combination with EChT

(D) Chinese herbs could improve immune system and inhibit growth of tumors, and may be a supplementary treatment to be combined with EChT.

The technical aspects are important. If possible, the needles should be inserted under direct vision. And the distribution of and the distance between electrodes should be rational and adjusted when necessary. The electric quantity should be adjusted to the type and the size of the tumor.

5. Summary

In 1987, Professor BJ Nordenström was invited to come to Beijing giving lectures on BCEC theory and demonstrated the use of EChT on malignant tumor.

Following three years of animal and clinical practice in China, good therapeutic effectiveness has been achieved. It was approved as a new therapeutic method to be used and spread clinically by the Ministry of Public Health of China

Over ten thousand cases of various kinds of tumors have been treated with EChT in China within 20 years. It could be used not only for malignant tumors, but also for some benign tumors, such as cavernous venous malformations. The effectiveness of it is even admiring with no bleeding, no scars left and no harm to the appearance and function.

EChT was also applied on breast hypotrophy and endometriosis in abdominal wall and satisfactory result has been achieved.

Typical cases

1.



M. 67ys. Right up lung cancer (Photo 1). Electrodes were inserted to the tumor (Photo 2). During EChT (Photo 3).

2.



Male, 42y. Cancerous ulcer in right thingt. 5.5x8.0 cm. (Photo 1). After 2 times EChT (Photo 2). No recurrence through 6 years following up (Photo 3).



M. 34y. Melanoma in left foot. Recurred after surgical resected. The wound didn't heal up and the tumor grew to 4.5x5.0 cm (Photo 1). 2 days after EChT (Photo 2).



4 weeks after EChT (Photo 3). The wound healed 7 weeks after EChT and no recurrence developed through 4 years following up (Photo 4).

4



M. 30 ys. Right upper limb soft tissue sarcoma recurred after 2 times surgery combing pulmonary metastasis, 13x21 cm (Photo 1). Tumor turned necrosis and fall off 5 days after EChT. The wound was healed 6 weeks after EChT (Photo 2). He died of lung metastasis after following up 20 months.



M. 67 y. Squamous cell carcinoma of low lip. The tumor became necrosis and formed a scar after EChT (Photo 2). A good figure of the patient 12 months after EChT (Photo 3).



M. 67 y. Lower lip cancer of squamous epithelium, recurred after surgical resection (Photo 1). Photo 2 shows the result 1 year after EChT.

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F. 52 y. Local recurrence after resection of right mammary cancer. Carcinoma ulcer grew to 12x10 cm (Photo 1). The tumor necrosed and surface of wound obviously reduced 7 weeks after EChT (Photo 2). The wound heated completely 9 weeks after EChT (Photo 3).

8



F. 62 ys. Breast cacner. Photo 1 shows the electrodes during EChT. Photo 2 shows the same patient 6 months after EChT.

9



F. 92 ys. Melanoma in left face (Photo 1), 6 months after EChT (Photo 2).



F. 61 ys. Recurrent cancer after operation on right eye (Photo 1). The tumor necrosed and dropped out after 1st EChT (Photo 2). The patient recovered well after second EChT was applied in 2 weeks later (Photo 3).



M. 4y. Venous malformations in right forehead. Operation failed due to uncontrolled bleeding. The diameter was 7.8x9 cm (Photo 1). The tumor disappeared and no recurrence developed after 3 years after EChT (Photo 3).

12



M. 32 y. Huge venous malformations in maxillofacial region. Many therapies had been tried but all failed (Photo 1). Photo 2 showed 1.5 years after EChT.

13



F. 2 y. Venous malformation in left maxillofactal region (Photo 1). During EChT (Photo 2), 2 years after EChT (Photo 3).



M. 32 y. Huge hemangioma in tongue. The tongue drop out of mouth and had a malfunction (Photo 1).



F.16y. Venous malformations in right maxillofacial region,tongue & lips. Speaking and foodintake were hindered (Photo1). 11 weeks after 1st EChT (Photo2). No recurrence for 3.5 years follow up. The well function of tongue and feature recovered.

16



F. 19ys. Venous malformation in tongue (Photo1). 1year after EChT(Photo2).

17



F,21ys. Maxillofacial & tongue venous malformation (Photo1,2). One year after EChT (Photo3, 4).

18



F.5ys. Up lip venous malformation reccured after surgical resection (Photo1). The patients' appearance after EChT (Photo 2, 3).

19



F. 7 ys. Venous malformation on left neck (Photo1, 2).



The same patient's MRI before treatment (Photo3, 4).



The same patient's appearance and MRI 1 year after EChT (Photo 5, 6, 7).



F. 14 ys. Severe maxillofacial vascular malformation (Photo1-4).



During EChT(Photo5). 3 years after 3 times EChT(Photo6,7).



M. 20 ys. Severe maxillofacial vascular malformation (Photo1-4).



During EChT (Photo5). 1 year after 3 times EChT (Photo 6). 3 times EChT and plastic surgery (Photo 7).

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