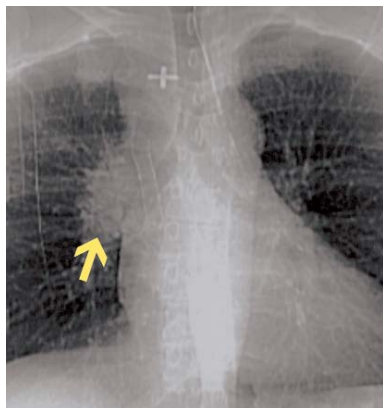


Lung Cancer

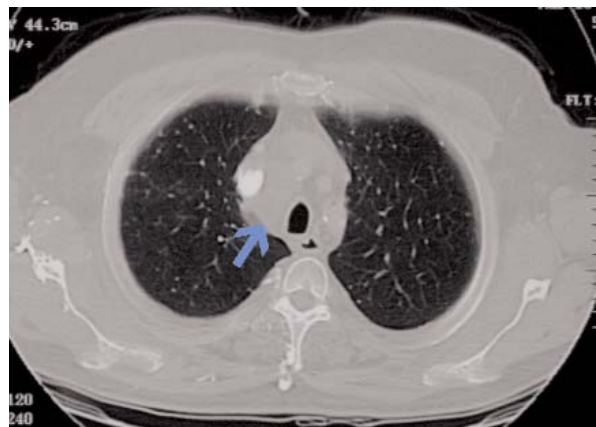
Adenocarcinoma With Sustained Remission After Brain and Adrenal Metastases - Earl Daniels' Extraordinary Survivorship

This lung cancer victim was treated with immunotherapeutic intent. Objective evidence accumulated during the course of this treatment supports the operation of a host-mediated immune response believed central to this patient's sustained remission status.



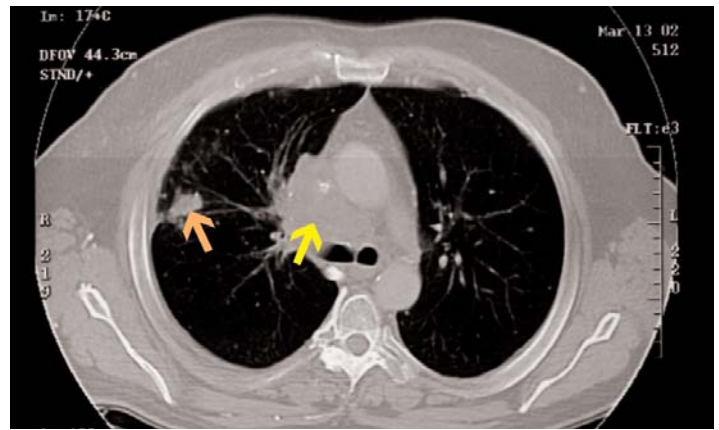
Earl Daniels presented in March 2002 with a swollen face, shortness of breath and weakness. His chest X-ray revealed a prominent mass in the right hilar region and a markedly widened upper mediastinum (area between the lungs). His CT scan of the chest, below left, with vascular contrast showed delayed emptying next to the right collar bone and absence of blood on the left side indicating nonfunction of veins on that side, probably due to clot. These findings indicated a blockage of venous return to the heart. This causes what is known as superior vena cava syndrome, because large vessels returning blood to the heart in the upper chest are blocked (purple arrow). Red arrow on the CT scan designates numerous vessels adjacent to the right collar bone (green arrow) containing stagnant blood and not seen on the other side.

