Acute Myelogenous Leukæmia: An Orthomolecular Case Study

Erik T. Paterson, M.B., Ch.B., D.Obst.R.C.O.G., F.B.I.S.

Abstract

A case is presented of a 55 year old male who developed Acute Myelogenous Leukæmia of sudden onset. There being insufficient time for Orthomolecular therapy to be effective, he was obliged to risk chemotherapy, which he survived despite numerous expected and unexpected complications. In between the three rounds of chemotherapy he tried to use Orthomolecular means to improve his condition and enhance his survival. He is now in "Complete Remission" and feeling well, using such techniques. The issue requiring resolution is the advisability of using chemotherapy with Orthomolecular techniques concurrently to improve survival of patients with Acute Myelogenous Leukæmia.

Key words: Leukæmia, Acute myelogenous, chemotherapy, Orthomolecular.

Introduction

Within the memory of many physicians now living, the diagnosis of Acute Myelogenous (or Myeloid) Leukæmia (AML) was an automatic sentence of death for the patient.[1] Hope for the management of all the leukæmias dawned in the 1960s when chemotherapy began to bring about complete remission for most, but not all, patients with Acute Lymphoblastic (Lymphatic) Leukæmia (ALL), an illness which strikes patients in the age range from early childhood to the early twenties. Chronic Lymphocytic Leukæmia (CLL) remains almost resistant to chemotherapy, although it has the best prognosis of the leukæmias with some patients surviving from time of diagnosis as much as twenty five years or more. Chronic Myelogenous Leukæmia (CML), with a much poorer prognosis than CLL, is starting to yield to chemotherapy, the most favourable form being the cytokines, Interferon in particular. With chemotherapy or bone marrow transplants new hope has come for patients with AML.

AML is not an uncommon illness. In fact its incidence in the population has been rising in recent decades. The age distribution tends to be from the early twenties to old age. While generally its cause remains unknown, there is a strong statistical relationship between AML and exposure to radiation–an almost linear relationship between the risk of AML and the total exposure to X-rays, for example. Another strong relationship exists between AML and previous chemotherapy for other cancers, Hodgkin's Lymphoma in particular. The role of pollutants is strongly suspected but unproven (the absence of proof never meaning proof of absence).

There are two currently accepted lines of management of AML.

That which has received the most publicity is bone marrow transplant because of its promise of "cure." In conventional allogeneic bone marrow transplantation, a donor of tissue type close to that of the patient provides bone marrow. The bone marrow of the patient is, hopefully, destroyed either by radiation or aggressive chemotherapy. The donated marrow is transplanted and the almost inevitable rejection reactions are suppressed by Cyclosporin. In autologous bone marrow transplantation, still experimental, the patient receives chemotherapy. When the marrow recovers it is harvested and grown in the laboratory, hopefully without the blast cells which are the origin of the leukæmia. The patient then receives the same aggressive chemotherapy to destroy his/her marrow,

1. 12-1000, Northwest Boulevard, Creston, B.C., Canada V0B 1G6

and the harvested marrow is re-implanted.

The other accepted line of management is chemotherapy. This consists of Cytosine arabinoside (Ara-C), or less commonly Idoxuridine, in combination with other agents such as Mitoxantrone and Etoposide. Formerly this was performed as two rounds of chemotherapy followed by maintenance oral chemotherapy. More recently the recommended regime consists of three rounds of chemotherapy without the oral medication afterwards.

Recent results suggest that chemotherapy is marginally superior in outcome to bone marrow transplantation. In either case the mortality rate is about fifty percent by six months after the date of diagnosis. In one centre, if the patient shows no recurrence by two years following the date of diagnosis, the survival curve becomes flat at approximately thirty percent (although there are trends suggesting forty five percent survival). This, of course, means that 55-70% of patients are dead within two years.

The operative word in the above account is "accepted" since most major Leukæmia treatment centres do not recognize additional nutritional support as an aid to enhancing the effectiveness of therapy either during the chemotherapy or after.

