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Neuroendocrine Tumor-II as a Primary in the Central Nervous System

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Abstract:- Malignancies known as neuroendocrine neoplasms (NENs) have sporadic instances of developing central nervous system. It was discovered that a 36-year-old lady had a primary Neuroendocrine tumor of the brain who presented with headache, vomiting, and hearing difficulty from the left ear and was diagnosed with a left cerebellopontine angle solid mass. After subtotal excision, histology revealed a Neuroendocrine tumor-II. Adjuvant radiation was administered following a thorough search for an extracranial main tumour, which included the use of Ga-68 DOTANOC-PET-CT. This led to the identification of a primary central nervous system Neuroendocrine tumor. The patient was free of metastatic or recurrent disease at 9 months of follow-up.

Keywords:- *Neuroendocrine Tumor; Cerebello-Pontine Angle; Radiotherapy, Subtotal Excision.*

I. INTRODUCTION

The human body's neuroendocrine system is made up of a sophisticated network of cells that have the ability to become neuroendocrine neoplasms or NENs. These cells are well-described in the respiratory tract, gastrointestinal tract, and central nervous system (CNS), and they are distributed diffusely across several organs (1). The synthesis and distribution of physiologically active chemicals are regulated by neurotransmitters, and neuroendocrine cells play a role in this process. Clinically, NETs can be classified as either non-functional or functional based on whether increased hormone production is linked to them. They can also be grouped based on their grade [(1)] and anatomical location. The lungs, liver, gastrointestinal system, and pancreas are the most frequent sites of genesis for NETs. A primary CNS origin for NETs is uncommon, however, it can happen with metastasis, particularly the high-grade form, involving the central nervous system (CNS). In the brain, intracranial neuroendocrine tumours occur 0.8% of the time [(2)]. We report here a case of a cerebello-pontine angle tumour, a primary brain NET that has been pathologically established to be positioned in the left cerebello-pontine angle.

II. CASE SUMMARY

A 36-year-old woman came into the emergency complaining of a headache, vomiting, and trouble hearing out of her left ear over the previous four months. There was no past medical history of cancer or any other illness. The patient had an ECOG Performance Score of 2. General physical examination and motor examination were normal. NCCT Head was suggestive of extra-axial SOL in the left cerebello-pontine angle. She underwent the right MPVP shunt procedure for raised intracranial tension.

Magnetic resonance imaging of the brain showed a left-sided extra-axial CP angle SO(4.5cm*5cm) (Figure 1 A, B, C,). The patient was taken up for surgery and underwent RMSO craniotomy with subtotal excision of the tumor. Post-op CEMRI BRAIN showed lobulated heterogeneous lesions measuring 2.1 cm & 2.3 cm in the left CP angle involving the inferior and middle cerebellar peduncle and left medulla oblongata and pons (Figure 2 A, B, C).

The biopsy of the lesion was suggestive of a Neuroendocrine tumor Grade II. An extensive IHC panel was done which showed positive for synaptophysin, dot-like positivity for cytokeratin, patchy positivity for GFAP and diffuse S100 positivity. The tumor cells were negative for CK20, OLG2, Prolactin, ACTH, GH, FSH, LH, PIT-1, TBX-2, TTF-1, PAX-8, CDX-2 and SATB2 and GATA3, KI67 Index- 5-6% which further confirmed the diagnosis of Neuroendocrine tumor Grade II. The Serum Chromogranin was 25.14 ng/ml. The patient underwent extensive workup to ascertain any site of the primary lesion given the rare occurrence of Primary CNS neuroendocrine tumors. Upper and lower Gastrointestinal endoscopies were normal. Laryngeal endoscopy was suggestive of a left vocal cord biopsy. The patient underwent a 68-GA DOTATATE PET Scan which showed tracer avid ill-defined heterogeneously enhancing soft tissue lesions 2.1 & 1.3cm in left CP angle. Another tracer avid heterogeneously enhancing soft tissue lesion 1x1cm in the suprachiasmatic and suprasellar region. No other lesion was seen. The case was discussed in the Tumor Board, and it was planned to be treated as a primary CNS neuroendocrine tumor. The patient received an adjuvant Radiotherapy for residual lesion. The patient was free of metastatic or recurrent disease at 9 months of follow-up.