March 2002 - Chest CT scan at presentation shows bulky mediastinal tumor causing superior vena cava syndrome



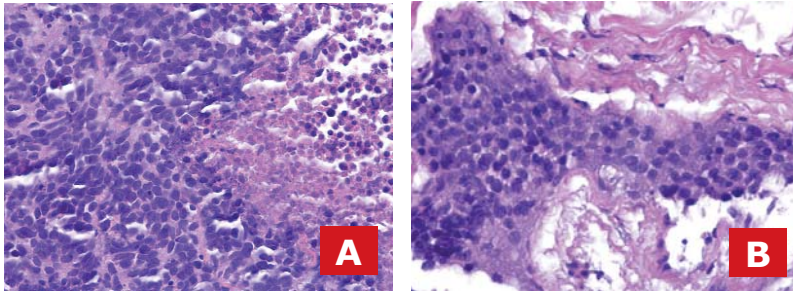
Slightly lower in the chest, a mass begins which extends throughout the upper chest down to the branching of the trachea. This mass protrudes in the root of the right lung (blue arrow) where blood comes and goes from the right lung. It was along the path of this large mass that the superior vena cava was compressed causing the superior vena cava syndrome.

You will also notice (orange arrow) a mass in the right upper lung which was suspected to be the site of origin for the tumor that spread between the lungs. The cancer was secreting CEA at a high level. The serum carcinoembryonic antigen (CEA) was 156. This degree of CEA elevation is found in lung cancer almost exclusively with adenocarcinoma.