The following case report illustrates one attempt by a patient to ensure his survival using Orthomolecular means.

Case Report

At the time of diagnosis the patient was a fifty-five year old, family physician, in practice in a western Canadian rural community. He was a non-smoker and his use of alcohol was slight. Other health problems included asthma, allergic rhinitis, and a minor degree of temporal lobe (partial complex) seizures. He had no known drug sensitivities except for gastric intolerance of niacin. In the course of practice he had been exposed to X-rays and, as a patient with other health problems, had been subject to barium studies of the gastrointestinal tract. For nineteen years he had been a practicing anæsthetist exposed to unvented anæsthetic gases, but had given this up five years before becoming ill with AML.

The first symptom suggestive of the onset of AML was unusual bleeding of his gums after brushing his teeth. About five to seven days later he developed nausea of sudden onset followed less than one hour later by a rapidly rising temperature accompanied by mild R chest discomfort. In the emergency department of the local community hospital his family physician discovered that his white blood cell count (WBC) was $41x10^9$/L (upper level of normal being 11). Intravenous antibiotics began to be administered. The following morning, at a regional hospital, the diagnosis of AML was established, and transfer to the Bone Marrow Transplant/ Leukæmia (BMT) unit of a tertiary care hospital was arranged.

In the BMT unit investigation revealed a WBC of 37.5 with a differential including 22,000 blast cells, hemoglobin (Hb) of 114 g/L, platelets of $15x10^9$/L (the normal range being >150), normal coagulation studies, normal creatinine, glucose and uric acid, and normal liver function tests apart from elevations of LD and AST.

Following a bone marrow biopsy to establish the diagnosis and sub-type the AML for prognostic purposes [It was FAB (France-America-Britain) type M4, or Acute Myelomonocytic Leukæmia, carrying a better prognosis than some of the other types, but not the best. Cytogenetic analysis was unremarkable otherwise.], a first bolus of Ara-C was administered at 6.75g IV over two hours, the WBC then being 36.6. Near midnight, over 48 hours after the acute illness began a Hickman line (a triple lumen, long term catheter) was established into the patient's superior vena cava or right atrium. Over a period of about 72 hours further Ara-C (3.38 g/day) and

Mitoxantrone (27 mg/day) were administered, followed for a further 17 hours by Etoposide (1,800 mg). Steroid eye drops were administered every four hours. This being completed the WBC had fallen to 3.0, with a Hb of 81 and the platelets were 10.

With persistence of the pyrexia, four antibiotics, Vancomycin, Tobramycin, Ceftazidime and Metronidazole, were continuously administered intravenously. Allopurinol was given orally to prevent renal failure due to the hyperuricæmia which is such a common feature of early therapy for AML. Acyclovir was also administered to prevent viral superinfections. Seventeen transfusions of packed cells were administered, the Hb reaching a minimum at one stage of 45. Even more frequently, 112 platelet infusions were administered, the count at one stage reaching a minimum of 3. He also received nineteen units of Albumin. All the blood products were CMV negative irradiated.

The following complications of treatment occurred during this first round of chemotherapy:

1. Vomiting, anorexia, diarrhœa and hair loss as is almost routine with aggressive chemotherapy.

2. Rhabdomyolysis. This was accompanied by a fever which was reported to the patient's wife as being 47° C. Vigorous cooling of the patient by his family restored survivable temperatures. No action was taken by either the medical or nursing staff.

3. A widespread, blistering eruption of the skin which was initially presumed to be due to a viræmia, but later shown to be caused by a severe reaction to the Allopurinol. By the time this drug was stopped, the hyperuricæmic threat was over.

4. Marked œdema caused by fluid overload, and resulting in a mild form of Adult Respiratory Distress Syndrome (ARDS). This was managed by appropriate diuresis and more careful control of fluid balance.

