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## Case Report

# Tuberous sclerosis complex associated intracranial lesion found by antenatal ultrasound ☆,☆☆

Ilana Hanes, MD, MSc<sup>a</sup>, Katherine Muir, MD<sup>b</sup>, Nishard Abdeen, MD<sup>c</sup>, Erick Sell, MD<sup>b,\*</sup>

<sup>a</sup> University of Ottawa, Ottawa, Canada

<sup>b</sup> Division of Neurology, Department of Pediatrics, Children's Hospital of Eastern Ontario, University of Ottawa, 401 Smyth Road, Ottawa, Ontario K1H 8L1, Canada

<sup>c</sup> Department of Medical Imaging, Children's Hospital of Eastern Ontario, University of Ottawa, Ottawa, Canada

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## ABSTRACT

Tuberous sclerosis complex (TSC) is characterized by the growth of benign tumors in the skin, brain, kidneys, lung and heart [1]. Prognosis is mostly determined by the extent of brain involvement as tumors in the brain lead to seizures, cognitive impairment and behavioral problems. Current evidence suggests anti-epileptic treatment before the onset of seizures reduces epilepsy severity and risk of cognitive impairment in TSC however identifying these children prior to the onset of seizures is challenging. Our case shows retrospectively reviewed antenatal ultrasounds of a male child diagnosed postnatally at 12 days of life with TSC. Analysis found a soft tissue mass in the right ventricle on antenatal ultrasound which was not captured in the initial ultrasound report. Though there are no reports of sensitivity of neurosonography for the antenatal detection of intracranial abnormalities associated with TSC, our case suggests that antenatal ultrasound could be used as a screening modality for antenatal diagnosis of TSC.

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Tuberous sclerosis complex (TSC) is characterized by the growth of benign tumors in the skin, brain, kidneys, lung and heart [1]. Prognosis is mostly determined by the extent of brain involvement as tumors in the brain lead to seizures, cognitive impairment and behavioral problems [2]. Epilepsy in particular is highly associated with cognitive abnormalities in TSC [3]. Current evidence suggests anti-epileptic treatment before the onset of seizures reduces epilepsy severity and risk of

cognitive impairment in TSC [4]. However, seizures are one of the most common presenting symptoms and identifying these children prior to the onset of seizures is challenging [3]. Currently, there are no screening tests for identifying children with TSC.

Cortical tubers are more common in TSC than cardiac rhabdomyomas, yet antenatal detection is not frequently reported. Only a handful of cases identifying intracranial lesions

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\* Corresponding author.

E-mail address: [esell@cheo.on.ca](mailto:esell@cheo.on.ca) (E. Sell).

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associated with TSC on antenatal ultrasound have been published [5]. Prenatal diagnosis of TSC by identification of intracranial lesions could lead to prophylactic treatment postnatally, capturing this population before the onset of seizures and possibly improving neurodevelopmental outcomes in children with TSC.

## Case report

A child was born at 36 weeks gestation by induced vaginal delivery for abnormal fetal heart rate. The patient's birth weight was 2615 grams and Apgar scores were 8 at 1 minute and 9 at 5 minutes. The baby cried spontaneously at birth and received routine newborn care. Electrocardiogram (ECG) found an irregular heart rate with premature atrial complexes, prolonged QT interval and flattened T waves. Post-natal echocardiogram showed multiple intracardiac masses consistent with cardiac rhabdomyoma, which were not identified in utero. Subsequent investigations including head ultrasound revealed bilateral subependymal nodules and bilateral cortical and subcortical echogenic areas. Abdominal ultrasound showed bilateral renal cysts. The patient also had 2 small hypopigmented plaques that fluoresced under Wood's lamp. Magnetic resonance imaging (MRI) brain at 12 days of life revealed many subependymal nodules, cortical and subcortical tubers and subependymal giant cell astrocytoma (SEGA) in the right frontal horn of the lateral ventricle. The patient met clinical criteria for diagnosis of TSC. Diagnosis was confirmed by genetic testing which revealed a heterozygous mutation in TSC2.

Retrospective review of the mother's antenatal ultrasounds at 34 weeks and 4 days gestation revealed a soft tissue mass in the right ventricle (Fig. 1). All other ultrasounds including exams performed at 19, 25 and 35 weeks gestation showed no intracranial abnormalities as only limited images of the brain were obtained during these studies. Postnatal transcranial ultrasound at 37 weeks corrected gestation age (Fig. 2) confirmed the presence of mass in the right lateral ventricle at the foramen of Monro and showed multiple subependymal nodules as well as cortical tubers. Findings were later confirmed and further delineated by MRI performed at 12 days of life (Fig. 2).