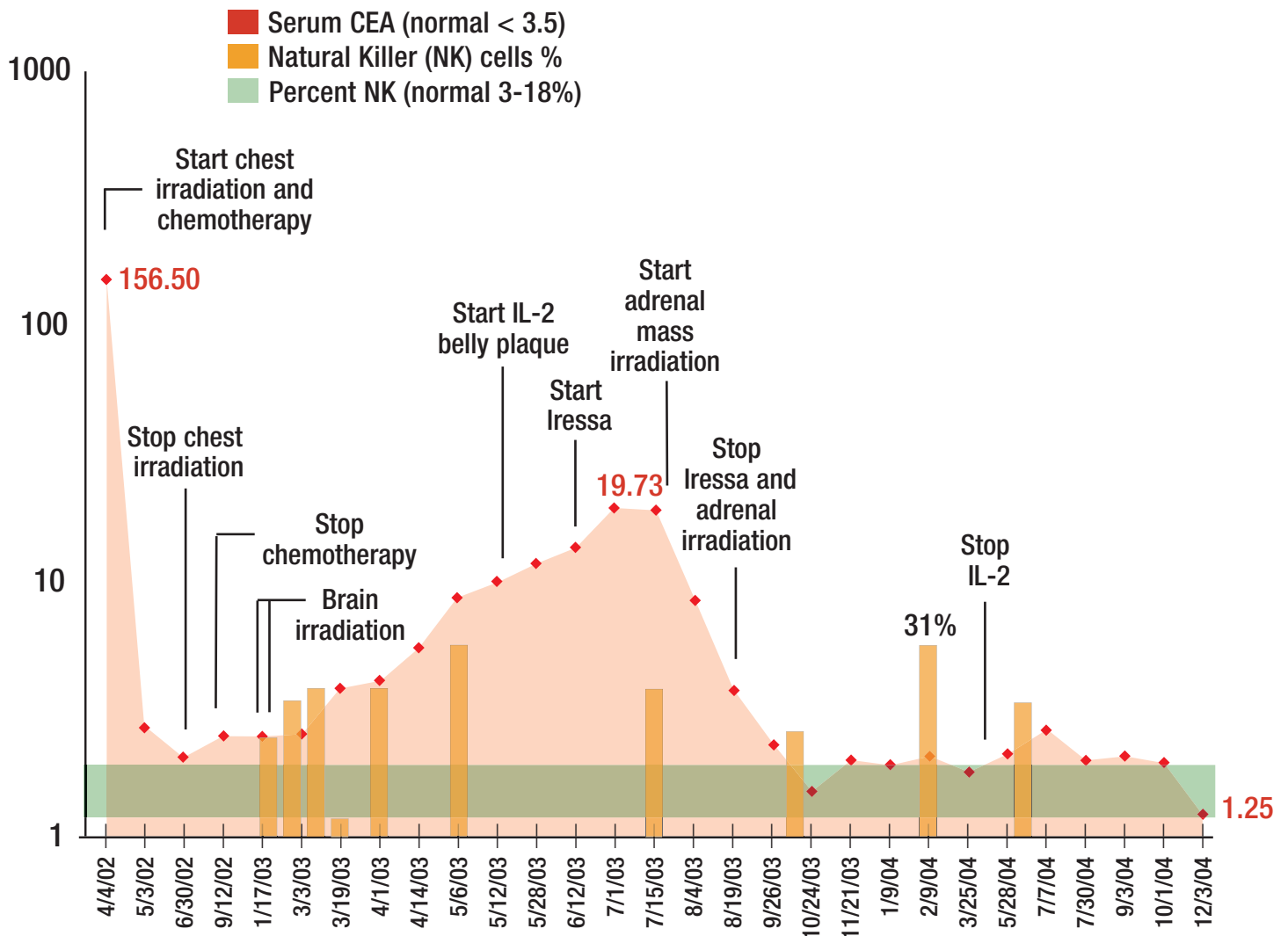
Pathology

Biopsy of the mediastinum revealed a tumor consisting of small cells in some areas (A) and other areas containing larger cells with moderate cytoplasm (B).

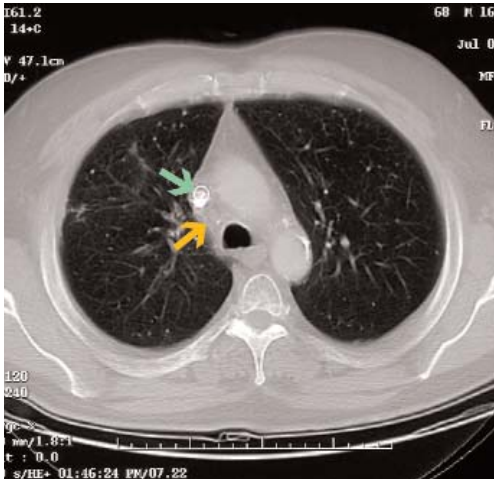


The stain for neuronal origin was negative. The tumor was interpreted as a mixed small cell and large cell adenocarcinoma with characteristics of adenocarcinoma.

Under initial combined concurrent radiotherapy and chemotherapy, the markedly elevated CEA returned to normal.



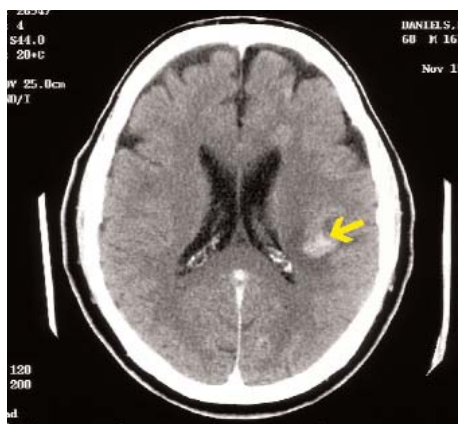
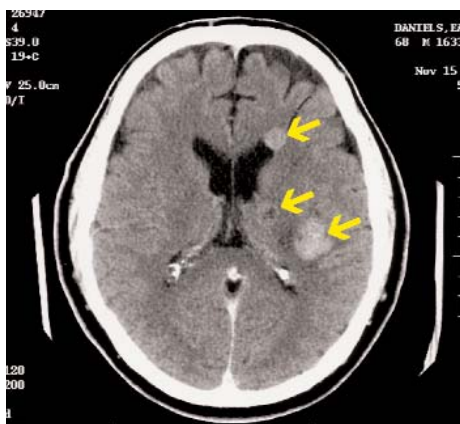
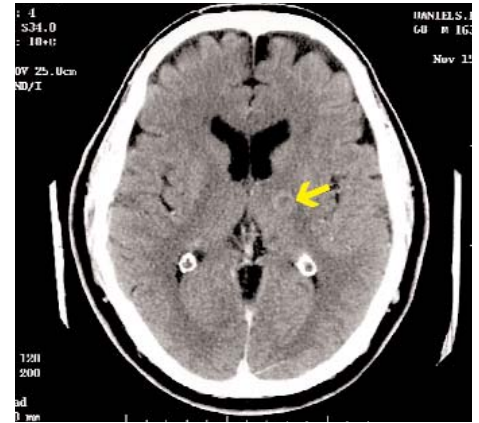
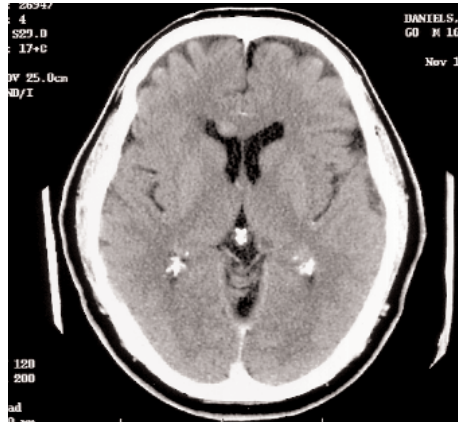
Taxotere "consolidation" chemotherapy was poorly tolerated ("like to have killed me"), not an unusual experience for chemotherapy recipients after repeated cytotoxic cycles. This patient, like many others, declined further chemotherapy as his independent decision. We respect this decision was prudent. After further chemotherapy was declined, the conventional treatment would have been "watchful waiting". This is a euphemism for doing nothing. In this case multi-agent immunotherapy including IL-2 immunotherapy was discussed with the patient and begun in earnest with his informed consent.



