EXPERT MEDICAL OPINION REPORT

[redacted]

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Docspert Health

Medical opinions from leading international doctors

Dear Client,

This is your expert opinion report.

How to read the report?

- Always consult and discuss the findings with your doctor.
- Kindly bear in mind that the report is based only on the information you provided and that our www.docspert.com specialists have not had the opportunity to examine you personally.
- If you or your doctor may have questions related to this report, You can ask your www.docspert.com specialist any follow up questions within 10 days of receiving this report.
- For more in-depth discussion, you can request a video consultation with your www.docspert.com specialist to discuss your questions. Please note that there is an extra fee for this service.
- If you want to receive treatment or have an operation in the US, UK or Europe, you can contact us to assist you and arrange all inquiries and procedures.
- Please feel free to contact us anytime. We are here to support you on your way to recovery.

We wish you a speedy recovery and hope that this report will contribute to helping you achieve a piece of mind,

Your DOCSPERT HEALTH team

Docspert Health Case Report

Case number [redacted]

Created on: [redacted]

Consultant

Prof. [redacted]

[redacted]

[redacted]

Profile link:

[redacted]

Patient's information

Name: [redacted]

Gender: Female

Date of birth: [redacted]

Nationality: [redacted]

Patient's personal history

A female patient, 52 years old, lives in Dakahlia, Egypt. She is married, with 4 offspring, the youngest of which is 26 years old. She is a housewife with no special habits of medical importance.
Weight: She was 104 kg and lost weight to 89 kg.

Patient's complaint

The patient has metastatic right breast cancer to brain only (Her2neu positive).

History of present illness

In 2018, the patient developed right breast mass with right axillary lymph nodes BIRADS V on mammogram. True cut biopsy showed Grade II invasive duct carcinoma with ER and PR negative and Her2neu positive score 3+ and KI67 20% and metastatic work up was free.

She received neoadjuvant chemotherapy 6 cycles FEC 100 ended on 06-2018 with subjective and objective response, then underwent Right MRM on 07-2018 and pathology showed residual high-grade duct carcinoma in situ with no invasive component and negative lymph nodes (Tis N0) then received 9 weeks Taxol-Herceptin as adjuvant.

On week 9 of adjuvant Taxol-Herceptin, the patient developed lower limb weakness and headache and MRI brain showed single brain lesion and PET-CT free except for brain, so she received 10 fraction WBI on 10-2019 then shifted to kadcyla where she received 9 cycles then progressed, so she received stereotactic radiotherapy 3 fractions over the brain lesion then shifted to Tykerb-Xeloda for 2 months but she progressed again.

The patient then shifted to Taxol–Herceptin –Perjeta for 6 cycles ended on 11– 2020 with stationary course in MRI for your kind opinion.

The patient has a history of fall since 2 weeks for which she performed MRI on her left knee for follow up.

General enquiry

Constitutional – NAD

Eyes – No jaundice, changes in vision, double vision, blurry vision, not wearing glasses.

ENT – No congestion, changes in hearing, does not wear hearing aids. Mouth– No fetor hepaticus or any other abnormal mouth odor, no dental cares. Skin/Breast – No rashes/ petechiae / pigmentations / spider nevi /nodules/ or discharge.

Cardiovascular – No chest pain, or heart palpitations.

Pulmonary – Repeated chest infections manifested as fever and productive cough.

Gastro–Intestinal – No nausea/vomiting/diarrhea or constipation, No changes in the appetite, No melena/fresh bleeding per rectum

Genito Urinary – No increased frequency or pain on micturition.

Musculo Skeletal – No changes in strengths, no joint tenderness or swelling.

Neurologic – Lower limb weakness, Headache. No seizure.

Psychology – No anxiety or depression.

Haem/Lymph – No easy bruising, history of hematemesis/hemorrhoids, Anemia, Polycythemia

Past medical history

The patient is hypertensive on loop diuretic.

No history of DM.

No history of HCV/ HBV/ HIV.

No history of previous blood transfusion.

Medication history

Phenytoin 100 mg three times per day

Dexamethasone (Epedrone) amp.

Lasix 40 mg tab once daily

Betahistine 16 mg tab once daily

Mepacure (Silymrin) once daily

Ursofalk (Ursodeoxycholate) 250 mg caps once daily

Osteocare (Ca, Mg, Zn,) tab once daily

VitD3

Liver albumin caps twice daily

Paracetamol tab once daily

Patient's hospitalization history

Hospitalized once for thyroidectomy in 1993, currently not on replacement therapy.

Allergies to drugs and other allergies

No history of drug or skin allergy

Family history

No history of similar condition in the family, no other history of malignancies except for her father who had urinary bladder carcinoma.

Allergies to drugs and other allergies

No history of drug allergy

Menstrual history

Menopause for 3 years, Menses was regular with average volume. As for ontraception she only used IUD.

Working diagnosis

The patient has metastatic right breast cancer to brain only (Her2neu positive).

Patient investigations:

1) Investigations of 2018:

Pathology report 4-3-2018

Chemotherapy report 27-6-2018

Case report 27-6-2018

Pathology report 14-7-2018

2) Investigations of 2019:

MRI brain 31-3-2019

3) Investigations of 2020:

Pathology report 21-2-2020

Echocardiography 14-7-2020

PET scan 10-11-2020

MRspectroscopy 15-11-2020

MRI brain 15-11-2020

MRI knee 15-11-2020

Patient questions:

1. Regarding the management plan , What's after Taxol–Herceptin?

2. Is there any recommended modification to the management plan you would like to add?

3. When should we hold the next follow up MRI scan and PET CT?

4. What is the prognosis of the case?

Kindly Note

This is a second opinion and not a prescription or a treatment plan. We always advise that all treatment and follow up should be undertaken by your local doctor.

