

## **Explosive Progression of Brain Metastases from Lung Adenocarcinoma after Radiotherapy and Significant Reversal after Inhalation of Hydrogen-Oxygen Gas**

### **Study Type & Overview**

- A case report published in *Annals of Medical Case Reports* (2022) by oncologists at Fuda Cancer Hospital, Jinan University, China. It documents the first reported case of explosive progression of brain metastases following whole-brain radiotherapy (WBRT) that was then significantly reversed through hydrogen-oxygen gas inhalation alone.

### **The Patient**

- A 51-year-old woman was admitted in October 2019 with left arm pain. CT and MRI confirmed stage IV-B lung adenocarcinoma with multiple brain metastases, mediastinal lymph node metastasis, and rib bone metastasis. Genetic testing revealed an EGFR exon 21 L858R mutation.

### **Prior Treatment Failures**

- The patient was treated with Gefitinib (a first-generation targeted therapy) from December 2019, but after three months showed progression in both lung and brain lesions. Repeat genetic testing at two separate centres showed the original EGFR mutation had turned negative, suggesting the tumour had genetically evolved. She was then switched to Osimertinib (a third-generation TKI), which also failed to prevent progression.
- From May 2 to May 29, the patient received whole-brain radiation therapy (WBRT) at an intensity of Dt50Gy/25f, five days per week.

### **The Explosive Progression – The Critical Event**

- One week after completing radiotherapy, the patient suddenly developed difficulty walking, severe headache, vomiting, confusion, and incontinence. MRI re-examination showed that the number and size of metastases in the brain had increased explosively, covering the entire brain.
- Radiation can promote the growth and invasion of cancer cells, especially metastasis. Evidence from in vivo and in vitro experiments indicates that ionising radiation applied to cancer cells or host cells may stimulate the metastasis process – a known phenomenon called the Tumour Bed Effect.
- The mechanisms behind radiation's pro-metastatic effect include upregulation of G-CSF signalling, triggering of Epithelial-Mesenchymal Transition (EMT) in cancer cells, and increased production of Reactive Oxygen Species (ROS) – all of which promote metastasis and invasion.

### **Hydrogen Inhalation – The Intervention**

In the following month after the deterioration, the patient received no special anti-cancer therapy except symptomatic and supportive treatment. On July 16, she began hydrogen inhalation therapy, inhaling a mixture of hydrogen and oxygen (66% H<sub>2</sub> and 34% O<sub>2</sub>) at a flow rate of 3,000 ml/min via nasal cannula for at least 6 hours per day, intermittently or continuously.

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## The Recovery – The Remarkable Outcome

After half a month of inhalation, the patient's condition began to improve. One month later, her headache had disappeared; she was able to walk, and her eating, consciousness, urination, and bowel movements returned to normal. MRI re-examination showed that more than 90% of the brain metastases had disappeared.

Since then, the patient successfully received further treatments including Sintilimab (a PD-1 inhibitor), Carboplatin, and Bevacizumab. At 15 months follow-up after starting hydrogen inhalation, the patient felt well, was able to perform light physical labour, lung lesions were further improved, and brain metastases remained stable and continuing to improve.

## Why Hydrogen May Have Worked – The Proposed Mechanisms

Based on the role of ROS in promoting radiation-induced metastasis, hydrogen inhalation's ability to selectively scavenge toxic ROS – including hydroxyl radicals ( $\bullet\text{OH}$ ) and peroxynitrite ( $\text{ONOO}^-$ ) – provides a logical explanation for how it reversed the brain metastasis progression in this case.

- Hydrogen molecules inhibit the viability, migration, and invasion of cancer cells, promote cancer cell apoptosis, and can inhibit lung cancer progression through multiple molecular pathways including suppression of STAT3/Bcl2 signalling, downregulation of CD47 (a "don't eat me" signal cancer cells use to evade the immune system), and reduction of cell cycle regulators cyclin D1, CDK4 and CDK6.
- The potentially better effect of hydrogen on brain metastases may also be related to its unique physical properties – hydrogen molecules are the smallest known molecules and highly dispersive, making it easy for them to penetrate the blood-brain barrier into the brain – an advantage no conventional chemotherapy drug enjoys.
- Hydrogen's inhibitory effect on NSCLC may also be related to immune regulation, including decreasing exhausted PD-1+ CD8+ T cells and restoring depleted lymphocyte subsets – effects documented in prior studies by the same team.

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### Conclusions

Although it is difficult to be certain that hydrogen can completely control the disease, at least when the patient was in a critical state, it reversed the condition and provided an opportunity for further treatment. Radiotherapy is a double-edged sword, and doctors should pay attention to its adverse effects, especially for brain metastases complicated by lung cancer. Molecular hydrogen's role in cancer treatment is worthy of attention and further research.

### Limitations to Keep in Mind

- This is a single case report – the lowest level of clinical evidence. No generalisable conclusions can be drawn.
- The patient subsequently received immunotherapy (Sintilimab), chemotherapy (Carboplatin), and anti-angiogenic treatment (Bevacizumab), making it impossible to attribute long-term stabilisation solely to hydrogen.
- No immune profiling was performed on this patient, so the proposed immune mechanisms remain speculative in this specific case.
- The dramatic MRI improvement (>90% of metastases disappearing) is extraordinary and has not been replicated in a controlled trial setting.
- The case report comes from the same research group (Fuda Cancer Hospital) responsible for several other hydrogen studies in this series, so independent replication from other centres is important.

To Read The Full Study Please

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