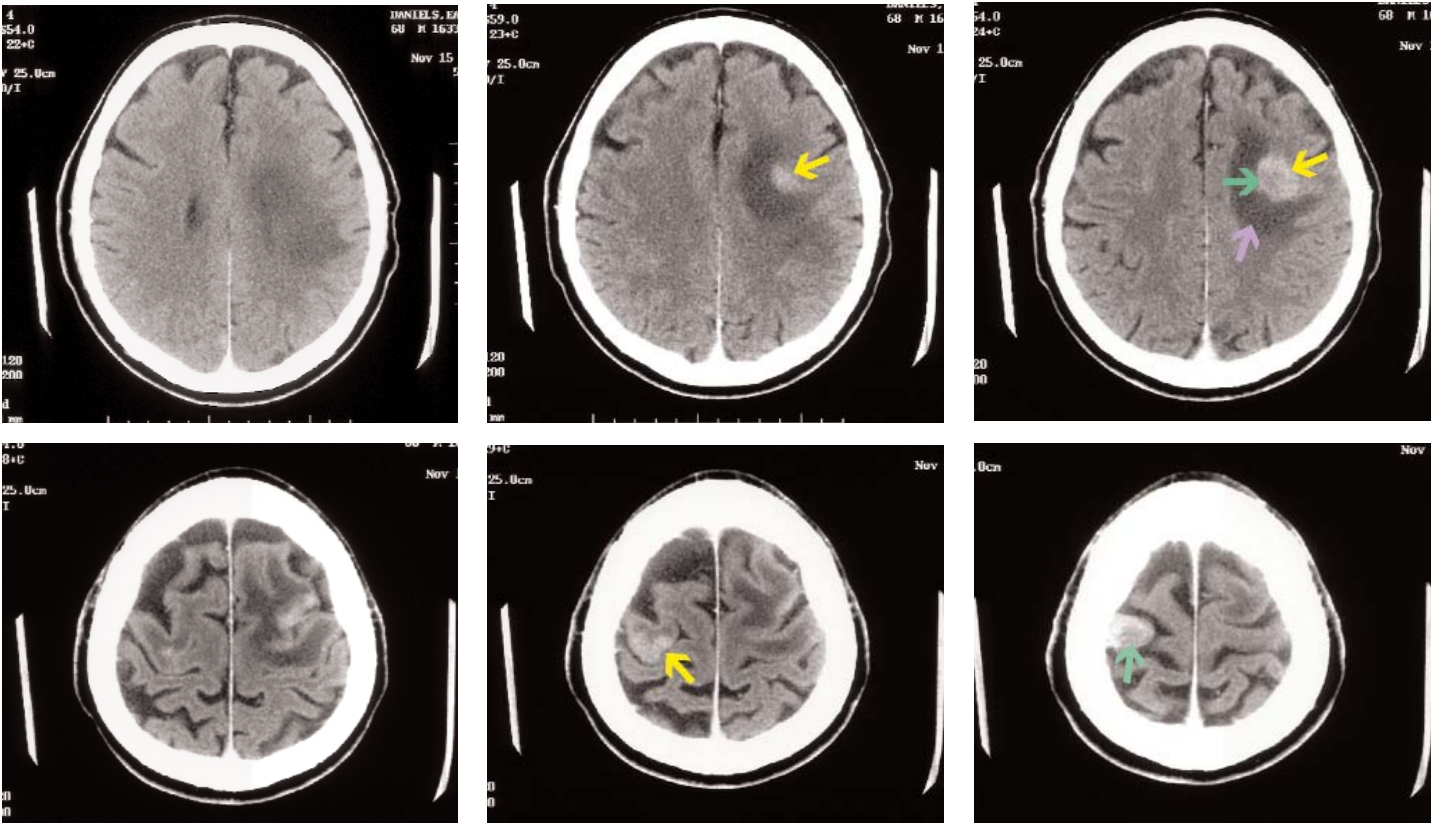
July, 2002 - CT chest after radiotherapy

