IMPACT OF HEALTHY DIET AND LIFESTYLE CHANGES ON VARIOUS PATHOLOGICAL PARAMETERS AND WELL BEING OF A DIABETIC PATIENT SUFFERING FROM TERMINAL HEPATO CELLULAR CARCINOMA:

Pandey H. M.; Chaudhary Nikhil

www.nikhilchaudhary.com

+Abstract

Introduction: A terminal case of Hepato Cellular Carcinoma (tumor of dimension- 12cm X 10cm, right lobe of liver) with history of diabetes (>10years), hypertension was referred to us for palliative care and if possible some improvement in her condition. Her diagnostic parameters like Alkaline Phosphatase, AST, ALT, etc were abnormally high. With a prognosis of maximum 25 days of life, any conventional treatment was not advised to her. She was advised to be on a customized diet and lifestyle without medications. After about a month, her blood and urine parameters showed almost normal levels. Time and again her blood and urine reports were taken. It has been seven months, and with diet and lifestyle approaches she is still succeeding to live. Compliance with the healthy diet is directly correlated to her well being and improvement in her condition.

Keywords: Hepato Cellular Carcinoma (HCC); Healthy Diet and Lifestyle; Pathological Calcification; Abnormally high Alkaline Phosphatase; Terminally ill Cancer patient.

Case Presentation of the patient:

On Day I a female patient, 65 years old, diabetic for more than 10 years, had jaundice with was diagnosed with Hepato Cellular Carcinoma based on Ultrasonography and Triple Phase CT scan reports along with certain blood reports. The findings were as follows: Random Blood Sugar- 224 mg/dL, earlier recent reports were 460 mg/dL. Serum SGOT: 190 U/L, Serum SGPT: 220 U/L, Serum Bilirubin: 2.1 mg/dL. Ultrasonography- Mass Lesion in Liver (Mixed echogenic area seen of size 10 x 8cm in right lobe of liver), multiple echogenic polyps in Gall Bladder. CT Scan– findings are likely suggestive of Liver Mass [? Hepatocellular Carcinoma] (Heterogenous mass lesion showing mild enhancement on arterial phase with early washout noted in the segment 5,6,7 & 8 of right lobe of liver, measuring 12X 10 cm. Her Urine contained high levels of albumin; sugar and also calcium oxalate crystals. Physically she was not able to even talk or walk.

On 21st August 2014,(5 days prior to the family's contact with us) the doctors examined her condition and told that she had a maximum of 25 days to live with such a high degree of illness. There was no treatment possible for a carcinoma of this type which has spread over such a huge portion of the liver. No chemotherapy, Radiotherapy or surgery was advisable for the patient. Therefore the doctor did not even advice them to go

for further diagnosis of any type. He advised that the patient be taken home and looked after.

She was not informed about the diagnosis neither was her husband. The Daughter in Law (DIL) was her primary caretaker and point of contact for us. She lived in a joint family with approximately 15 members including kids. The entire treatment plan devised and advised by us was only through phone. The patient is almost 2000 kms away from chennai (where we are located). The parameters and physical condition was monitored through phone, emails.

The tablets she was consuming were advised for both diabetes and her problems associated with HCC like nausea, vomiting, pain etc. We discussed with the family to discontinue the tablets prescribed:

1. Ultracet (Combination of Tramadol and Acetaminophen): Tramadol and Acetaminophen have led to severe poisoning in large number of cases with fatal consequences [1][2]. Acetaminophen poisoning accounts for at least 40% of the US acute liver failure cases seen at tertiary care centres and one third of the total deaths. Acetaminophen is the most common cause of acute liver failure in both the US and the UK.[3]
2. Sorafenib Tab : Sorafenib has been found to be highly toxic to liver resulting in severe allergy and also death in many cases.[4][5]
3. Razo D (Combination of Domaperidone and Rabeprazole Sodium): Should not be given in patients suffering from hepatic insufficiency.[6]
4. Ondace MD Four (Ondansetron): In case of severe hepatic impairment and various liver diseases, Ondansetron should be avoided.
5. Triglynase 2 Forte (Combination of Pioglitazone, Metformin[7] and Glimepiride): Pioglitazon has been found to increase the risk of Bladder cancer either alone or in combination with metformin and Glimepiride is contra indicated for patients suffering from liver disease.[8][9]
6. Galvus 50 mg (Vildagliptin): It should not be used in patients with hepatic impairement.[10]

