



**INTERNATIONAL JOURNAL OF
PHARMACEUTICAL SCIENCES**
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: <https://www.ijpsjournal.com>



Case Study

Pilocytic Astrocytoma Induced Neutropenia: Case Report

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ARTICLE INFO

Published: 25 Aug 2025

Keywords:

Pilocytic astrocytoma,
tumor, BRAF, neutropenia

DOI:

10.5281/zenodo.16940746

ABSTRACT

Pilocytic astrocytoma (PA) is a kind of benign brain tumor. The most prevalent age group for PA, a brain tumor grade I according to the World Health Organization, is 0–14 years old. This tumour usually located in the cerebellum. PA is slow-growing, benign, and have a high survival rate. The location of tumor plays a role in executing symptoms and they include headache, vision problems, and CNS defects. MAPK alterations, KIAA1549-BRAF fusion plays a role in occurrence of PA. Diagnosis relies on imaging techniques like CT / MRI and biopsy. Treatment includes surgical resection, chemotherapy and radiation therapy. Neutropenia is a side effect of treatment for PA.

INTRODUCTION

"Gliomas" refer to tumors that originate in the brain's glial or supporting tissue. Astrocytoma is one kind of glioma. According to World Health Organization (WHO), astrocytoma's are of 4 groups. They are divided based on the growth rate and propensity to infiltrate (spread) to surrounding brain tissue. The non-infiltrating astrocytoma exhibits slow progression. Astrocytoma occurs in various parts of brain like cerebrum, cerebellum and on nervous system (1).

DEFINITION

Among both adults and children, pilocytic astrocytoma is the most prevalent primary tumor. It ranks first among glial neoplasms of the central nervous system in children and the most prevalent tumor in the cerebellum. There is a survival rate of 94% after 10 years with this tumor, and it is benign (2). According to World Health Organization pilocytic astrocytoma comes under grade I category of tumors. These tumors arise from the cerebellum, hypothalamic region, brainstem, and spinal cord (3). Based on data collected from the Central Brain Tumor Registry of the United States (CBTRUS), about 19.5% of central nervous system tumors in children 0–14 years old are pilocytic astrocytomas (4).

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



EPIDEMIOLOGY

The most prevalent juvenile glioma and cerebellar tumor is pilocytic astrocytoma. About 85% of PAs have cerebellar astrocytomas, while 10% have cerebral astrocytomas. Among intracranial neoplasm PA accounts for 0.6% - 5.1% and 1.7% - 7% of all glial tumors.

Of all NF1 individuals, pilocytic astrocytoma most frequently affects 15%–21%. 75% of instances of pilocytic astrocytoma occur within the first 20 years of life, and it most frequently affects children and young people. There is no gender variation in the occurrence of PA (2).

CLINICAL FEATURES

Symptoms of PA varies from site of origin. The clinical features include-

| Site of origin | Symptoms |
|----------------------|--|
| Brain stem | Nausea, vomiting, ataxia, papilledema, nystagmus. |
| Tectum | Headache, vomiting, paresis, abnormal headache, vomiting, paresis, abnormal gait, somnolence, Parinaud syndrome, diplopia. |
| Optic pathway | Visual loss, optic disc pallor, optic nerve atrophy. |
| Hypothalamus | Obesity, diabetic insipidus. |
| Cerebral hemispheres | headache, seizure activity, hemiparesis, ataxia, nausea, and vomiting. |

Some of the most typical symptoms are nausea, vomiting, trouble walking, double vision, impaired vision, and soreness in the neck (1,2,5).

PATHOLOGY

“Subtypes of juvenile pilocytic astrocytoma often exhibit molecular changes in the MAPK pathway, including NF1, BRAF, KRAS, FGFR1, PTPN11, NTRK, RAF1, and SRGAP3. One possible mechanism that causes multiple Pas is the

Ras/Mitogen-activated protein kinase (MAPK)/RAF/extracellular signal-regulated kinase (ERK) (1).These alterations drive cells, both healthy and cancerous, to grow, proliferate, and eventually die. Tandem duplication at 7q34 is the genetic abnormality that allowed the KIAA1549 and BRAF genes to fuse. Because of this fusion and the constitutive kinase activity of the Ras/ERK pathway, the amino-terminal BRAF autoregulatory domain is eliminated. PAs with cerebellar origins are more likely to have the KIAA1549-BRAF fusion, which is present in 60-94% of PAs.”

A fusion of the FAM131B and BRAF genes is another known BRAF mutation that initiates PA (2).

DIAGNOSIS

- **COMPUTED TOMOGRAPHY (CT)-** The majority of cerebellar and cerebral pilocytic astrocytomas look well-defined on computed tomography (CT), with smooth edges, cystlike characteristics, a round or oval form, and sporadic calcifications. They are smaller than 4 cm in size (2).
- **MRI-** PAs are usually hyperintense on T2-weighted or FLAIR images and hypo- or iso-intense on T1 sequences on MRI. Usually, they are diffusely and significantly enhancing. They might have tumor nodules inside of them or contain cysts (2).
- **BIOPSY-** A biopsy will assist in distinguishing a tumor from other lumps, including an infection. When grading the tumor, its microscopic structure will be crucial (2).
- **OTHER TESTS** Patients with astrocytoma-related seizures may have their epileptiform activity assessed and tracked using electroencephalography (EEG). Radionuclide



scans, such as technetium-based imaging, positron emission tomography (PET), and single-photon emission tomography (SPECT), may be used to study tumor metabolism and brain function (2).

