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Case Report

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Chemotherapy in a patient with metastatic duodenal cancer and idiopathic thrombocytopenic purpura: a case report and review of literature

Abstract

Metastatic duodenal adenocarcinoma is a rare disease, and it's coexistence with idiopathic thrombocytopenic purpura is still very rare. Here we report first case of metastatic duodenal adenocarcinoma with coexistent ITP treated with palliative chemotherapy protocols. We initially managed ITP, after which having had a safe platelet count (above 75000/uL.), we safely administered chemotherapy protocols like FOLFOX4, FOLFIRI, XELIRI/CapeIRI. Management of idiopathic thrombocytopenic purpura was done initially by treating with steroids, and afterwards by administering intravenous immunoglobulins after which platelet count increased up to 182,000/uL. The PFS for first line chemotherapy-protocol FOLFOX4 was approximately 9 months. Presently undergoing second line palliative chemotherapy-protocol FOLFIRI/XELIRI until publishing of this manuscript. PFS for second line palliative chemotherapy and OS still not achieved.

Keywords: cape IRI, IVIG-intravenous immunoglobulin's, ITP, FOLFOX4, chemotherapy, H. pylori

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Piyush Vyas,[1] Krzysztof Wózniak,[1] Marta Dudek,[1] Ewa Zurawinska Grzelak,[1] Leszek Kraj,[1] Mateusz Cieslak,[1] Anna Dryja,[1] Seema Vyas[2]

[1]Medical University of Warsaw, Poland
[2]Maria Sklodowska Curie Centre and Institute of Oncology, Poland

Correspondence: Piyush Vyas, Consultant Clinical Oncologist, Department of Hematology, Oncology and Internal medicine, Medical University of Warsaw, Poland, Email vyas_piyush20@yahoo.co.in

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Abbreviations: ITP, idiopathic thrombocytopenia purpura; CapeIRI, capecitabine/irinotecan; PNS, paraneoplastic syndrome; TPO Mimetics, thrombopoetin mimetics; H. Pylori, helicobacter pylori; PFS, progression free survival; OS, overall survival

Introduction

Since metastatic duodenal carcinoma is not a frequent cancer in everyday oncology practice, and if it occurs with ITP, it remains a challenge to treat such a patient. Duodenal cancers comprise only 1-2% of all gastrointestinal cancers; they are a third of all small intestine cancers and comprise only 0.4% of all malignancies.[1] There are no standard treatment protocols, no guidelines, and no randomized phase III clinical trials conducted in this disease. And if such a patient with metastatic duodenal cancer has other serious co morbidities like ITP, many of us search medical literature, online journals etc, to find answers. So did we search literature, we performed an electronic search on MEDLINE, EMBASE, SCOPUS and the Cochrane Library. And to our surprise we did not find even a single case study published on the treatment of metastatic duodenal adenocarcinoma with coexistent ITP.[2] Thus we report here this first published case report with a patient who presented with ITP and metastatic duodenal adenocarcinoma simultaneously, and was treated with palliative chemotherapy protocols.

On the basis of our literature review, we treated our metastatic duodenal cancer patient with chemotherapy protocols generally administered as standard regimens in colorectal adenocarcinomas. We treated metastatic duodenal cancer with FOLFOX4 as first line chemotherapy protocol. As a second line treatment we administered FOLFIRI protocol. We also demonstrated that single day hospitalization chemotherapies like XELIRI can be safely administered among patients with metastatic duodenal adenocarcinoma with coexistent ITP without any significant bleeding complications.[3–5] Chemotherapy among patients with coexistent ITP has been administered at various cancer centers as shown by various case studies published in literature, mainly among breast cancer and lung cancer patients. Risk of life threatening complications is not significant if platelet counts are at safer levels of more than 75,000 /uL. As far as management of ITP is concerned, steroids and/or IVIG are probably treatments of choice in patients with metastatic solid tumors.[6] Special precautions are to be taken when establishing the diagnosis of ITP. Bone marrow biopsy should be consistent with ITP and should exclude metastasis, bone marrow infiltration by tumor. The significance of ITP as a para neoplastic syndrome in metastatic duodenal cancer remains unknown. Krauth et al.[7] have analyzed 68 published cases of an association of ITP and solid cancers. As shown by Krauth et al.[7] in some cases surgical removal of tumor, chemotherapy administration gave complete response to ITP, but for metastatic cases probably steroids are treatment of choice. And we further propose that if patients do not respond to steroids, then IVIGs can be the administered with good results as was the case with our patient. Surgical approaches like removal of primary tumor, splenectomy or lobectomy etc. can induce long term complete responses of ITP in some patients mainly with non-metastatic disease.