Two other tablets, Enterogermina (Antibiotic resistant Bacillus Clausi) and Beplex Forte (Multivitamin) were not pressed upon to be stopped. Voluntarily they accepted the idea and proposed to stop the medicines as stopping them had hardly any risk as the patient's condition was already very critical and the outer limit of her survival was 20 days from this day as per the doctor.

A week later to the start of the therapy when the patient's family started gaining confidence and there was little improvement in the condition of the patient, we requested the family to take some diagnostic tests to have a clarity on her current health status. Results of the test (can be considered as the initial parameters which would have prevailed before the start of the therapy) is Alkaline Phosphatase:1624 U/L (first diagnosis); Total Cholesterol: 503 mg/dL; Total Bilirubin: 3.6 mg/dL; SGOT: 195 U/L; SGPT: 145 U/L; Albumin: 3.0 g/dL; Fasting Blood Sugar: 326 mg/dL, HbA_1c: 9.6%; Urine- presence of sugar, albumin and oxalate crystals.

Our treatment approach considered th patient's past medical history as well as her present health status.We had some experience in dealing with diabetic patients and last stage cancer patients. We concluded the following things which must be considered while designing the diet for the patient:

It is a known fact that the blood of diabetic patients is acidic compared to the non diabetic patients. A relationship between raised levels of Alkaline phosphatase and other liver enzymes with high blood sugar levels among diabetics has been established [11]. Alkaline phosphatase has been found to directly take part and promote both physiological bone mineralization and pathological soft tissue calcification [12-18][30-31]. Such high levels of Alkaline Phosphatase have rarely been reported in scientific literature. As we did not have any biopsy reports, we hypothesized that the tumor in the liver was a calcification due to high alkaline phosphatase and also acidic environment prevailing in the patient's body. We also hypothesized that she must be suffering from severe deficiency of certain Vitamins and minerals generally found in patients suffering from Diabetes, Cancer or other metabolic problems. These included Magnesium, vitamin C, vitamin D, vitamin B Complex, Folate etc.

Therefore, a diet plan was devised with the following parameters: To increase the pH of the patient by giving alkaline foods like vegetables. A dietary approach was planned in such a way that it would contain compounds (of biological origin) like PPi (Pyrophosphates), Magnesium, Inositol hexa Phosphates (IP6) which are found to be antagonistic for further calcification and may also de calcify the liver [19-24).Chemicals like Inositol hexa phosphates (IP6) which is naturally found in germ and the kernel of seeds and grains prevents calcification or even leads to de calcification. A diet plan which was advised to reduce her sugar levels and provides her body with all necessary nutrients and anti oxidants to fight cancer is shown below:

Food items to be used liberally: Bran Rice; Vegetables; Green Chutney- Coriander + mint chutney; Salads; Lemons and Amla; Sprouts; Vegetable Soup; Spices; Green Tea; Flaxseed.

Food items to be completely avoided: Refined Carbohydrates; Meat and Egg; Fruits and Fruit Juices; Fried Food; Trans-Fat; Packaged Products; Over Cooked Food; Dairy Products; Soft Drinks or Energy Drinks; Alcohol; Oils and Fats

Lifestyle changes advised: To expose skin to direct sunlight for about 20 minutes every day to increase vitamin D in the body; to exercise, if not exercising, to start mildly and increase the duration. It is important to exercise for over all good health, and should have stamina to walk for at least 30 minutes every day without fail. To use Magnesium Sulphate (Epsom salt) in her bathing water.

Dietary energy restriction: The patient was advised to eat 1 meal of whole grain brown rice (Also known as Red rice/ Bran Rice/ Puttu Arisi) per day. This would be the only carbohydrate rich grain she was allowed to consume in a day. Other times she was advised to eat rest of the items which included vegetables, sprouts, nuts, seeds, green tea, etc. The customization of their daily menu is left to them according to their convenience.

