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Idiopathic Intracranial Hypertension in a Breast Cancer Patient Receiving Adjuvant Paclitaxel: A Case Report and a Review of the Literature

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Abstract:-

- ***Background:***

Paclitaxel is a cytotoxic drug belonging to the taxane family, widely used in medical oncology, such as in breast cancer, in which it has demonstrated great efficacy, whether as metastatic or adjuvant treatment. Paclitaxel's main toxicities are immediate anaphylactic reactions and peripheral neuropathy. The occurrence of idiopathic intracranial hypertension is an unusual event.

- ***The Clinical Case:***

This is a 53-year-old Moroccan woman, treated for breast cancer; she was put on sequential adjuvant chemotherapy after surgery. She received 3 courses of Doxorubicin and Cyclophosphamide without incident and then we started weekly Paclitaxel. From the very first courses, the patient presented with continuous but moderate headaches, and a cerebral Magnetic Resonance Imaging (MRI) showed signs of idiopathic intracranial hypertension, which was confirmed and treated in the neurology department. The patient progressed well, allowing the 12 courses of paclitaxel to be continued.

- ***Conclusion:***

Idiopathic intracranial hypertension is an unusual complication of paclitaxel. The occurrence of headache or other neurological symptoms in a patient being treated for breast cancer requires an urgent brain MRI, particularly to look for brain metastases.

Keywords:- *Breast Cancer, Idiopathic Intracranial Hypertension, Paclitaxel.*

I. INTRODUCTION

Breast cancer is the most common cancer and the most common cause of cancer-related death in women worldwide [1][2]. Early detection and the development of targeted therapies have reduced the mortality rate from breast cancer, but there are disparities between countries in terms of access to care and screening programmes [3]. In the case of localised breast cancer, surgery represents an important stage in treatment, with the aim of achieving R0 surgery [3]. For luminal like breast cancer, in addition to hormonal treatment, the indication for chemotherapy depends on the risk of recurrence and is linked to a number of high-risk markers; in case of doubt, genomic signature tests can be used [4].

Many adjuvant chemotherapy regimens have demonstrated efficacy, the most recent being the introduction of taxanes, in particular paclitaxel, given sequentially on a weekly basis after treatment with doxorubicin and cyclophosphamide [5]; It is a cytotoxic molecule widely used in medical oncology, belonging to the taxane family. It is an anti-mitotic agent that blocks depolymerisation of microtubules and inhibits chromosome segregation, leading to arrest of cell division and induction of apoptosis. Paclitaxel has side effects, the most common of which are hypersensitivity reactions and peripheral neuropathy [6].

We report a clinical case of idiopathic intracranial hypertension (IIH) in a patient treated for breast cancer with paclitaxel.

IIH tends to affect obese women of childbearing age [7][8], its prevalence has risen sharply in recent years as a result of the increase in obesity rates [9]. It is an increase in intracranial pressure with no obvious cause [10][11]. The diagnosis is based on a number of criteria: papilledema at the fundus, an increase in cerebrospinal fluid (CSF) pressure and normal CSF composition, with imaging showing no aetiology at the origin of this hypertension [12]; however the diagnosis is not always obvious in the face of atypical presentations requiring the presence of indirect radiological signs given their specificity [10].

IIH is not known to be a side-effect of Paclitaxel, its appearance in our patient prompts us to describe the case and to consider the circumstances that led to it.

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II. CLINICAL CASE

This is a Moroccan patient, 53 years old, postmenopausal and mother of 4 children; She has no personal medical history except for moderate obesity with a body mass index of 32 kg/m2, treated for luminal left breast cancer, she underwent partial mastectomy with axillary curage, there was an indication for adjuvant chemotherapy given the axillary lymph node invasion.

Sequential chemotherapy was started and the patient received 3 courses of Doxorubicin and Cyclophosphamide without incident. Then we initiated Paclitaxel on a weekly basis (12 courses planned).

