Introduction
Pleomorphic xanthoastrocytoma (PXA) is a brain tumour that occurs most frequently in children and teenagers. The average age at diagnosis is said to be 12 years.

Pleomorphic xanthoastrocytoma usually develops within the supratentorial region (the area of the brain located above the tentorium cerebelli). It is generally located superficially (in the uppermost sections) in the cerebral hemispheres, and involves the leptomeninges (the inner two meninges, the arachnoid and the pia mater, between which the cerebrospinal fluid circulates). It rarely arises from the spinal cord. In about 20% of cases, tumours exist in more than one lobe.

Pleomorphic Xanthoastrocytoma (PXA)
Pleomorphic Xanthoastrocytomas are a type of rare, low-grade astrocytoma (WHO Grade II) found in young patients who typically present with temporal lobe epilepsy. Pleomorphic Xanthoastrocytomas affect males and females equally.

“Pleomorphic xanthoastrocytoma (PXA) is a rare central nervous system tumor occurring mostly in children and young adults. Next-generation sequencing of 295 cancer-related genes was used to investigate the molecular profiles of 13 cases of PXA. We found that BRAF V600E (5/13; 38%), FANCA/D2/1/M (5/13; 38%), PRKDC (4/13; 31%), NF1 (3/13; 23%), and NOTCH2/3/4 (3/13; 23%) alterations were the most frequent somatic gene mutations. However, neither PTEN nor EGFR

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February 2019
mutation, which is frequently present in glioblastoma, was detected. The KRAS mutation in PXA is reported for the first time in these tumors. Microsatellite stability was present in all cases. Because mutations of FANCA and BRAF and copy number variations of CDKN2A/B are more frequent in PXA than in glioblastoma, they might be used to distinguish the two tumors. The MAPK pathway is involved in the pathogenesis of PXA and may be an effective target for treatment.”

Incidence of Pleomorphic Xanthoastrocytoma (PXA) in South Africa

The National Cancer Registry (2014) does not provide any information regarding the incidence of Pleomorphic Xanthoastrocytoma.

Differential Diagnosis of Pleomorphic Xanthoastrocytoma (PXA)

Main differential diagnosis is that of other cortical tumours, with helpful distinguishing features including:

- Ganglioglioma
- Dysembryoplastic neuroepithelial tumours (DNET)
- Oligodendroglioma
- Desmoplastic infantile ganglioglioma
- Cystic meningioma

Diagnosis of Pleomorphic Xanthoastrocytoma (PXA)

Diagnosis is usually made by utilising:

- Computerised tomography (CT scan)
- Magnetic resonance imaging (MRI)
- Digital subtraction angiography (DSA): a fluoroscopy technique used in interventional radiology to clearly visualise blood vessels in a bony or dense soft tissue environment.


**BACKGROUND AND PURPOSE:** Anaplastic pleomorphic xanthoastrocytoma, which has been recently defined as a distinct entity in the 2016 World Health Organization classification, may exhibit aggressive clinical behaviour and relatively worse prognosis than pleomorphic xanthoastrocytoma. This study aimed to investigate whether there were any differences in MR imaging characteristics between these 2 tumors.

**MATERIALS AND METHODS:** This retrospective study included 9 patients with anaplastic pleomorphic xanthoastrocytoma and 10 patients with pleomorphic xanthoastrocytome who underwent MR imaging before an operation. DWI was performed in 17 patients (8 with anaplastic pleomorphic xanthoastrocytome, 9 with pleomorphic xanthoastrocytome); and DSC-PWI, in 9 patients (5 with anaplastic pleomorphic xanthoastrocytome, 4 with pleomorphic xanthoastrocytome). Demographics, conventional imaging characteristics (location, size, cystic degeneration, enhancement, peritumoral edema, and leptomeningeal contact) minimum relative
ADC ratio, and maximum relative CBV ratio were evaluated between the anaplastic pleomorphic xanthoastrocytoma and pleomorphic xanthoastrocytoma groups.

**RESULTS:** Anaplastic pleomorphic xanthoastrocytoma was more likely to demonstrate high-grade features than pleomorphic xanthoastrocytoma, including greater maximum tumor diameter (4.7 ± 0.6 cm versus 3.1 ± 1.1 cm, \( P = .001 \)), more frequent heterogeneous contrast enhancement of solid portions (88.9% versus 20.0%, \( P = .01 \)), more obvious peritumoral edema (2.3 ± 0.9 cm versus 1.0 ± 0.9 cm, \( P = .008 \)), lower minimum relative ADC on DWI (1.0 ± 0.2 versus 1.5 ± 0.4, \( P = .008 \)), and higher maximum relative CBV on DSC-PWI (2.6 ± 0.8 versus 1.6 ± 0.2, \( P = .036 \)).

**CONCLUSIONS:** Anaplastic pleomorphic xanthoastrocytomas often have more aggressive MR imaging features mimicking high-grade astrocytomas than pleomorphic xanthoastrocytomas. DWI and DSC-PWI might be useful in the characterization and differentiation of anaplastic pleomorphic xanthoastrocytomas than pleomorphic xanthoastrocytomas.