5. Dyspnœa accompanying mild pain of the lower one third of the left Soleus muscle with a negative Homan's sign. This was presumed to be Pulmonary Thromboembolism which was investigated excessively with no such state being found. It was, in fact, due to the combination of the ARDS and the patient's asthma.

6. Atrial flutter or fibrillation. This resolved spontaneously with more careful management of his fluid balance.

7. Stomatitis. This required intravenous Morphine until it resolved spontaneously.

About four weeks after the onset of the illness the WBC had recovered enough that the feverishness had settled. The antibiotics could be stopped.

Six days later a repeat bone marrow biopsy showed the number of blast cells as being less than five percent of the total, defined as "Complete Remission".

In all this time the patient was not permitted to receive any more than 500 mg ascorbic acid per day, even though his usual, premorbid dose had been 10g per day (with vitamins E, A, D, B_1, B_6 and a potent multivitamin preparation, along with supplementation of calcium and magnesium).

He was discharged to the care of his family in a small rental apartment near the hospital and was followed in the BMT Day Care Unit. He was advised that the second round (first "consolidation" round) of chemotherapy would begin after two weeks.

Four weeks later, at the time of the second admission, his condition had spectacularly improved. During this interval he had undertaken increasing exercise and consumed increasing doses of vitamin C. Nevertheless the vomiting still occurred at times provoked by the slightest digestive mis-step. This last was investigated endoscopically in another tertiary care hospital and infection by Helicobacter pylori was suggested but unproven. The patient elected to delay therapy for this until it was clear that he was able to survive the subsequent rounds of chemotherapy.

He also experienced episodes of de-

pression but the oncological Psychiatrist felt that it was best to leave these untreated, a conclusion with which the patient agreed.

The drug regime of the second round of chemotherapy was exactly the same as the first. The antibiotics used this time were Ceftazidime, Tobramycin and Vancomycin. None of the above noted complications occurred except the first. However, an acute necrotising mucositis involving the buccal cavity, tongue and pharynx occurred.

This was managed by Total Parenteral Nutrition and intravenous morphine for a period of about eleven days. Blood transfusions of 10 units and 30 units of platelet infusions were administered as before. After thirty seven days the patient was again discharged.

The initial recovery period was marked by an infection of the Hickman line which had to be removed, antibiotics failing to control the infection. It is not on record what dose of vitamin C the patient reached during this seven week interval but continued gastrointestinal delicacy did not permit a rapid increase in dosage.

At the start of the final round of chemotherapy the patient showed a granulocytopenia with a WBC of 2.3 necessitating another bone marrow biopsy, which turned out to show no abnormality. A fresh Hickman line was established and treatment with the Ara-C and Mitoxantrone only was given as chemotherapy, the same doses as before. Again intravenous antibiotics (with the addition of Acyclovir and Amphotericin-B as prophylaxis for viral and fungal infections), blood transfusions (eight units) and platelet infusions (34 units) were administered. The problems in this round included a more prolonged recovery time for the bone marrow, and elevated creatinine, along with low potassium and magnesium levels. This was almost certainly due to renal tubular trauma caused by the Amphotericin-B, a problem which has persisted to the time of this writing and which is unlikely to resolve. The other significant problem was the development of a low grade allergic reaction to the platelets, treated prophylactically with Benadryl at the cost of considerable sedation to the patient each time it was administered.

Eight days after discharge, the Hickman line was removed by the oncologist in charge of the final round of chemotherapy, who advised the patient that there was nothing further to offer by way of after care except regular blood tests. Only in the event of a recurrence of the AML would any other active therapy be considered. This the patient was not prepared to accept.