From the first courses of paclitaxel, the patient presented with continuous headaches of moderate intensity; analgesic treatment was prescribed but without improvement. After the 3rd injection of Paclitaxel, a cerebral MRI was requested, suggesting that secondary cerebral localisations were likely. The MRI showed indirect signs of idiopathic intracranial hypertension (see Figure 1 and Figure 2).

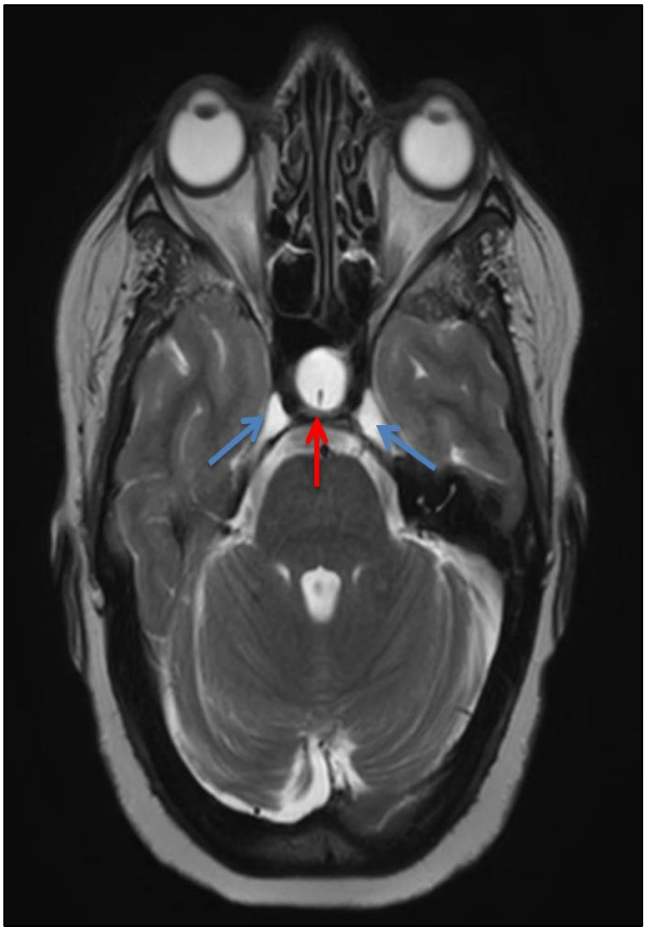

Fig 1: T2 Axial Sequence, Showing Signs of IIH: Empty Sella Turcica with an Intrasellar Arachnoidocele (Red Arrow) + Bilateral Symmetrical Enlargement of Meckel's Cavum (Blue Arrow).

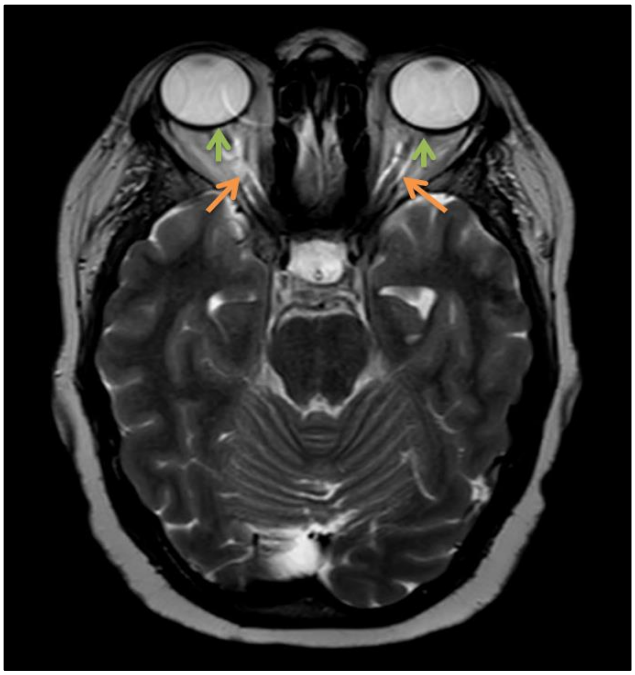

Fig 2: T2 Axial Sequence, Showing other Signs of IIH: Dilatation of the Optic Nerve Sheath (Orange Arrow) + Flattening of the Posterior Surface of the Eyeball (Green Arrow).