CT chest of July 2002, taken after radiotherapy to the chest and chemotherapy, shows stent (green arrow) in superior vena cava that had been inserted prior to radiotherapy to relieve acute symptoms of compression of this large vein (vena cava). This mechanical compression had caused severe symptoms when Mr. Daniels first sought medical attention. There was marked shrinkage of mass effect in the mediastinum (orange arrow) after initial treatment. Chest radiotherapy and chemotherapy were associated with CEA falling to normal range.

November, 2002, three months after chemotherapy stopped, CT brain shows multiple brain metastases



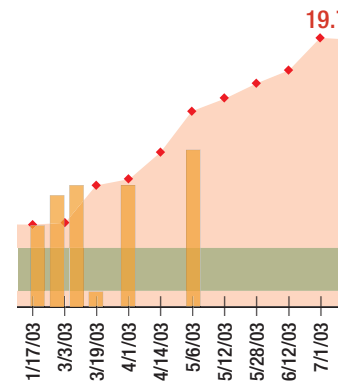
Mr. Daniels' presenting complaints with brain metastasis (yellow arrows) were headaches, confusion and incoordination.



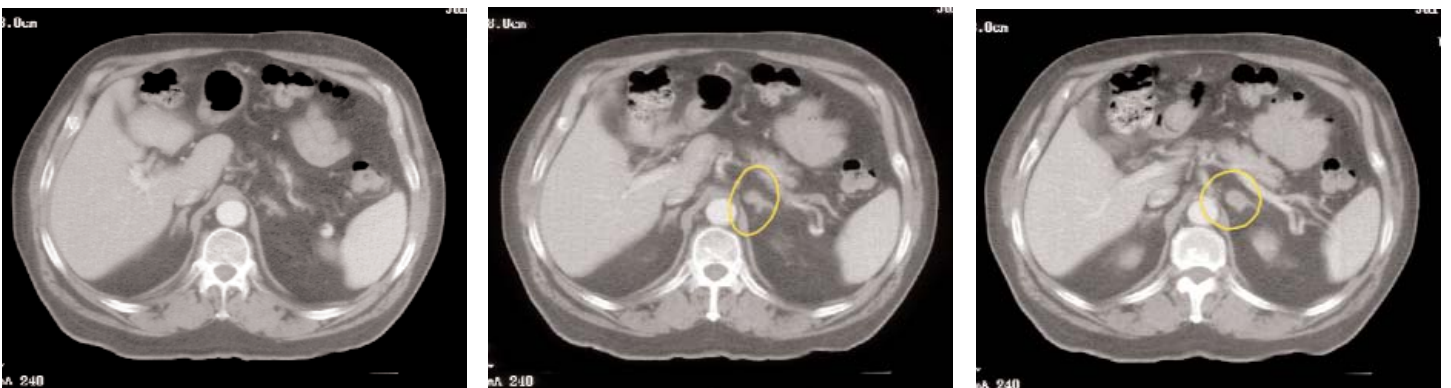
The dark centers in several of these tumors (green arrow) are evidence of central necrosis, which is indicative of dead tumor that has lost its blood supply. Central necrosis is commonly seen in adenocarcinoma and is less common in small cell carcinoma. The dark area around the tumor nodules is cerebral adema (purple arrow).