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III. DISCUSSION

Neuroendocrine tumours are uncommon neoplasms that emerge from enterochromaffin and argentaffin cells. These cells are commonly found in the gastrointestinal tract or bronchopulmonary tree, but they can also originate from the pancreas, thymus, or other locations. Because the tumour grows slowly, there is a higher chance and rate of metastasis. Although this tumour frequently metastasises to bone tissue, the central nervous system (CNS) is seldom affected. A CNS carcinoid tumour without a primary source is extremely uncommon [(3)].

Neuroendocrine tumors are identified by their histopathological features which usually give an appearance of "salt and pepper" nuclei. There is cellular uniformity with the central oval nucleus. It may show a varied architecture like trabeculae, glands, pseudo rosettes etc. For immunohistochemistry, Chromogranin A and synaptophysin are currently considered the most specific markers for Neuroendocrine neoplasms. Ki-67 labelling index is accepted as a proliferative marker for NENs being independently correlated with survival and representing the most reliable prognostic factor of neuroendocrine tumors [(4)].

The Ki-67 index and/or mitotic activity of gastrointestinal neuroendocrine tumours (NETs) are used to grade them. Along with other factors such as tumour size, lymphovascular invasion, and disease stage, the grade is crucial for NET prognosis and therapy choices. Neuroendocrine neoplasms are classified into three categories by the World Health Organisation (WHO): poorly differentiated neuroendocrine carcinoma (NEC), mixed neuroendocrine-non-neuroendocrine neoplasms, and well-differentiated NETs. Grade 1 (Ki-67 index <3% [mitotic count < 2 per 10 high-power fields (HPF)]), grade 2 (Ki-67 index 3%–20% [mitotic count < 2–20 per 10 HPF]), and grade 3 (Ki-67 index >20% [mitotic count >20 per 10 HPF]) are the three categories into which NETs are divided by the WHO [(5)].

Our patient had a negative DOTATATE PET scan and no prior history of primary carcinoid cancer. One cutting-edge functional imaging technique for evaluating well-differentiated NETs is gallium-68 DOTATATE PET/CT. It is the favoured imaging modality for determining the location of unidentified primary tumours, making early diagnoses, and choosing patients for peptide receptor radionuclide treatment. With a 97% sensitivity and 93% specificity, this scan has been utilised to detect neuroendocrine tumours [(6)]. In our instance, it only showed aberrant activity in the brain's Left CP angle area and not anywhere else, including the gastrointestinal tract, liver, spleen, or urinary tract. This suggests that our case may represent a primary intracranial neuroendocrine tumor. We reviewed the available literature and found that to date, less than 10 cases of primary CNS NETs have been reported.

The first documented case in the literature was published by Tamura et al. A 77-year-old man who was experiencing headaches and difficulty with skilled motor skills was the patient in this instance. A large malignant lesion that originated in the left parietal and temporal lobes and produced a mass oedematous effect was visible on the CT scan. A complete and gross excision of the tumour was performed. Based on histopathology, the tumour was identified as NET. FDG-PET and CT scans did not identify any further origin location. Following that, the patient experienced two local recurrences, which were treated by gamma knife radiosurgery and resurgery, respectively. At the 2-year follow-up, the patient was clear of illness [(7)].

A case of a 71-year-old man who presented with a changed mental state was documented by Greenberg et al. A complicated, intensifying, hemorrhagic mass was visible on the brain's MRI of the left parietal lobe. A CT scan of the pelvis, abdomen, and chest revealed no further tumour sources. The patient lumped surgically removed, and the histology revealed that it was a high-grade, poorly differentiated small-cell neuroendocrine carcinoma. After that, the patient had postoperative cavity stereotactic radiosurgery [(2)].