The prognosis of the patient is divided into 3 parts –

Part I - between Day 1 and Day 50 Starting the therapy of dietary and lifestyle changes and reports taken on Day 50: Slowly the patient's condition started stabilizing. When the patient changed to the new diet and lifestyle changes, she never had a single episode of vomiting and rarely any loose motions at all and anti-emetic drug was never required. She started to feel the change and became a lot more confident. On Day 5, she started walking on her own though only for 2 minutes. On Day 6, she spoke to us over the phone and said that she was able to talk. The same day she walked up to a nearby temple. Her fasting blood sugar levels were between 250 and 326 mg/dL. On Day 9, lot of guests kept visiting her and she was able to talk to them. She started to consume more food and drink, and a lot of water. She started developing new habits like drinking water empty stomach in the morning. On Day 32, she got loose motions. Her fasting blood sugar started shooting very high about 250 mg/dL and above, and up to 540 mg/dL in postprandial. Later we had learnt that she was deviating from our diet. At this point the deviation was not so much though. On Day 33, we were informed that the patient's mouth seemed to be distorted in one side and she was not able to speak properly. She also had boils inside her mouth. After the revelation she made about the deviations being done in the diet, we advised and requested her to make sure that she sticks to the dietary regimen. From Day 39, her fasting blood sugar values (125,115 mg/dL) started to show improvement. On Day 50, the following tests were done and results are shown: Fasting Blood Sugar: 95 mg/dL; Alkaline Phosphatase: 399 U/L; Total Choleterol: 185 mg/dL; Total Bilirubin: 0.9 mg/dL; SGOT: 81U/L; SGPT: 54U/L; Albumin: 3.3 g/dL; HbA_{1c}: 7.2%; urine had trace of albumin, and absence of either sugar or crystals.

The parameters showed tremendous improvement with Liver Function coming close to normalcy. Alkaline phosphatase had reduced remarkably along with SGOT while Total Bilirubin and SGPT had come to normal levels. A diabetic for over a decade had now achieved normal fasting blood glucose and cholesterol levels, and HbA_{1C} also improved tremendously without taking any medication. Absence of sugar and crystals in her urine was a sign of great improvement in her kidney function, overall health and also her internal (Extra cellular) environment.

Alkaline phosphatase has been closely linked with the prognosis of the disease in patients suffering from HCC. A direct relationship between the levels of Alkaline Phosphatase and disease free survival as well as overall survival was found among patients of HCC.[25-28] Another study also found that there was a similar connection between Alkaline phosphatase and Albumin ratio to disease free and overall survival among patients suffering from HCC.[29] In our case the Alkaline phosphatase had reduced markedly while Albumin had increased to normal levels from being low earlier.

By now the physical condition of the patient had improved drastically. She was able to talk with ease, walk for long durations without any support, do some household activities, her

Jaundice was completely gone and there was no yellowness in her skin or eyes at all. These results were a proof of better prognosis in the patient. It gave us immense hope to achieve complete remission of HCC in this case.

Part II – Day 50 to Day 84 (First Diagnostic report to second): On day 65, the patient along with her family visited the same doctor with the new reports. The doctor is not informed about the dietary therapy being given. He was happy to see the reports as almost all critical parameters were normal by then and informs the patient's family that she is fine now. Doctor did not even advice to get a CT scan done at this moment. The patient very innocently asked the doctor, "Doctor I feel very hungry and feel like eating Paneer Paratha." To this the doctor replied, "Madam you can eat whatever you feel like." Since the consultation done with the doctor, the patient started to deviate from our prescribed diet once in a while with increasing frequency. But she was still adhering to a great extent to the prescribed diet. During this time, she frequently encountered episodes of very high glucose in her blood. This also led to problems like feeling uncomfortable, Boils in her stomach which were very frequent before we started the dietary changes.