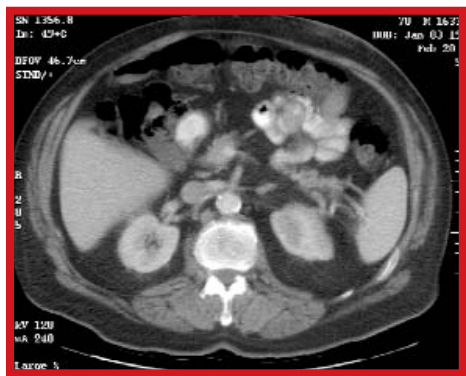
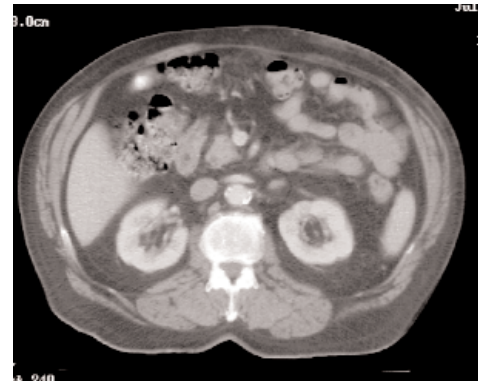
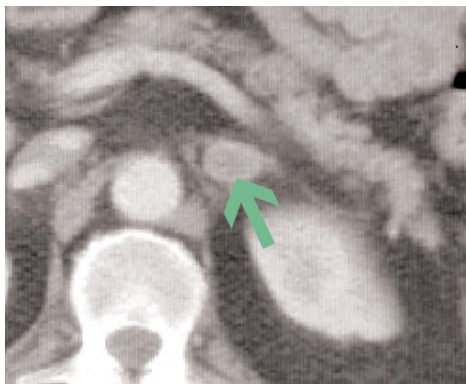
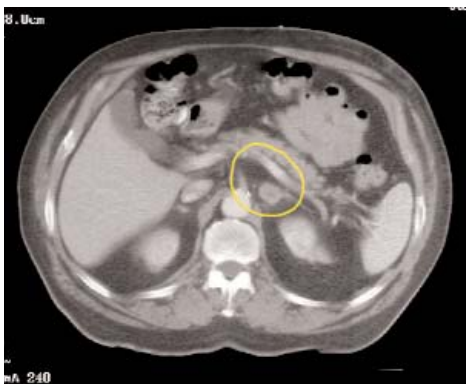
These metastases required treatment with radiotherapy. The brain metastases shrank markedly after radiotherapy. Radiotherapy to the brain consisted of 4000 cGy in 4 weeks, a regimen far more protective of higher cognitive function than the often used 3000 cGy in two weeks. Immunotherapy with IL-2 belly plaque and other agents was continued before and after the brain irradiation.

After brain radiotherapy was complete, the CEA cancer marker began a disappointing steady rise (see graph).