Expert Opinion on [redacted]

This patient with an HER2-positive ER/PR negative breast cancer has had state-of the-art treatments but despite these treatments, suffers from metastatic brain disease.

To understand the philosophy of next-treatment planning, a closer look at the medical history is necessary.

- The neoadjuvant treatment with FEC 100 resulted in a complete remission of the invasive part of the disease. The DCIS typically is only marginally affected because of the intact basement membrane.

- Brain metastasis was diagnosed during the 9th week of Taxol-Herceptin. Both products don't pass the blood brain barrier (BBB). That is the case also with pertuzumab, lapatinib, neratinib, afatinib and tucatinib (Duchnowska R, Loibl S, Jassem J. Tyrosine kinase inhibitors for brain metastases in HER2-positive breast cancer. Cancer Treat Rev. 2018 Jun;67:71-77. doi: 10.1016/j.ctrv.2018.05.004. Epub 2018 May 9. PMID: 29772459. But also Kadcyla has limited penetrance through the BBB.

Basically, all treatments were effective for HER2-positive breast cancer but could not pass the BBB. The first thing to do is to irradiate the whole brain and this was administered in October 2019. After this treatment Kadcyla worked for 9 cycles and even less with lapatinib-capecitabine.

Besides radiotherapy, other techniques can lower the BBB. Examples are Focused ultrasound (Arvanitis CD, Askoxylakis V, Guo Y, Datta M, Kloepper J, Ferraro GB, Bernabeu MO, Fukumura D, McDannold N, Jain RK. Mechanisms of enhanced drug delivery in brain metastases with focused ultrasound-induced blood-tumor barrier disruption. Proc Natl Acad Sci U S A. 2018 Sep 11;115(37):E8717-E8726. doi: 10.1073/pnas.1807105115. Epub 2018 Aug 27. PMID: 30150398; PMCID: PMC6140479.) and Elacridar, a permeability P-glycoprotein inhibitor (Dash RP, Jayachandra Babu R, Srinivas NR. Therapeutic Potential and Utility of Elacridar with Respect to P glycoprotein Inhibition: An Insight from the Published In Vitro, Preclinical and Clinical Studies. Eur J Drug Metab Pharmacokinet. 2017 Dec;42(6):915-933. doi: 10.1007/s13318-017-0411-4. PMID: 28374336.

Newer treatments depend on extensive molecular profiling. For example, measurement of PD-L1 in the tumor infiltrating lymphocytes predict for response and immunotherapy (Hou Y, Nitta H, Wei L, Banks PM, Parwani AV, Li Z. Evaluation of Immune Reaction and PD-L1 Expression Using Multiplex Immunohistochemistry in HER2-Positive Breast Cancer: The Association With Response to Anti-HER2 Neoadjuvant Therapy. Clin Breast Cancer. 2018 Apr;18(2):e237-e244. doi: 0.1016/j.clbc.2017.11.001. Epub 2017 Nov 9. PMID: 29198959; PMCID: PMC7219558.). Many new approaches are currently under clinical investigation (Pernas S, Tolaney SM. HER2-positive breast cancer: new therapeutic frontiers and overcoming resistance. Ther Adv Med Oncol. 2019 Mar 19;11:1758835919833519. doi: 10.1177/1758835919833519. PMID: 30911337; PMCID: PMC6425535 and can be seen and followed at Home - ClinicalTrials.gov.

1-Regarding the management plan , What's after Taxol-Herceptin

After WBI (whole brain irradiation), the combination of Taxol-Herceptin is capable of inhibiting brain metastases as well as FEC-chemotherapy. In fact, all chemotherapies that affect cancer will (as seen in the neoadjuvant phase), after treatment of the BBB, affect brain metastases as well.

Effective treatment examples are (in combination with Herceptin):

- Epirubine monotherapy
- Combination of Gemcitabine-Vinorelbine
- Carboplatin-Taxol, etc….

2-**Is there any recommended modification to the management plan you would like to add?**

The whole brain radiotherapy has already been added. Now protracted chemotherapy is indicated for longer periods with toxicity (e.g. lower doses, monotherapy ,..) that is well supported and provides an excellent quality of life.

3-**When should we hold the next follow up MRI scan and PET CT?**

I would not concentrate too much on regular diagnostic means but on a well tolerated chemotherapy. In particular, since the brain localizations give early symptoms in case of progression I would perform only new examinations in case the symptomatology predict progression and change of treatment.

4-**What is the prognosis of the case?**

Prognosis depends on the response to treatments and if treatments are possible, there is a reasonable chance for longer survival. The same holds for the constant affluence of new treatment options that can be learned from Home - ClinicalTrials.gov.

Many thanks and best wishes,

Yours sincerely

[redacted]

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Appendix: Investigation Reports Provided

(Investigations are removed from the report for the patient`s privacy)

Docspert Health

+201280958411

support@docspert.com

@DOCSPERT

UK: 44 Buryfield Road, Solihull, B91 2DG

Egypt: 12 Ezz Eldin Taha st., Nasr City, Cairo