Case study

A 57 year old Caucasian female was admitted to our department in Febuary 2015 with presenting complaint of persistent mild epigastric pain. She had a medical history of celiac disease, chronic gastritis and Helicobacter Pylori infection. She had no history of prior blood transfusions, recent medications, or human immunodeficiency virus risk factors. Pertinent negative findings on physical examination included no evidence of lymphadenopathy, splenomegaly, ecchymoses, or petechiae. Due to persistent epigastric pain an endoscopic procedure (gastroduodenoscopy) was administered. The endoscopic finding revealed that she had an ulcerating lesion in the duodenum. The biopsy specimen taken from the ulcerating lesion confirmed that she has an adenocarcinoma of duodenum. After which a further diagnostic workup was done for staging.

The computer tomography examination showed that she has numerous metastases in liver. Thus she was diagnosed metastatic duodenal adenocarcinoma. Laboratory workup included no evidence of disseminated intravascular coagulopathy, however she had mild thrombocytopenia. .A bone marrow biopsy was done and the biopsy report showed that the changes in bone marrow were typical of ITP-increased megakaryocytopoeisis, absence of bone marrow infiltration by cancer cells. So as a diagnosis of exclusion, she was diagnosed with ITP. She had thrombocytopenia (platelet count less than 100000/uL.), had increased number of megakaryocytes in bone marrow evaluation, no history of intake of drugs causing thrombocytopenia, no other causes of thrombocytopenia detected like viral infections, no bone marrow infiltration by tumor etc.

Treatment of metastatic duodenal adenocarcinoma

Since she had mild thrombocytopenia (platelet count above 75000/uL. but less than 100,000/uL.), had good performance status, no significant abnormalities in laboratory results, no significant co-morbidities, she was qualified for treatment with palliative chemotherapy protocol FOLFOX4, which was administered from 2015 February until December 2015 (10 cycles of standard FOLFOX4 protocols). A computer tomography scan was done after administering 6 cycles of chemotherapy as per FOLFOX4 protocol where the disease was stable and we continued the treatment up to 10 cycles (November 2015). After 10 cycles of I line chemotherapy (FOLFOX4), the patient had a computer tomography scan which showed progression of disease. Thus the first line treatment with protocol FOLFOX4 was stopped. As a second line treatment she was offered a further treatment with FOLFIRI protocol which was administered from November 2015 until March 2016 - 4 cycles. We could not maintain an ideal 2 week interval as is recommended for these protocols due to thrombocytopenia levels below 75,000/uL. And need to administer dexamethasone pulses or IVIG.[12] After 4 cycles of FOLFIRI regimen, she further continued palliative chemotherapy with CapeIRI protocol (popularly known as XELIRI- capecitabine, oxaliplatin). Protocol FOLFIRI was changed to XELIRI due to bad psychological tolerance of continuous 22 hours infusions of 5Fluorouracil in FOLFIRI protocol by the patient.

Chemotherapy protocols

FOLFOX4: Oxaliplatin was administered on day 1 at the dose of 85mg/m^2 as a 2 h infusion, concurrently with FA 200mg/m^2/day, followed by bolus 5-FU 400mg/m^2 and a 22 h infusion of 5-FU 600mg/m^2 for two consecutive days, every 2 weeks.

FOLFIRI: Irinotecan 180mg/m^2 IV over 30-90 min on day 1 plus leucovorin 400mg/m^2 IV infusion to match duration of irinotecan infusion on day 1 plus 5-FU 400mg/m^2 IV bolus on day 1, then 1200mg/m^2/day for 2-d (total 2400mg/m^2 over 46-48h) continuous infusion, every 2 weeks.

XELIRI(CapeIRI): Irinotecan 250mg/m i.v. on day 1 + capecitabine 1000 mg/m orally twice daily on days 1 to 14, every 3 weeks.