July 2003 - Repeat chest CT scan shows active mass in adrenal gland





In July 2003, a PET scan was ordered in an attempt to define the site of origin for the rising CEA. A CT scan through a solitary area of intense PET uptake revealed a mass in the left adrenal, which had developed since the CT scan taken at presentation. It was hypothesized that this adrenal mass was metastatic cancer largely responsible for the progressive rise in CEA. Note the dark center inside this mass (green arrow) similar to that seen on several of the brain metastases. Such dark areas are felt to represent central necrosis or poor blood flow and are commonly seen in adenocarcinoma.

The adrenal gland is the source of cortisone and hydrocortisone, known immunosuppressive hormones. These hormones cause lysis (death) of lymphocytes. The brain and adrenal gland are well documented as preferred metastatic recurrence sites for adenocarcinoma of the lung. The brain is a common site for recurrences as chemotherapy does not penetrate the blood-brain barrier in sufficient quantities to have anticancer effects. The adrenal acts as "fertile soil" for recurrences likely due to the immunosuppressive micro environment hostile to natural killer lymphocyte mediated immunotherapy.

The same CT demonstrating the adrenal mass also memorializes several prominent areas of IL-2 generated belly plaque (orange arrows). Contrast these areas on different cuts with the opposite side (above in red box), and you will note the difference.

Blood determinations at around this time revealed substantial elevation of natural killer (NK) lymphocyte blood levels (see graph). This elevation supports our theory that the belly plaque is a factory for NK cells. NK cells escape the plaque into the general circulation.

Most medical oncologists would have recommended more chemotherapy at discovery of the adrenal metastasis, the indication being systemic recurrence or relapse. This was a critical decision fork. (See end of section for other treatment decision forks.) The adrenal recurrence was treated with local radiotherapy, hopefully reducing the body burden below the IIT and blocking corticosteroid production by the adrenal. The tumor was radiosensitized with Iressa. IL-2 belly plaque was continued, but was later stopped.

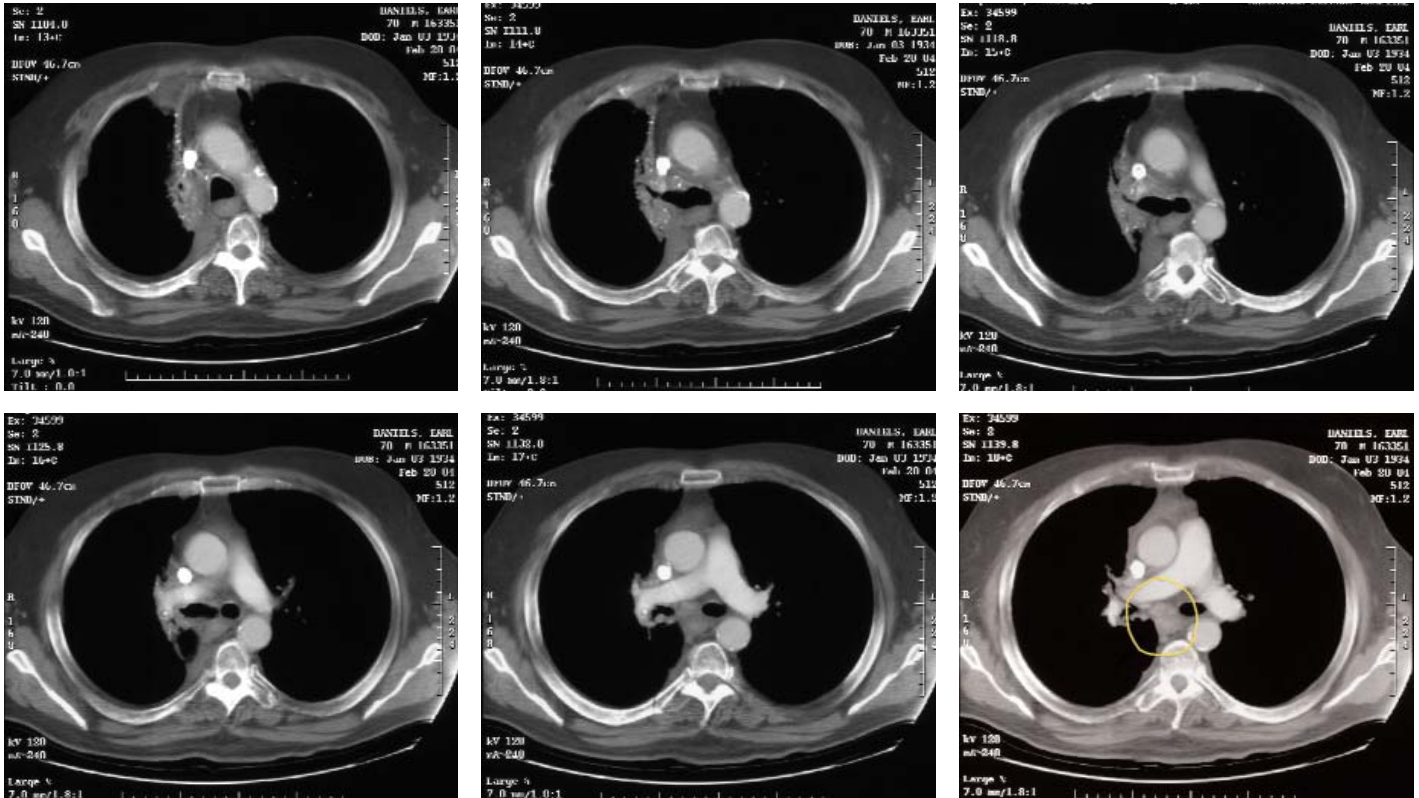
The CEA fell rapidly during adrenal irradiation to normal, and CEA has remained normal for 15 months. The patient has remained physically and mentally active with an excellent quality of life (see video).