Another instance, described by Reed et al., was a 34-year-old woman who had been healthy until exhibiting signs of intracranial hypertension, which was thought to be the result of a primary NEN of the brain. After receiving four rounds of cisplatin and etoposide as adjuvant intensity-modulated radiation treatment (IMRT), she experienced a locoregional recurrence of the initial NEN in the same location ten years later. Despite extensive diagnostic testing, no further sources of a primary tumour were ever found. The patient ultimately passed away from complications resulting from a ventriculoperitoneal shunt that was implanted to address the disease's hydrocephalus [(1)].

In 2009, Vernieri et al. reported the diagnosis of a cerebellum well-differentiated neuroendocrine tumour in a 38-year-old patient. Initially, it was thought to be a metastasis from an unidentified WDNET that originated outside of the cerebellum. But even after a thorough 6-year follow-up, no extracranial WDNET was ever discovered. The patient underwent radiation and surgery for the twice localised recurrences of the tumour throughout this period [(8)].

Because Primary CNS neuroendocrine tumours are uncommon, there are currently no clear guidelines for their care. The prognosis for individuals with brain NETs may differ significantly from that of patients with metastatic brain NETs since the primary cause of mortality in these patients is attributable to the advancement of systemic illness. Compared to non-metastatic NETs, which have a 47% ten-year overall survival rate, primary brain NETs seem more similar.

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IV. CONCLUSION

We present a very uncommon scenario of a brain's primary intracranial neuroendocrine tumor. Because the patient was a young female, she underwent subtotal excision due to the location of the tumor followed by intensity-modulated radiotherapy. The patient needs a routine three monthly MRI brain and 68-GA DOTATATE PET Scan for the first two years followed by 6montly for the next three years and annually for a lifetime to detect recurrence.