Treatment of ITP

The platelet counts at various stages of her treatment varied from 10 thousand/uL to 182 thousand/uL. Since initially she did not react to steroids (dexamethasone pulse), thus was administered intravenous immunoglobulin's at a dose 1mg/kg body weight on day 1 and day 2 whenever her platelet count decreased to levels below 75 thousand/uL. And after the administration of IVIG the platelet count rose to a maximum of up to 182,000/uL.

As far as complications are concerned she did have dark stools once, after which immediately IVIG were given, and the platelet counts increased to a very safe level of more than 100 thousand /ul. After a careful observation, treatment with proton pomp inhibitors and with safe levels of haemoglobulin not requiring blood transfusion, she was safely relieved from hospital. Presently this female patient which we report still is undergoing palliative chemotherapy (II Line FOLFIRI/XELIRI), is in a good condition and as per our last imaging results (CT scan), she still has a stable disease (April 2015).

Discussion

It remains unclear whether ITP associated with solid tumors can be considered as para neoplastic syndrome. Occurrence of Immune-mediated hematological para neoplastic syndromes (PNS) is well known in lymphomas, but in solid tumors whether immune mediated hematological PNS coexists? And if there is any association between these two entities, then can the occurrence of ITP can predict a future probable occurrence of a malignancy, should a patient with ITP be put on surveillance? These questions remain unanswered.[8,9] Some authors however say if a malignancy and ITP coexist, then such type of ITP should be considered as para neoplastic and should be termed secondary ITP.

The cause of such an association among solid tumors remains a research interest. Needed is more interest on the subject, especially oncologists should report more such cases so that more data is available for further analysis. After an extensive literature review we found that by and large most of the centers administered steroids for treating ITP among metastatic solid tumor patients. In case a patient does not respond to steroids, IVIG can be the next option. Indications of treating ITP in a patient without malignancy are platelet count below 20,000-30,000/uL; in case of a cancer patient undergoing chemotherapy the platelet count it seems should be minimum 75,000/uL to avoid bleeding complications. Thus the indication for treating ITP in a patient undergoing chemotherapy is platelet count less than 75,000/uL. It seems the treatment should rather be individualized as we found other approaches like splenectomy, chemotherapy (especially with cyclophosphamide or vincristine as immunosuppressive agents), tumor resection (lobectomy in lung cancer patients) were also offered as other potential treatment options which produced good results as far as treatment of ITP is concerned in such patients.

Cancer patients with ITP refractory to steroids, IVIG, splenectomy can be treated with TPO -mimetics like Eltrombopag or Romiplostin lastly approved by EMEA and FDA. Case reports with the use of these novel agents among patients with chronic lymphocytic leukemia and among patients with breast cancer with successful treatment of refractory ITP have been published.[10]

As our patient had H. Pylori infection confirmed on endoscopic procedures, there are arguments to use H. Pylori eradication therapy for treating ITP in such patients. Some studies have shown that eradication of H. Pylori can also induce long term complete responses as far as treatment of ITP is concerned. Some studies have shown a correlation between ITP and H. Pylori infection, and thus some researchers advocate classifying such ITP with coexisting H. Pylori as secondary ITP. In a simplified version the pathophysiology behind such association is production of autoantibodies directed towards platelets by H. Pylori infection which triggers such a mechanism of production of autoantibodies.[11–13] Probably it's a favorable prognostic factor if ITP and H. Pylori coexist as far as treating ITP is considered. As far as our patient was concerned we did treat her by giving her

antibiotics for H. Pylori eradication, but her ITP was refractory to H. Pylori eradication therapy.

Conclusion

To our knowledge, this is the first reported and published case of metastatic duodenal adenocarcinoma with coexistent ITP, treated with palliative chemotherapy.[14] Chemotherapy protocols (FOLFOX4; FOLFIRI, XELIRI) can be safely administered among patients with metastatic duodenal adenocarcinoma with coexistent ITP.[15,16] After an initial treatment of ITP, probably it is possible to treat patients with coexisting metastatic duodenal adenocarcinoma with chemotherapy protocols like FOLFOX4 and FOLFIRI/XELIRI without significant risk of bleeding. However during the whole treatment process an active surveillance and monitoring of any bleeding signs from the gut or elsewhere is no doubt required.

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Conflicts of interest

The authors declare there is no conflict of interests.

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