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Received: 27 October 2012 / Accepted: 23 November 2012 / Published online: 20 December 2012
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Abstract The uptake of fluorodeoxyglucose Positron Emission Tomography in the tumors of various cancer types demonstrates the key role of glucose in the proliferation of cancer. Dichloroacetate is a 2-carbon molecule having crucial biologic activity in altering the metabolic breakdown of glucose to lactic acid. Human cell line studies show that dichloroacetate switches alter the metabolomics of the cancer cell from one of glycolysis to oxidative phosphorylation, and in doing so restore mitochondrial functions that trigger apoptosis of the cancer cell. Reports of dichloroacetate in human subjects are rare. The authors contacted individuals from Internet forums who had reported outstanding anti-cancer responses to self-medication with dichloroacetate. With informed consent, complete medical records were requested to document response to dichloroacetate, emphasizing the context of monotherapy with dichloroacetate. Of ten patients agreeing to such an evaluation, only one met the criteria of having comprehensive clinic records as well as pathology, imaging and laboratory reports, along with single agent therapy with dichloroacetate. That individual is the focus of this report. In this case report of a man with documented relapse after state-of-the-art chemotherapy for non-Hodgkin’s lymphoma, a significant response to dichloroacetate is documented with a complete remission, which remains ongoing after 4 years. Dichloroacetate appears to be a novel therapy warranting further investigation in the treatment of cancer.

Keywords Dichloroacetate · DCA · non-Hodgkin’s lymphoma · NHL · PET · PET/CT · Glycolysis · Metabolomics · Warburg
Abbreviations

DCA (dichloroacetate)
NHL (non-Hodgkin’s lymphoma)
PET (Positron Emission Tomography)
CT (computerized tomography)
FDG (fluorodeoxyglucose)
SUV (standardized uptake value)
mg (milligrams)
kg (kilograms)
R-CHOP (rituximab-Cytoxan, Hydroxydaunomycin, Oncovin, Prednisone)

Background

The metabolic profile of malignancy has been characterized as one associated with metabolic adaptations directed to preferentially utilize pathways involved with glycolysis (Warburg et al. 1927), which in the recent literature has been termed the glycolytic phenotype of cancer. (Bui and Thompson 2006; Fang et al. 2008; Gatenby and Gawlinski 2003) In essence, this glycolytic phenotype is a Darwinian adaptation in that the cancer cell diminishes and undermines the metabolic pathways of glucose oxidation used by normal cells for energy production, and also for tumor cell elimination (Fang et al. 2008). One crucial normal cell function compromised in the battle with cancer involves mitochondrial programmed cell death or apoptosis. On the basis of the above observations, agents that target tumor metabolism, and specifically the mitochondrial ATP-producing pathways, are currently in clinical trials.

Dichloroacetate (DCA) has been used over the past 30 years to treat congenital lactic acidosis—a rare metabolic disease that occurs mostly in children and young adults. (Berendzen et al. 2006; Kuroda et al. 1986; Stacpoole et al. 1997, 2008, 2006). Congenital lactic acidosis is associated with various inborn errors of mitochondrial dysfunction, and almost a thousand peer-reviewed medical publications are focused on the clinical use of DCA for this disorder. Numerous additional articles on various aspects of DCA pharmacology, metabolic effects and toxicity have also been published, but only a dozen or so papers on DCA relate to its anti-cancer activity (Bonnet et al. 2007; Bui and Thompson 2006; Cao et al. 2008; Chen et al. 2007; Christofk et al. 2008; Madhok et al. 2010; Michelakis et al. 2010, 2008; Vander Heiden 2010; Wong et al. 2008), with many of these restricted to evaluation of DCA in tumor cell lines, or in non-human animal models (Cao et al. 2008; Madhok et al. 2010; Wong et al. 2008; Sun et al. 2010). Only the publication by Michelakis et al. (2010) evaluated DCA in five human patients with glioblastoma multiforme (Michelakis et al. 2010). This, however, is the first report of a cancer patient undergoing monotherapy with DCA with the induction of a complete remission post-relapse after state-of-the-art chemotherapy with rituximab-CHOP.

Methods

Patient population

The authors SS and OA solicited all individuals who had reported favorable anti-cancer responses to DCA on Internet forums, and asked if they would agree to make their complete medical records available for detailed analysis, at no charge. Such parties were informed that the purpose of the study was to ascertain whether monotherapy with DCA could be confirmed as an active anti-cancer therapy.

Medical legal issues

Written informed consent to use detailed medical data as well as radiologic images was obtained from the subject of this case report. A copy of the written consent is available for review by the editor of this journal.

Patient exclusion criteria

Copies of all consultations and office visits, pathology reports, imaging and laboratory studies, surgical reports, radiation therapy data and chemotherapy details were requested. Of 10 possible candidates, 5 provided grossly insufficient medical records to allow for any assessment of DCA efficacy. In 3 other candidates, another treatment was commenced just before or soon after DCA was started. In 1 candidate, DCA had never been started. One of the five individuals with insufficient records was diagnosed with a non-Hodgkin’s lymphoma and appeared to have had a major response to DCA monotherapy but unfortunately he did not respond to our communications for complete medical records. In the remaining individual (TM), the subject of this report, full medical records were obtained. This individual, described in this report, was not treated by the authors.

Financial burden to participants

For every case where the initial reviews of medical records indicated a response to monotherapy with DCA, the full medical records were requested, reviewed and abstracted to an electronic health record by SS and OA. In such cases, the diagnostic pathology slides and/or tissue blocks were obtained and sent to an expert in hematopathology for a second opinion. Full imaging data in the form of Dicom files were obtained and reviewed by co-author RB, a board-certified radiologist.