On Day 81, the following parameters were assessed and reports shown below: Alkaline Phosphatase: 443 U/L; Total Cholesterol: 204 mg/dL; Total Biliurubin: 1 mg/dL; SGOT: 79 U/L; SGPT: 40 U/L; Albumin: 3.6 g/dL; Fasting Blood Sugar : 171 mg/dL; HbA_{1c}: 9.70 %; Urine had no albumin, sugar or crystals.

As can be seen from the results, we found that her Alkaline Phosphatase started showing increasing trend, though marginally, compared to her previous report. Her blood glucose levels and HbA_{1c} were also showing upward trend. Our contention all along has been that blood sugar levels as well as alkaline phosphatase levels are interdependent. After seeing these reports, we cautioned the caregiver and her family members that she should strictly adhere to our advice otherwise things may eventually go out of hands. To our shock, the caregiver started complaining that the non compliance is not because of lack on her part but rather because of increasing non cooperation from the patient's side. As expected her condition did not improve much. But the parameters were still better as she was complying with the diet though she was eating some quantity of restricted food as well. They were cautioned that unless and until the patient complies with the advice, her condition may not improve.

Part III – between Day 81(Second diagnosis) and Day 167(Third and final diagnosis): On day 128, her fasting blood sugar levels kept fluctuating and even reaching levels of 300 mg/dL. In fact she didn't even give us her fasting sugar values on a regular basis probably because she knew she has been deviating and her values will be quite high or maybe she checked the values, found them to be high so decided to rather hide it from us. The deviation kept on increasing. The adherence to the diet went down. There were problems of understanding among the patient and her caretaker. With time the problems kept increasing. On Day 167 blood tests were done and results are as follows: Alkaline Phosphatase: 723 U/L; Total Bilurubin: 2.2 mg/dL; SGOT:169 U/L; SGPT:109 U/L; Albumin: 3.0 g/dL; Fasting Blood Sugar: 200 mg/dL.

As seen in the reports her alkaline phosphatase and blood sugar levels were elevated. She had also started feeling very unwell during this period. Her condition was continuously deteriorating. We advised the caretaker and her family members that the patient should strictly adhere to the diet or else she may not recover. They realized the situation, and for next few days they complied with our advice and she started recovering physically. But this compliance was not sustained after few days and she slipped back to her condition (prior to the date when we started our treatment). On enquiries from the patient's caregiver, she expressed total helplessness in the matter.

Conclusion

The nutritious diet rich in Magnesium & Ip6 along with liberal use of non starchy vegetables resulted in the improvement of all relevant parameters in turn resulting in patients overall well being. Later on when the patient started eating processed and refined food, in contravention of our advice, her condition again started deteriorating. In the face of deteriorating parameters also, the non observance continued unabated and therefore the patient's condition could not be improved. Therefore healthy diet and lifestyle has the potential to convert HCC into cancer under remission (i.e metastatic and hypermetabolic nature of cancer can be reversed) and also cure it.

References

1) Fakhreddin Taghaddosinejab et al. (2009) Factors related to Seizure in Tramadol Poisoning and its Blood Concentration, Journal of Medical toxicology; September Vol. 5, No. 3.
2) Micaela Tjaderborn et al.; Micaela Tjaderborn et al. (2007) Fatal unintentional intoxications with tramadol during 1995-2005; Forensic science international, Vol 173, 2007, 107-111.
3) Anne M Larson et al. (2005) Acetaminophen induced acute liver failure: results of a United States Multicentre, prospective study; Hepatology, Vol 42, No. 6.
4) Anneleen Van Hootegem et al. (2011) Sorafenib induced liver failure – A case report and review of Literature; Case reports in Hepatology, Vol. 2011, 2011.
5) Benjamin Hagopian et al. (2010) Unusually severe Bullous skin reaction to sorafenib A case report; Journal of Medical cases, Vol. 1, No. 1.
6) Benoit Drolet et al. (2000) Domeperidone should not be considered a No risk alternative to Cisapride in the treatment of Gastrointestinal Motility Disorders; Circulation.
7) Jolien de Jager et al. (2010) Long term treatment with metformin in patients with type 2 diabetes and risk of Vitamin B 12 deficiency: randomised placebo controlled trails; BMJ, 2010; 340; C2181.
8) James D. Lewis et al. (2011) Risk of bladder cancer among diabetic patients treated with Pioglitazone; Diabetes care, Vol 34.
9) FDA Drug Saftey Communication: Update to ongoing safety review of Actos (Pioglitazone) and increased risk of bladder cancer; www.fda.gov/Drugs/Drugsafety/ucm259150
10) Summary of product characterstics; European Medicines Agency; http://www.ema.europa.eu
11) Elevation of serum alkaline phosphatase activity and related enzymes in diabetes mellitus – Goldberg et al.; Clin Biochem. 1977.
12) Edward D. Chan et al (2002) Calcium deposition with or without bone formation in the