**CEA normal for
14 months after
marked elevation;
off standard treatments**

Possible cure!

The 14-month, no-chemotherapy remission currently enjoyed by Mr. Daniels after two manifestations of distant spread (brain and adrenal) is an anomalous occurrence under the prevailing chemotherapy centric paradigm of cancer treatment. In our opinion, this protracted delay to recurrence in association with other evidence of immune activity strongly supports our case that our immunotherapy efforts were successful in arresting tumor regrowth.

February 2004 - Mediastinum CT



A repeat CT scan of the chest was obtained in February of 2004. A residual mass in the mediastinum may be a fibrous tissue scar left behind after the cellular part of a tumor is destroyed leaving behind only a contracted fibrous tissue scar from the connective tissue scaffolding of the previous cancer. Such masses are often seen after local control in bulky Hodgkin's disease masses.

Based on the well established radiobiology of bulky adenocarcinomas, combined radiotherapy and chemotherapy, the treatment Mr. Daniels initially received, rarely create local control of 8 cm masses like the one in Mr. Daniels' chest at presentation. Another interpretation of this case, one that we favor for management purposes, is that immunotherapy has induced growth arrest of residual tumor in a greatly shrunken tumor rather than total tumor eradication or cure.

Clonagens are individual cancer cells that can regrow to large masses. We believe the presumption should be that cancer clonagens are typically incorporated in residual masses after standard radiotherapy and chemotherapy. Clonagens also are likely to be found at one or more distant sites, and these clonagens will proliferate if immune surveillance is low.

It has been our experience over the years that patients who decrease or terminate their immunotherapy based on duration of remission often relapse. Relapses after known systemic spread have been universally fatal. These considerations lead us to the conclusion that disciplined immunotherapy carried out by the patient for years under physician supervision is worthwhile after initial treatment so long as elevated serologic marker determinations remain normal and no evidence of disease (NED) is the clinical condition of the patient.

This patient's quality of life during immunotherapy has been as good as it was prior to his developing cancer. This high quality survival would not likely have been the case if, at the first sign of dissemination, chemotherapy had been elected by the patient as further treatment.



Earl Daniels
Marks, Mississippi

Prohibited: Immune Restorative Therapy at Work



**Keeping the Grim Reaper at Bay
in a Deadly Condition**