At home, convalescent, the patient began a programme of increasing doses of nutrients, as well as maintaining the necessary replacement of potassium ("Slow K" 600 mg three times per day) and magnesium (in combination with calcium and vitamin D, 1000 mg per day). As far as vitamin C is concerned, see below. Depending on his gastric tolerance, he began to take vitamin E 1000 IU per day, a multivitamin and mineral capsule daily, Thiamine and pyridoxine 500 mg each daily, halibut liver oil (as a source of vitamins A and D) one capsule daily, Evening Primrose oil 800 mg capsules three times daily, Coenzyme Q_{10} (Ubiquinone) 150 mg daily, and Dehydroepiandrostenediol 333 mg daily.

The dosage of vitamin C is of particular interest. At first the patient's tolerance of this was governed by his gastric tolerance. As this improved he was able, over less than two months, to build the total daily dose up to 60 grams per day in divided doses. For the lower doses he used 1000 mg tablets. As the amounts built up he switched to calcium ascorbate powder dissolved in unsweetened juice–a level teaspoonful being equivalent roughly to 4 g, or a level commercial coffee scoop being equivalent to 10 g. The top dosage was determined by bowel tolerance, any higher dose than 60 g per day causing diarrhœa.

As the patient's convalescence pro-

ceeded and his condition improved the diarrhœa recurred forcing progressive reductions in dosage down from 50 g, gradually through to 10 g and, recently, 8 g daily.

Less than thirteen months after diagnosis of the AML, with persistently normal hæmatological tests, the patient returned to full time medical practice.

Discussion

A more detailed, but non-technical, account of the events described above has been published elsewhere.[2-16]

One fact omitted from the Case Report is that the patient had considered for the twenty years prior to the onset of the AML the possibility that he might develop one of the leukæmias at some time. Being a practicing Orthomolecular Physician he had decided that, in that eventuality, he would not accept standard chemotherapy. Equally he knew that for Orthomolecular therapy to work, time in the order of several months would be needed before the benefits of such therapy would become apparent.

At the onset of his illness he was forced to reconsider the above decision because of the acuteness of the AML. He had only days to live before he would succumb to renal failure from the hyperuricæmia (a death experienced by the sister of a close friend) or infection. He was not an acceptable candidate for renal dialysis. Survival for the time necessary for orthomolecular therapy to work was highly unlikely.

When he arrived at the BMT unit he was faced with further difficult decisions. There was a ten percent chance that the chemotherapy would not work at all, and he would die as a result. There was another ten percent chance that the complications of the chemotherapy would be lethal for him (and, indeed, at one stage it was presumed by the staff of the BMT Unit that he was dying of such complications). Two analogies were presented to him. The first was to imagine a garden overgrown with weeds. The garden was sprayed with gasoline and a lighted match was tossed in. The hope would be that something useful would survive the holocaust. The other was to imagine being poisoned to death and then there being an attempt to rescue him. The patient was too old for consideration for a bone marrow transplant. In any event the only likely donor, his sister, had breast cancer only a few years before and was, hence, not acceptable.

Having made the decision to proceed with the chemotherapy the patient was disturbed that no consideration was taken of his previous intake of vitamins. Indeed it was with considerable reluctance by the medical staff of the BMT Unit that he was given as little as the 500 mg vitamin C. As far as he could he tried to make up for this in the intervals between the rounds of chemotherapy when he was out of hospital, the limiting factor being his gastric tolerance. Having completed the chemotherapy he could proceed to be more aggressive with his use of nutrients. What was the rationale for this, and what so far has been the outcome?

That there may be a role for ascorbate in cancer therapy has been known for more than twenty years.[17] Even more specifically it has also been known that in vitro growth of the cell cultures of AML are suppressed by ascorbate as shown by Park et al.[18] That most forms of cancer might respond favourably in a clinical setting to ascorbate and other nutrients has been shown by Hoffer and Pauling[19,20] in terms of survival times, the word cure not being used, these writers not being the only ones making such a claim.[21, 22] It might be objected that the Mayo Clinic study [23] refuted the value of such vitamin C therapy in cancer. This objection is not sustainable because of two reasons. The first is that the Mayo study figures included patients who survived for too short a time for the vitamin C to have had an effect, e.g. one patient who survived only two days. The second is that no pla-

cebo controlled study in cancer patients (or most other diseases for that matter) is ethical.[24,25] On the other hand, whether vitamin C is given orally or intravenously the dose tolerated is a reflection of the current condition of patients (deteriorating or improving as the case may be) as determined by "titrating to bowel tolerance" as defined by Cathcart.[26]

Analogous considerations apply to the other nutrients the patient is using as listed above. It might be objected that niacin is missing. However the patient knows from previous experience that he has an idiosyncratic gastric intolerance of this.