lung; Am J Respir Crit Care Med, Vol 165, pp 1669.

13) Shuichi Jono et al. (2000) Phosphate regulation of vascular smooth muscle cell calcification; Circ Res. 2000; 87:e10-e17.
14) Donald W. Moss (1982) Alkaline Phosphatase isozymes; Clinical Chemistry, vol 28, No. 10.
15) Sonoko Narisawa et al. (2007) Novel inhibitor of alkaline phosphatase suppress vascular smooth muscle cell calcification; Journal of bone and mineral research, vol 22, No. 11.
16) M Schoppet et al. (2008) Role for alkaline phosphatase as an inducer of vascular calcification in renal failure?; Kidney international (2008) 73, 981-991.
17) Mathieu P et al (2005) Calcification of human valve interstitial cells dependent on alkaline phosphatase activity; The journal of heart valve disease, 2005, 14(3), 353-357.
18) F. Grases et al. (2004) Dietary myo-inositol hexaphosphate prevents dystrophic calcifications in soft tissues: a pilot study in wistar rats; Life Sciences 75 (2004), 11-19.
19) Cecilia M. Giachelli (2003) Vascular Calcification: In vitro evidence for the role of Inorganic phosphate; J Americal society of Nephrology; 14: S300-S304.
20) Adela Hruby et al. (2014) Magnesium intake is inversely associated with coronary artery calcification; JACC, cardiovascular imaging, vol 7, no. 1.
21) Dongbo Wang et al. (2009) Carboxylated molecules regulate magnesium content of amorphous calcium carbonates during calcification; PNAS, Vol 106, no. 51.
22) Silvia Salem et al. (2012) Relationship between Magnesium and clinical biomarkers on inhibition of vascular calcification; Am J Nephrol 2012.
23) Loic Louvet et al. (2013) Magnesium prevents phosphate induced calcification in human aortic vascular smooth muscle cells; Nephrol Dial Transplant (2013)28: 869-878
24) Kazimierz Pasternak et al. (2010) Biochemistry of Magnesium; J Elementol. 2010, 15(3):601- 616
25) Yu MC et al. (2011) Alkaline phosphatase: does it have a role in predicting hepatocellular carcinoma recurrence?; J Gastrointest Surg. 2011 Aug, 15(8): 1440-9.
26) Deborah L. Regidor et al. (2008) Serum Alkaline phosphatase predicts mortality among maintenance hemodialysis patients; J Am Soc Nephrol, 2008, 19: 2193-2203.
27) Jong Man Kim et al. (2013) The effect of alkaline phosphatase and intrahepatic metastases in large hepatocellular carcinoma; World Journal of surgical oncology 2013:11:40.
28) Xin-Sen Xu et al. (2014) Model based on gamma glutamyltransferase and alkaline phosphatase for hepatocellular carcinoma prognosis; World Journal of Gastroenterology, 2014, 20 (31).
29) Anthony W. H. Chan et al. (2015) Albumin to alkaline phosphatase ratio: A novel prognostic index for hepatocellular carcinoma; Hindawi, Disease markers, Vol 2015.
30) Lovisa Hessle et al. (2002) Tissue nonspecific alkaline phosphatase and plasma cell membrane glycoprotein 1 are central antagonistic regulators of bone mineralization; PNAS, 2002, vol 99, No. 14, 9445-49.
31) Hideo Orima (2010) The mechanism of mineralization and the role of Alkaline Phosphatase in health and disease; J Nippon Med Sch; 2010; 77