High-grade Glial Tumors Associated with *ETV6-NTRK3* Gene Fusion: Imaging Appearance with Pathological Correlate

Juliet M Alla, BA¹, Joshua P Nickerson, MD¹, Matthew Wood, MD, PhD¹, Mahmud Mossa-Basha, MD², Christopher G Filippi, MD³, Deborah Zarnow, MD⁴, Jianling Ji, MD⁵, Jaclyn A Biegel, PhD⁵, Yasmine Akkari, PhD⁶, Gisele Ishak, MD², Ramon Barajas, MD¹

¹OHSU, ²U of Washington, ³Northwell Health, ⁴Children's Hospital of Philadelphia, ⁵Children's Hospital of LA and Keck SOM, ⁶Legacy Health

Background

High-grade glial tumors in the pediatric population associated with the *ETV6-NTRK3* gene fusion are rare but treatable malignancies, with reports of response to first-generation TRK tyrosine kinase inhibitors.

Materials and Methods

Five pediatric patients (3 female and 2 male; age range, 11 days – 4 yrs) presenting with high-grade glial neoplasms associated with the *ETV6-NTRK3* gene fusion were evaluated via MRI.

Case 1

A 3-year-old female presented with a 2 mo history of morning emesis. Gadolinium-enhanced MRI showed (Fig 1):

- Extensive abnormal tissue at the margins of the lateral ventricles
- Mixed cystic and solid mass extending into the parietal lobe
- Tumor did not demonstrate enhancement or reduced diffusion
- Leptomeningeal CSF dissemination within the internal auditory canals, distal lumbar spine, and dura of the posterior fossa

Pathologic and genetic analysis confirmed *ETV6-NTRK3* gene fusion (Fig 3).

Treatment with a TRK tyrosine kinase inhibitor was initiated with marked clinical and radiological response (Fig 2).

FIGURE 1

FIGURE 2

FIGURE 3

Case 2

A 5-month-old male presented with macrocephaly.

MRI revealed (Fig 4):

- Large partially cystic mass with a solidly enhancing nodule
- Hydrocephalus and a large porencephalic cyst
- No diffusion restriction

The mass and cyst were resected; disease recurred 3 yrs later and was resected again.

Genetic evaluation revealed *ETV6-NTRK3* gene fusion.

TRK tyrosine kinase inhibitor therapy was initiated with no evidence of disease progression at 2 yr follow up.

FIGURE 4

Case 3

A female twin born at 27 wks gestation was found to have a brain mass on prenatal US and fetal MRI at 26 wks. Post-natal MRI on day 11 of life revealed (Fig 5):

- Large heterogeneous mass in left parietal lobe
- Large flow voids and areas of diffusion restriction within the mass
- Areas of intrinsic T1 shortening and susceptibility artifact within the mass
- Peripheral regions of avid, irregular, nodular contrast enhancement

Perfusion with arterial spin labeling revealed markedly elevated cerebral blood flow within the mass.

Genetic analysis confirmed *ETV6-NTRK3* gene fusion.

FIGURE 5

Case 4

A 4-year-old female presented with morning emesis and headaches.

MRI demonstrated (Fig 6):

- Large posterior fossa mass within left cerebellar hemisphere
- Cystic or necrotic central mass with peripheral rim of irregular, nodular enhancement
- Adjacent solidly enhancing tumor mass
- Trace susceptibility artifact on SWI imaging

Mass was resected and *ETV6-NTRK3* fusion was confirmed on genetic testing.

FIGURE 6

Case 5

A 2-year-old male presented with repeated seizure and severe headaches.

MRI revealed (Fig 7):

- Large mass within right temporal lobe
- Mixed areas of cystic or necrotic change
- Neovascularity and scattered foci of susceptibility artifact suggestive of intratumoral hemorrhage
- Irregular and nodular enhancement
- No diffusion restriction

ETV6-NTRK3 fusion was found following resection and genetic analysis.

FIGURE 7

Results

The cases in this series revealed a heterogeneous imaging appearance of *ETV6-NTRK3* fusion gliomas, with findings including mixed cystic and solid masses, irregular and nodular enhancement, neovascularity, and scattered foci of susceptibility artifact.

Conclusions

These data suggest that despite sharing a common genetic underpinning, imaging findings for *ETV6-NTRK3* fusion gliomas are heterogeneous. Advances in understanding the evolution and subtypes of these tumors may enable radiologists to further differentiate these neoplasms based on imaging appearance.

Contact

Joshua P. Nickerson, MD
OHSU Department of Radiology
3181 SW Sam Jackson Park Rd., Portland, OR 97239
nickerjo@ohsu.edu

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