**Treatment of Pleomorphic Xanthoastrocytoma (PXA)**

The following treatments may be used alone or in combination to treat Pleomorphic Xanthoastrocytoma (PXA):

- **Neurosurgery** to remove as much of the tumour as possible. If the tumour is completely removed, no other treatment is required other than serial MRIs to monitor for re-growth. A second surgical procedure may be performed if the tumour cannot be completely removed and increases in size, or if it comes back.
- **Gross total resection** usually eliminates seizures
- **Radiation therapy** may be considered, but does not influence long-term outcomes.
- **Biologic therapy**

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**OBJECTIVE:** The authors conducted a study to delineate the long-term results of the surgical treatment of pediatric pleomorphic xanthoastrocytomas (PXAs).

**METHODS:** All consecutive children and adolescents (0-20 years) who underwent primary tumor resection for a PXA during the years 1972-2015 were included in this retrospective study on surgical morbidity, mortality rate, academic achievement, and/or work participation. Gross motor function and activities of daily living were scored according to the Barthel Index.

**RESULTS:** Of the 12 patients, 8 patients were in the 1st decade of life and 4 in the 2nd. The male/female ratio was 6:6. No patient was lost to follow-up. One patient presented with severe progressive tumor disease and died within 3 months after repeated resection. Another child died 3 days following a second surgical procedure involving gross-total resection (GTR) 8 years after the initial operation. The other 10 patients were alive at the latest follow-up when they reached the median age of 34 years (range 11-60 years). The median follow-up duration was 22 years (range 2-41 years). Barthel Index score was 100 in all 10 survivors. A total 18 tumor resections were performed. Five patients underwent a second tumor resection after MRI/CT confirmed recurrent tumor disease, from 6 months up to 17 years after the initial operation. Only one of our patients received adjuvant therapy: a 19-year-old male who underwent resection (GTR) for a right-sided temporal tumor in 1976. This particular tumor was originally classified as astrocytoma WHO grade IV, and postoperative radiotherapy (54 Gy) was given. The histology was reclassified to that of a PXA. Seven of 8 children whose primary tumor resection was performed more than 20 years ago are alive as of...
this writing—i.e., 88% observed 20-year survival. These are long-term survivors with good clinical function and all are in full- or part-time work.

CONCLUSIONS: Pediatric patients with PXA can be treated with resection alone with rewarding results. Recurrences are not uncommon, but repeated surgery is well tolerated and should be considered in low-grade cases before adjuvant therapy is implemented. Follow-up including repeated MRI is important during the first postoperative years, since individual patients may have a more aggressive tumor course.

INTRODUCTION: Pleomorphic xanthoastrocytoma (PXA) is a rare Grade II and III glioma. Surgical resection is the mainstay of treatment, however, adjuvant therapy is sometimes necessary. Given the rarity of PXA, chemotherapeutic efficacy data is limited. The importance of the BRAF V600E mutation in the context of MAP kinase pathway inhibition is unknown. The purpose of this study was to perform an in vivo screen of a variety to agents to determine efficacy against both V600E mutant and non-mutant PXA.

METHODS: The efficacy of bevacizumab, temozolomide, lomustine (CCNU), irinotecan (CPT 11), a tyrosine kinase inhibitor (sorafenib), a selective MEK1/2 inhibitor (cobimetinib), and a BRAF inhibitor (vemurafenib) were assessed in two subcutaneous xenografts: D645 PXA (V600E-mutant) and D2363 PXA (V600E-non-mutant) (n = 5-10 mice). Select agents were also assessed in an intracranial model of D2363 PXA (n = 6-9). Subcutaneous tumor growth and survival were the endpoints.

RESULTS: Temozolomide, bevacizumab, CPT 11, and sorafenib significantly inhibited subcutaneous tumor growth in both V600E-mutant and V600E-non-mutant models (P < 0.05). MEK inhibition (cobimetinib) but not BRAF inhibition (vemurafenib) also inhibited tumor growth regardless of V600E mutation (P < 0.05). Temozolomide, CPT 11, and bevacizumab also prolonged survival in a V600E-non-mutant intracranial model (median overall survival (OS) 68.5, 62.5, and 42.5 days, respectively) in contrast to controls (31.5 days, P < 0.001).

CONCLUSIONS: These findings suggest that when adjuvant treatment is clinically indicated for PXA, temozolomide, CPT 11, or bevacizumab may be considered. Additionally, a trial of a MEK inhibitor or tyrosine kinase inhibitor could be considered for PXA regardless of V600E mutation status.

About Clinical Trials
Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:
- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.
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Sources and References Consulted or Utilised

Boston Children’s Hospital
http://www.childrenshospital.org/conditions-and-treatments/conditions/pleomorphic-xanthoastrocytoma

Dana-Farber Cancer and Blood Disorders Center
www.danafarberbostonchildrens.org/conditions/brain-tumor/pleomorphic-xanthoastrocytoma.aspx


Pathology Outlines.com
http://www.pathologyoutlines.com/topic/cnstumorpleomorphicxanthoastrocytoma.html

Pleomorphic Xanthoastrocytoma
http://neuropathology-web.org/chapter7/chapter7bGliomas.html

Radiopaedia.org
http://radiopaedia.org/articles/pleomorphic-xanthoastrocytoma


Wikipedia
https://en.wikipedia.org/wiki/Pleomorphic_xanthoastrocytoma
