Pleomorphic Xanthoastrocytoma

19

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19.1 Introduction [1–4]

- Pleomorphic xanthoastrocytoma (PXA) is a low-grade glial tumor constituting 1% brain tumors.
- Kepes et al. described it for the first time in 1993.
- Arises from subpial astrocytes.
- Most commonly affects second and third decade of life (10–30 years); Median age—33 years (Range 4.5–75).
- No gender predilection.
- Associated with seizure in young adults and considered a part of epileptogenic tumors spectrum.
- Nearly 50% of patients present with seizure and one-third present with headache.
- These tumors commonly arise from the temporal lobe (nearly 50%). Frontal, multi-lobar, and spinal location has also been described.
- Mostly localized but isolated reports of leptomeningeal dissemination.
- Most of the tumors are supratentorial, less than 10% are infratentorial.
- Tumor is superficial, proximal to dura but without involvement.

19.2 Classification

- Pleomorphic xanthoastrocytoma—WHO grade II tumors (80%)
- Anaplastic pleomorphic xanthoastrocytoma (APXA)—WHO grade III tumor (Anaplastic may be de novo or as progression from grade II)

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- Criteria
  - >5 mitoses per 10 high-power fields and increased cellularity
  - Presence of necrosis
  - MIB-1 labeling index >4%

19.3 Investigation

Anaplastic cases appear as high-grade glioma.

19.3.1 Appearance on CT Scan

- Solid and cystic component
- Appears hypodense or isodense
- Calcification rare
- With little or no surrounding edema
- Cause scalloping of the overlying bone

19.3.2 MRI

- Appears solid-cystic tumor with homogenous to heterogeneous contrast enhancement
- Peripheral eccentric cystic component (50–60%)
- Exhibit dural tail which is mostly reactive
- *T1*: Solid component iso to hypointense
- *T1 post contrast:* enhancement
- *T2*: Solid component iso- to hyperintense
- T2 FLAIR: Cystic areas show hyperintensity

19.4 Pathology

- Tumors are moderately cellular, predominantly pleomorphic and show foci of lymphoplasmacytic infiltration.
- Necrosis and mitoses rare.
- The tumor has been named pleomorphic as there is variable histological feature including spindle cells, polygonal cells, and multinucleated cells.
- Pathogenesis is driven by MAPK pathway.
- Nearly 60–70% patients harbor BRAF mutations; less common in anaplastic PXA.
- Mutation of BRAF confers better survival compared with wild variant.

- *Immunohistochemistry*
  - GFAP: Positive
  - S100: Positive
  - Vimentin: Positive
  - Reticulin: Positive
  - PAS: Positive
  - Synaptophysin, MAP2 and neurofilament: variable
  - Ki-67 proliferation index: <1%

19.5 Treatment

19.5.1 Surgical Excision [5]

- Surgical excision standard of care and a maximal safe resection is aim of surgery.
- Nearly 60% patients can undergo GTR.
- Patients with a GTR have good long-term survival.

	GTR (months)	STR (months)
PFS	48	14
OS	NR	62

19.5.2 Radiation [2, 3, 6–10]

- Data on adjuvant radiation is limited.
- Conflicting data about survival advantage in PXA.
- Radiation has been utilized more in salvage setting (76%).
- In APXA radiation may be more effective as these patients experience early failure.

19.5.2.1 Indications for Adjuvant RT

- PXA with GTR: Not required.
- PXA with STR or recurrence: RT should be considered.
- APXA: adjuvant radiation may be considered upfront even after GTR.

19.5.2.2 Target Volume

- In adjuvant or salvage setting:
  - Local radiation only (post-operative cavity plus any residual enhancing mass with 1 cm isotropic expansion as CTV and 3–5 mm additional as PTV)
- In CSF positive cases: CSI should be considered.

19.5.2.3 Dose

Local radiation: 54–60 Gy in conventional fractionation

CSI dose 30 Gy to the entire cranio-spinal axis followed by boost to the primary up to 56–60 Gy

19.5.3 Chemotherapy

- Role of chemotherapy controversial.
- V600E BRAF mutation in nearly 70% patients which constitutively activates RAS/RAF/MEK/ERK signaling pathway.
- BRAF inhibitor monotherapy or BRAF+MEK inhibitor are used in recurrent tumors.
- BRAF inhibitors, Vemurafenib and Dabrafenib showed promising result.

19.6 Results [2, 3]

Median OS of 183 months; PFS of 38 months.

	PFS (5 year)	OS (5 year)
PXA	Nearly 60%	Nearly 75%
APXA	Nearly 49%	Nearly 60%

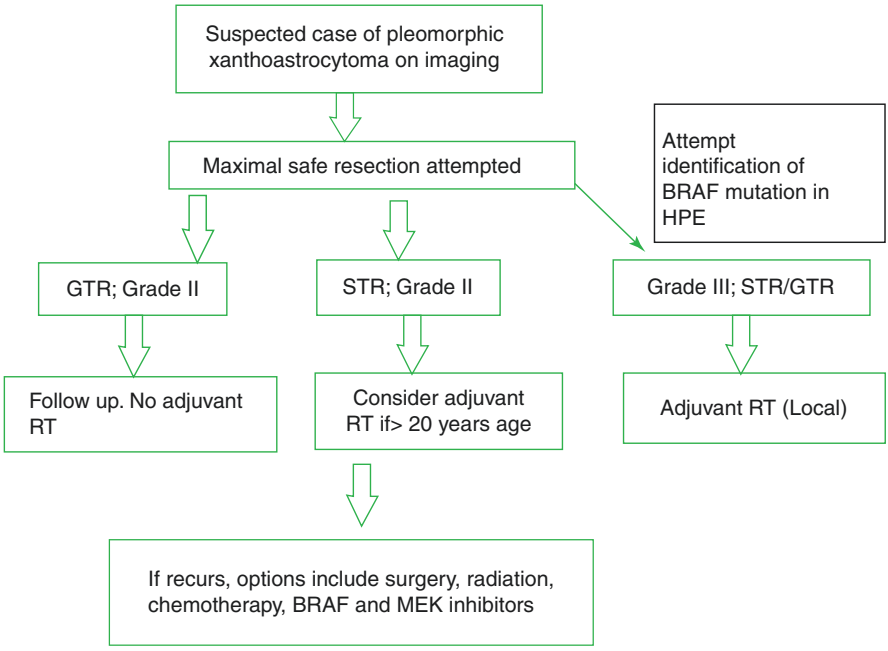
19.6.1 Prognostic Factors (Favorable)

- Patients younger than 20 years
- GTR
- Grade II [PFS: (48 vs 11.7 months) and OS: (209 vs 68 months)]
- Adjuvant treatment

19.7 Follow-up

- Nearly 50% patients experience progression within 3 years.
- Local recurrence is most common pattern of recurrence. Leptomeningeal spread seen in 7% patients.
- Follow-up should be done with clinical examination and CEMRI of brain every 3 months for first 3 years and thereafter every 6 months.
- Re-surgery followed by radiation or chemotherapy may be used to salvage.

19.8 Treatment Algorithm



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