None of the nutrients mentioned are known to have any adverse influence on the effectiveness of the chemotherapy or upon the measures taken to rescue patients from the complications of chemotherapy. As far as ascorbate is concerned Hoffer[27] has cited a meeting at Bethesda, Maryland in 1990, co-sponsored by the National Cancer Institute, at which ascorbate was shown to decrease the toxic effects of both radiotherapy and chemotherapy against normal tissue while sensitizing malignant cells against the same forms of therapy. Prasad and Rama[28] showed that pre-treatment with ascorbate yielded improved outcomes after radiotherapy. Since the effect of chemotherapy upon individual cells is the same as that of radiotherapy, similar efficacy of ascorbate as a protective agent for normal tissues and as a sensitizing agent of neoplastic tissues is to be predicted until proven otherwise. Vitamin B_3 has been shown in numerous animal studies to enhance the effectiveness of both chemo- and radiotherapy while being protective of normal tissues. Over fifty years ago it was shown[29,30] that this vitamin improved outcomes in cancer patients, along with other nutrients. And Canner et al.[31] showed that this same vitamin reduced the death rate from all causes including cancer, i.e. niacin is the only substance known to prolong people's lives over the long term. Vitamin E may have a protective effect against cancer. Studies of its role as protective of normal tissues against the toxic effects of chemotherapy are woeful by their absence. Ubiquinone (commonly known as Coenzyme Q_{10}), a central coenzyme in oxidative phosphorylation, has been shown to prolong life in cancer patients.[32] Minerals, selenium in particular, have an antineoplastic effect when given in deficiency states.[33]

These results consider nutrients given alone and should warrant more serious consideration by the oncological community. But what if they are given in combination? Is there evidence to suggest a synergistic effect? Rueff. [34] Kallistratos et al.[35] and Winn and Levin,[36] found that there was indeed such an effect.

Since all the nutrients mentioned here are safe in much higher doses than those of the RDAs, can be administered safely both orally and, in the event of gastric disturbance, intravenously, and are effective both in the prevention of the adverse effects of chemotherapy and radiotherapy while yet enhancing their efficacy, it seems strange that this patient was not offered their benefits during all three rounds of chemotherapy for his AML.

As of the time this is being written, the patient is at the third anniversary of the diagnosis of his AML and remains well. Does this mean that recurrence of the AML will not happen? After all he has not passed the fifth anniversary, let alone the tenth, the usually accepted criterion for cure of cancer. Time will tell.

By now it will be apparent that the patient described is the writer, myself. How do I feel about my situation? I am reminded of a conversation between myself and a very good friend of mine, Dr. Gary Deatherage, a Clinical Psychologist. I was between the first and second rounds of the chemotherapy and expressing my despondency about my future. He asked me what my response would have been if he had asked me how

long I was likely to live before I knew I was ill with the AML. I muttered and stuttered. Then he asked, "What has changed?" Of course, nothing has changed. I still cannot say how long I am likely to live.

But I am determined to bias my chances by continuing the fight against a recurrence of the AML using Orthomolecular techniques.

Afternote

Another Orthomolecularly oriented Physician developed AML a matter of a few months before myself. He received a bone marrow transplant, experienced many complications of this, and basically had to fight for his life. Using Orthomolecular techniques, including self-administered EDTA chelation therapy, he now is well and has built up a busy practice.

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