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Neuroendocrine Tumor and Psychosis: A case report

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I. INTRODUCTION:

Neuroendocrine Tumours (NETs) are tumours arising from the diffuse neuroendocrine cells in the body, with an estimated prevalence of 35 per 100,000(1).

They are often classified by their site of origin and their symptoms seem to vary according to various sites (2)(3). A peculiar characteristic of NETs is their potential to synthesize and secrete a wide range of metabolically active substances into the systemic circulation (e.g. hormones and amines, such as bradykinins, tachykinins, prostaglandins, and histamine) of which serotonin is the most prominent(4), leading to a wide range of clinical syndromes.

Approximately 10% of serotonin producing neuroendocrine tumours lead to carcinoid syndrome, which occurs when biologically active substances secreted by the tumour bypass liver metabolism either by way of the tumour not draining into the portal system or due to hepatic metastasis, and enter the bloodstream(5).

The synthesis of serotonin by tumour cells can deplete central serotonin, increasing the risk of psychiatric disorders. Psychiatric symptoms, including depression and anxiety, are common in metastatic carcinoid tumours. However, the precise mechanisms and treatment methods for associated psychotic symptoms are unclear.

This case report focuses on the management of psychosis in a 64-year-old female patient with a carcinoid tumour.

II. CASE REPORT:

A 64-year-old female patient, presenting with symptoms of sleep disturbance, fearfulness, gabhraman, hearing of voices of her neighbours (commanding in nature), suspiciousness that some unknown person was trying to harm her family for 2 months following a family function in January 2023. She would fear that something would happen to her family and would keep all the doors of the house closed, find injury marks over her husband's face and would repeatedly call her brother to check about their safety. These symptoms significantly affected the patient's functioning. With these complaints, the patient was started on psychiatric treatment.

After a few days, the patient had complaints of vomiting, abdominal pain, nausea and fever, so the patient was admitted to a private hospital for medical evaluation. On detailed investigation, CTscan Abdomen showed? neoplasticetiology, carcinoid/carcinoma/ ?koch's and USG showed two lesion of 10-25 mm in ileum and in gallium 68 dotatoc PET CT abdomen also showed local lymph node metastasis. Hence laparoscopic D3 right hemicolectomy was done on 17thFebruaary 2023. The biopsy specimen revealed well differentiated neuroendocrine tumour with lymphovascular and perineural invasion on histopathological examination and positivity for cytokeratin AE1 and AE3, synaptophysin and chromogranin on immunohistochemical examination. With above findings, the final diagnosis was given as well differentiated neuroendocrine tumour, grade 1, terminal ileum.

There was some improvement in psychotic symptoms after the operative measures but still hampering the patient's functioning, due to which the patient presented in SMIMER outpatient department in April 2023. The patient was already on Trifluoperazine 5mg, Risperidone 2mg and Aripiprazole 15mg at the time of presentation to SMIMER Hospital. The **Mental Status Examination (MSE)** of the patient revealed the following: The patient was restless, had labile mood, Delusion of Persecution and Auditory hallucination (Second degree, commanding type) were present. The cognitive status of the patient showed impaired attention and concentration, impaired immediate and recent memory and partially impaired abstract thinking.

The patient had first episode of psychotic complaints, in the form of suspiciousnessin 2006 with exacerbations in between precipitated by stressful events in the family as well as medical conditions(menopause in 2006,? Breast Fibroadenoma in 2007)until 2008when her symptoms resolved after taking psychiatric treatment. After this, the patient would develop

occasional suspiciousness in between along with intermittent episodes of irritability, but no treatment was taken. The patient also had a positive family history for schizophrenia in maternal side cousins in third degree relative, but no history of schizophrenia in parents and siblings.

The patient was started on treatment and after few changes in dosage of ongoing medications, currently, the patient is significantly better on Tab. Trifluoperazine (5 mg) + Tab. Trihexyphenidyl (2 mg) one in the morning and two tablets at night, Tab. Risperidone (2 mg) + Tab. Trihexyphenidyl (2 mg) one tablet at nigh at 2 months follow up.

III. DISCUSSION:

In daily clinical practice, the neuropsychiatric alterations were commonly observed in NET patients, which includes a wide variety of symptoms, from slight irritability to anxiety, depression, and psychosis and sleep disorders, which can lead to social dysfunctioning(6). Two case reports have been reported in the past for psychosis associated with Carcinoid Tumour.(7)The reported frequency of depression in patients with Carcinoid Syndrome varies from 50 % to less than 1 %(7).Serotonergic brain dysfunction is hypothesized to occur in these patientsdue to peripheral over-consumption of tryptophan, an essential amino acid. This leads to decreased central serotonin levels, affecting dopamine synthesis and activation through NMDA and GABA-mediated action.

Carcinoid syndrome, can further exacerbate these symptoms by diverting tryptophan from niacin synthesis to serotonin formation(8). Additionally, some patients may experience unmasking of carcinoid symptoms when prescribed selective serotonin reuptake inhibitors (SSRIs). Surgical removal of the tumor, the primary treatment for NETs, often necessitates the use of somatostatin analogues that reduce serotonin levels, potentially worsening psychotic symptoms.

Monitoring serotonin dysfunction after tumor removal can be done by measuring 5-hydroxyindoleacetic acid (5-HIAA) levels in urine. Quetiapine, which acts on both serotonin and dopamine receptors, has been suggested for psychosis management in carcinoid tumors(7). The complexity of managing both the tumor and psychotic symptoms underscores the importance of a comprehensive approach in the care of NET patients.

IV. CONCLUSION:

Carcinoid tumors have a slow growth rate, with an average time of 53.8 months from symptom onset to diagnosis. Early detection and treatment are crucial for a favorable prognosis, as gastric carcinoids tend to metastasize to the liver and increase serotonin production.

However, there is limited research on treating psychosis in carcinoid syndrome and understanding the complex interactions between serotonin level changes, antidepressant use, and antipsychotic medications.

This case report contributes to the existing literature by supporting the connection between serotonergic brain dysfunction, psychiatric symptoms, and carcinoid syndrome. It emphasizes the importance of recognizing the overlap between endocrine-oncology and psychiatry and gaining a deeper understanding of the neurobiology of organic illnesses.

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