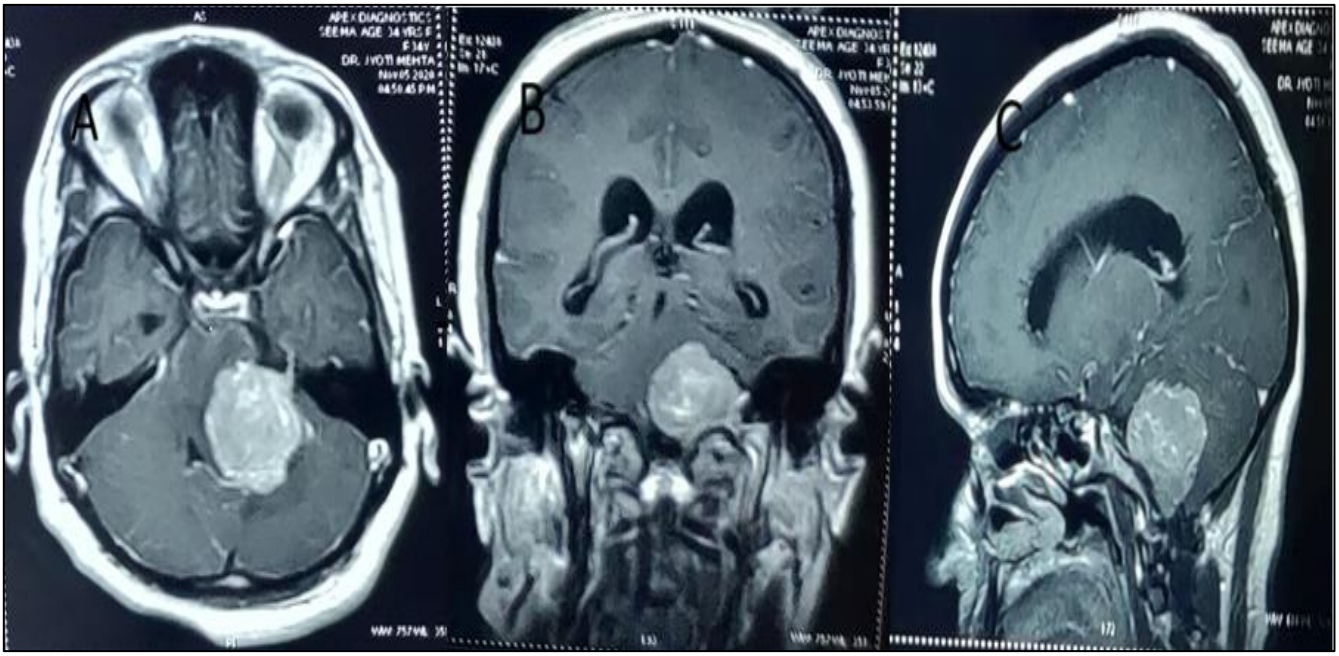

Fig 1. MRI Brain Images of the Patient T-1 Contrast Weighted Imaging. The Lesion Appears View Iso-to-Hyperintense in Nature. A- Axial View, B- Coronal View, C- Sagittal

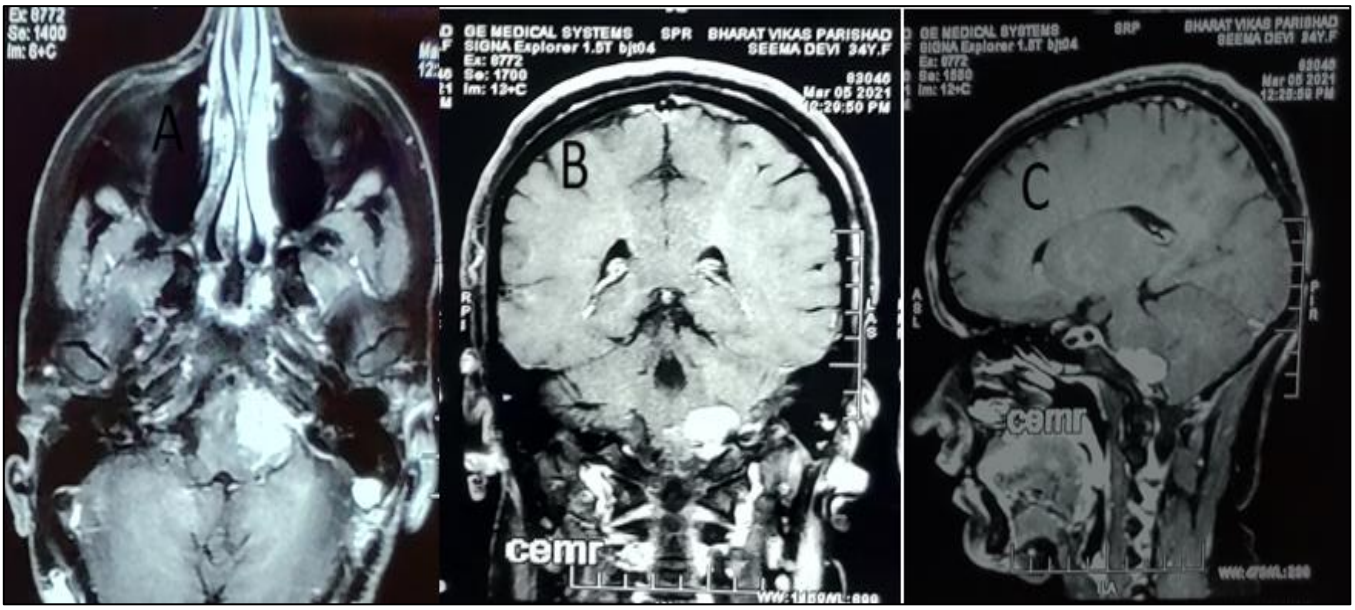

Fig 2. MRI Brain Images of the Patient T-1 Contrast Weighted Imaging. There is a Residual Lesion Present in the Post-Op Imaging. A- Axial View, B- Coronal View, C- Sagittal

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No conflicts of interest.

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