A fundus showed papilledema; the patient was referred to neurology, where the diagnosis was confirmed by a high opening pressure and normal CSF composition; she underwent regular lumbar punctures until her symptoms improved, in addition to anti-epileptic treatment with Topiramide and Acetazolamide. The patient's progress was favourable, allowing her to complete 12 courses of paclitaxel.

III. DISCUSSION

Paclitaxel is a chemotherapy molecule belonging to the taxane family, considered to be anti-mitotic, it inhibits microtubule depolymerisation by binding to β-tubulin, leading to mitotic arrest and subsequent activation of apoptosis[13]. The main limitation of this drug is the presence of side effects dominated by hypersensitivity and neuropathy; Hypersensitivity reactions are usually immediate, appearing within the first few minutes of infusion, these reactions may include respiratory signs (bronchospasm, dyspnoea), skin signs (urticaria, erythema or even angioedema) and in some cases hypotension with anaphylactic shock; Fortunately, these reactions can be prevented by proper premedication with corticosteroids and antihistamines [6].

As for neuropathy, the main symptoms are pain, paresthesia and dysesthesia in the hands and feet. The pathophysiology is complex, involving an alteration in axonal transport and oxidative stress resulting from the stabilisation of microtubules, as well as a disturbance in mitochondrial function [14].

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The presence of these side effects has encouraged the development of new forms with greater efficacy and less toxicity, in particular albumin-bound Paclitaxel (nab-Paclitaxel) [15].

There is no direct association in the literature between the use of paclitaxel and the appearance of idiopathic intracranial hypertension. Could this be triggered by a progressive increase in weight, given the repeated premedication with corticosteroids and post-chemotherapy corticosteroid therapy? We have very little data in the literature in this respect, but stopping or reducing the dose of long-term corticosteroid therapy could trigger idiopathic intracranial hypertension, even though corticosteroids are considered to be one of the therapeutic weapons against this condition…[18][19] A paediatric case reported the occurrence of idiopathic hypertension associated with inhaled corticosteroid therapy for asthma [20].

The pathophysiology of IIH is still poorly understood, with a strong link to obesity [7][11]. The validated diagnostic criteria include elevated intracranial pressure, normal CSF composition, the absence of hydrocephalus or neurological lesions explaining this intracranial hypertension, in addition to papilledema at the fundus[11][12]. In our patient, indirect radiological signs were also present, which are very useful to help diagnose atypical forms; according to a prospective study, the diagnosis of HII can be made if two of the following three components are present: papilledema, CSF opening pressure ≥25 cm and ≥3 neuroimaging signs. The presence of 3 neuroimaging signs has a sensitivity of 59.5% and a specificity of 93.5%[10].

In addition to the standard management of intracranial hypertension, it would be interesting to control the main risk factor, which is obesity, Recent studies support the use of GLP-1 (glucagon-like peptide 1) receptor agonists, which may be effective not only in weight loss but also in reducing CSF secretion, given the presence of GLP-1 receptors in the choroid plexus[16]; In our patient, weight loss will help to potentiate the effect of treatment and reduce the risk of her breast cancer relapsing[17].

It is important to remember to ask without hesitation for a cerebral MRI in the event of headaches or any neurological sign occurring in a patient being treated for breast cancer, in order to rule out the presence of cerebral metastases[21].

IV. CONCLUSION

Idiopathic intracranial hypertension is an unusual complication of Paclitaxel. Any headache or other neurological sign in a patient undergoing treatment for breast cancer requires an emergency cerebral MRI to rule out the presence of cerebral metastases. Therapeutic management of IIH includes not only a medical component but also a dietary hygiene component aimed at eliminating obesity, the main risk factor.

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- **Competing Interests :** The authors declare they have no competing interest.

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