TREATMENT

SURGICAL TREATMENT

Surgical removal is typically the recommended course of therapy since it usually has favorable results, including recovery and good overall survival. The main therapy for PA, according to the National Comprehensive Cancer Network (NCCN) recommendations, is excision. Usually, patients who get a complete resection don't need any more care. The National Comprehensive Cancer Network (NCCN) recommends radiation therapy (RT) for neurologic symptoms or tumor growth, monitoring in instances of partial resection in adults, and BRAF/MEK inhibition for tumors mutated to BRAFV600E. There is a high chance of positive outcomes, good recovery and overall survival. Stereotactic resection can be used to lesions in less advantageous sites, such as the basal ganglia.

Adjuvant treatments like radiation and chemotherapy are reserved for cases where surgical resection is not a possible. Children less than five years old are not candidates for radiation treatment due to the risk of morbidity it carries (4).

RADIATION THERAPY

Radiation treatment involves the destruction of tumor cells with high-energy X-rays or other particles. External beam radiation therapy is the standard method of administering radiation to patients. Internal radiation treatment refers to radiation that is administered via implants (4).

CHEMOTHERAPY

Adolescents in their pre-puberty years may benefit from carboplatin and vincristine chemotherapy if their low-grade astrocytomas are incurable because of their location, have an early recurrence rate, or are progressing. Alternate dosing regimens may also be effective. Patients with high-grade malignancies do not benefit much from chemotherapy, despite the fact that some chemotherapy regimens do provide significant tumor response rates (4).

NEUTROPENIA-

“After one year of life, the condition known as neutropenia, when the absolute neutrophil count (ANC) is less than $1.5 \times 10^9 / L$ (less than 1500 / μL), is present (6).

CLASSIFICATION (6,7)

| ANC LEVEL | CATEGORY | RISK FACTOR |
|-----------------------------|-----------------|--------------------------------------|
| $1.0 - 1.5 \times 10^9 / L$ | Mild | Doesn't impair host defence |
| $0.5 - 1.0 \times 10^9 / L$ | Moderate | Acute risk of infection |
| $0.2 - 0.5 \times 10^9 / L$ | Severe | Increased risk of infection |
| $\leq 0.2 \times 10^9 / L$ | Agranulocytosis | Severe, life-threatening infections” |

ETIOLOGY-

- Nutritional deficiencies like vitamin B₁₂, folic acid, copper, protein-calorie malnutrition.
- Neonatal iso immune neutropenia occurs when antibodies developed during pregnancy are unable to cross the placenta and instead target certain epitopes, most often HNA-1a, HNA-1b, and HNA-1c antigens.
- Lupus erythematosus and rheumatoid arthritis also a reason of neutropenia.

Some chemotherapeutic agents and some range of drugs also responsible for occurrence of



neutropenia. Drugs like carbamazepine, valproate, sulphonamides, penicillin, olanzapine, methimazole, propylthiouracil, rituximab, etc, share a huge role in occurrence of neutropenia (6).

DIAGNOSIS OF NEUTROPENIA

Important diagnostic methods include genetic testing, anti-neutrophil antibodies, bone marrow aspiration, and a full blood cell count (6).

THERAPY

For acute infections of neutropenia, a wide range of antibiotics are used. To treat chronic neutropenia, G-CSF therapy is employed.

For a subject suffering from chemotherapy induced neutropenia G-CSF therapy is highly employed. Recombinant human G-CSF increase the production of Neutrophils in the body (6).

CASE DISCUSSION

A 11 years old male patient was admitted in the oncology, haematology and BMT ward on 17/4/2025 with the chief complaints of pancytopenia. Patient has no h/o right frontotemporal craniotomy and biopsy of optic hypothalamic glioma + right ventriculoperitoneal shunt on 17/4/2024. Patient was diagnosed with Pilocytic astrocytoma WHO-grade-1

GFAP positive, BRAF 600E positive, Ki 67-2%

- Post cycle 1 chemotherapy- PLV on 23.10.2024
- Post cycle 2 chemotherapy- PLV on 12.12.2024
- Post cycle 3 chemotherapy- PLV on 23.01.2025
- Post cycle 4 chemotherapy- PLV on 06.03.2025

- Febrile Neutropenia and anemia 17.04.2025-2 units of PRBC transfused.

Now admitted for supportive care and management.

- On examination the patient heart rate was 136/min, Respiratory rate was 22/min, blood pressure was 142/83mmHg, and temperature and spO2 was afebrile.
- 2 units of leukodepleted, irradiated PRBC transfusions has been done and was uneventful.
- On 18/4/2025 patient hemogram shows hemoglobin 9.5gm%, WBC count was 3000, platelet count was 44000.
- On 19/4/2025 patient hemogram shows hemoglobin was 10.8gm%, WBC count was 4500, platelet count was 52000. The laboratory investigations of HB was found to be 9.5gm%, polymorphs 78%, lymphocytes 10%, eosinophils 02%, monocytes 10%, haematocrit(PCV)28.1vol%, RBC count was 3.29mill/cells, WBC count was 3000cells/cumm, RDW17.1%.
- INJ. Magnex forte 3gm BD, INJ. Neukine 300mcg S/C OD, IVF Ns@100ml/hr has been advised to take on 18/4/2025 and 19/4/2025 days.

CONSLUSION

Thus, the main motive of this written report is to create awareness in hospital sectors about the side effects of treatment given for pilocytic astrocytoma and treat Neutropenia.

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HOW TO CITE: Dr. Ramadevi Pemmereddy, Mattam Pavani, Dornala Manoj, Pilocytic Astrocytoma Induced Neutropenia: Case Report, *Int. J. of Pharm. Sci.*, 2025, Vol 3, Issue 8, 2686-2690. <https://doi.org/10.5281/zenodo.16940746>

