Case report
UDC: 616.22-006:616-098.1:615-085:504.06

Case report of a laryngeal squamous cell carcinoma treated with artesunate

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This present report describes the treatment of a laryngeal squamous cell carcinoma patient with the water-soluble artemisinin analog, artesunate. Artemisinin is a novel anti-cancer drug with demonstrated results in killing cancer cells. Artesunate injections and tablets were administered to the patient over a period of nine months. The tumor was significantly reduced (by 70%) after two months of treatment. Overall, the artesunate treatment of the patient was beneficial in prolonging and improving the quality of life. Artemisinin and its analogs offer promise for cancer therapy.

KEY WORDS: *Laryngeal Neoplasms; Carcinoma, Squamous Cell; Antimalarias*

Archive of Oncology 2002,10(4):279-280©2002,Institute of Oncology Sremska Kamenica, Yugoslavia

INTRODUCTION

Approximately one percent of all cancers originates in the larynx and laryngeal cancer comprises 45% of the carcinomas of the head and neck (1). The majority of laryngeal carcinomas are squamous cell carcinoma. Cancer of the larynx is most often found in males over the age of 50. It is often associated with heavy tobacco and alcohol use. The most common treatment options for laryngeal cancer patients are radiation therapy, surgery and chemotherapy.

In this case report, we implemented a novel therapy for the treatment of laryngeal cancer using artesunate, an analog of the antimalarial drug artemisinin. Artemisinin is a sesquiterpene lactone, isolated from the plant Artemisia annua L. (sweet wormwood). The artemisinin molecule contains an endoperoxide bridge that reacts with an iron atom to form free radicals (2), which causes macromolecular damage and cell death. Since cancer cells have a significantly higher iron influx via the transferrin receptor mechanism, they should be more susceptible to the cytotoxic effect of artemisinin. The anti-cancer potential of an analog of artemisinin has been studied in vitro with promising results (3,4). This report is the first on the use of artemisinin as an anti-cancer therapy in humans.

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The manuscript was received: 10. 08. 2002.

Provisionally accepted: 27. 09. 2002.

Accepted for publication: 08. 10. 2002.

CASE REPORT

A seventy-two year old vegetarian male with a long history of tobacco chewing and smoking was admitted to Vivekanand Hospital (Meerut, India) on December 15, 2000. The patient complained of progressive hoarseness, and loss of appetite and weight for the last eight months. For the last six months, he noticed a periodic difficulty in swallowing solid food that increased with time. Four months before coming to the clinic, the patient noticed pain in the right ear. The pain was piercing, of moderate intensity, and intermittent without any radiation. Two months prior to admission, he also noticed pain in the right side of neck below the mandible. This pain was of mild intensity, intermittent, and without any radiation. The patient was unable to swallow food 15 days before admission. As soon as he took solid food, it was immediately vomited out with a coughing reflex. The vomitus was blood stained. On the day of admission, the patient showed: 1) significant difficulty in swallowing of solid food; 2) hoarseness of voice; and 3) complaint of pain in the right ear and the right side of neck below the mandible. Physical examination revealed enlarged cervical lymph nodes on the right side of the neck. Laryngoscopic examination showed a growth on the right side of the larynx. The growth was covering the right vocal cord, right pyriform fossa, ventral aspect of epiglottis, and adjacent area of the lateral pharyngeal wall. The surface of the growth was irregular, nodular, ulcerated and bled on touch. Its size was approximately 3 cm x 2.5 cm x 3 cm=22.5 cm^3. The diagnosis was a stage II cancer of the larynx (T2 N1 M0). A diagnosis of differentiated squamous cell carcinoma was established after histopathological examination of a biopsy from the growth.

After obtaining consent from the patient, artesunate treatment was started on 01/22/2001. On day one of treatment, a capsule con-

taining ferrous sulfate (150 mg) and folic acid (0.5 mg) was given orally at 2:00 PM after a meal. Injections of artesunate (60 mg I.M. per day; Cadila Healthcare Ltd., Ahmedabad, India) were given from day one (01/22/2001) to day 15 (02/05/2001) at 10:00 PM of each day. One tablet of artesunate (50 mg; Cadila Healthcare Ltd., Ahmedabad, India) was taken orally at 10:00 PM after the evening meal every day from day 16 (02/06/2001) onward. The patient had been doing weight-bearing exercises since the treatment began. More details regarding the therapy can be obtained by contacting the first author.

The patient had a fever (100-101°F) from day four to day seven of the treatment. After starting the treatment his hoarseness of voice gradually reduced. Within two weeks of the treatment, his voice became clear. The patient was able to take solid foods quite comfortably. He regained a good appetite. Clinical examination revealed cervical lymph nodes were reduced in size. Laryngoscopic examination on 03/25/2001 showed a growth involving the right vocal cord, right pyriform fossa, and ventral aspect of epiglottis and adjacent lateral pharyngeal wall. The size of the growth was approximately 2.25 cm x 2 cm x 1.5 cm=6.75 cm^3, which was significantly reduced by 70% from its original size (22.5 cm^3 - 6.75 cm^3 = 15.75 cm^3, this equals a reduction of 70%). The growth was non-nodular and non-ulcerating. The patient gained two kilograms of weight in the two months since starting the treatment and felt physically and mentally strong. In an unrelated note, the patients had extensive patches of leukoderma around his mouth, on fingers of both hands, which responded well to artesunate treatment over the nine months of observation.

DISCUSSION

This is the first report on the use of a daily dose of artesunate for cancer treatment. We have previously reported that artemisinin selectively killed MOLT-4 lymphoblastoid cells (a human leukemia cell line) after incubation with holotransferrin (3), whereas the same treatment had significantly less effect on normal human lymphocytes. A similar effect was observed in human breast cancer cells (4). Furthermore, we found that oral administration of an artemisinin analog and ferrous sulfate retarded the growth of implanted fibrosarcoma tumors in the rat (5). A more recent study has also shown that artesunate can effectively retard the growth of various types of human cancer cells *in vitro* (6). Without treatment, laryngeal cancer patients die within an average of 12 months (1). The patient lived for nearly one year and eight months (until his death on 1/11/02 due to pneumonia) after the appearance of symptoms, although treatment was discontinued after nine months. Considering the complicating factors in this case, including the discontinuation of treatment and the late stage diagnosis, we feel artemisinin was successful in both prolonging and improving the quality of the patient's life.

The observations that the patient regained his voice, appetite, and weight after a short term treatment with artesunate and the fact that the tumor significantly reduced in size (by 70%), whereas no apparent adverse side effect was observed, indicate that this can be an effective and economical alternative treatment for cancer, especially in cases of late detection where available treatments are limited. Since this case, several patients with different types of cancers have begun treatment with artemisinin and its analogs with promising results. We feel that this emerging new therapy has promise to prevent and treat different types of cancers since it works via a simple mechanism which is common to all cancer cells (i.e. an increase in iron influx).

Acknowledgements

The authors are grateful to Miss Himani Singh for her help in preparation of the manuscript.

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