## Discussion

The neurological sequelae of TSC are the most common and often the most debilitating aspect of the disease [2]. Up to 80% of patients with TSC will be affected by epilepsy, many of whom will develop epilepsy in the first year of life [6]. Neurodevelopmental disorders, such as intellectual disability, autism spectrum disorder (ASD) and behavioral difficulties, are highly prevalent amongst children with TSC [2]. The association between early age at seizure onset and poor neurodevelopmental outcome is widely reported [4]. Given these associations, there have been several studies examining the impact of treatment of seizures on neurodevelopment outcome. In a prospective cohort study, preventative treatment with anti-seizure medication was shown to reduce

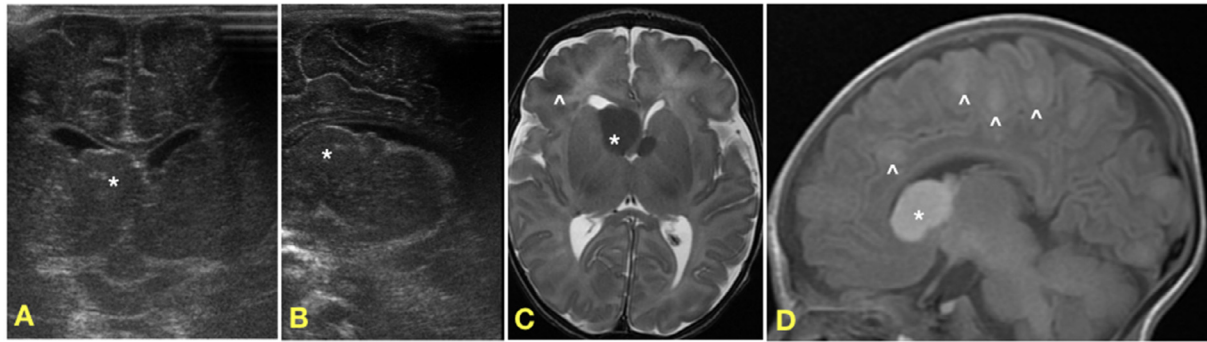


**Fig. 1 – Coronal view of antenatal ultrasound at 34 weeks and 5 days gestation with soft tissue mass filling the right frontal horn of the lateral ventricle (ventricle indicated with callipers 2 and mass indicated by \*) while the left frontal horn appears normal (indicated by callipers 1).**

the risk of epilepsy and epilepsy severity [4]. IQ scores were also higher and intellectual disability was less severe in those treated preemptively with anti-seizure medication compared to those who were not [4]. However, it is challenging to identify children with TSC prior to seizure onset, as seizures are the most common presenting symptom [2]. Cardiac rhabdomyomas are a well described marker of TSC when detected antenatally however only 50% of patients with TSC have cardiac rhabdomyoma [7]. This is compared to brain involvement in over 90% of individuals with TSC. The sensitivity of ultrasound in the antenatal detection of intracranial abnormalities associated with TSC is unknown and only a handful of cases have been reported [5].

Ultrasound is the primary imaging technique for the assessment of the fetal brain. While there are advantages, such as real time imaging and low cost, there are several limitations to antenatal ultrasound in assessing the fetal brain, including acoustic attenuation and shadowing from the bony calvarium, beam attenuation by adipose tissue or polyhydramnios and engagement of the fetal head in the maternal pelvis. Furthermore, routine ultrasound in the third trimester focus on growth and only a few standard views for head circumference and biparietal diameter are obtained. In our case, the subependymal mass was noted only when reviewed retrospectively. Other findings such as subependymal nodules and cortical tubers were not seen on the limited images available. The limitations to antenatal sonography likely contribute to the limited detection of intracranial abnormalities associated with TSC (Fig. 2).

Our case is unique as no previous report has retrospectively reviewed antenatal ultrasounds of children diagnosed



**Fig. 2 – Coronal (A) and sagittal (B) images of post-natal transcranial ultrasound on second day of life compared to axial T2-weighted and sagittal T1-weight MRI images on the 12th day of life (C and D respectively). The SEGA in the right foramen of Monro is seen with both modalities (indicated by \*). Multiple cortical tubers (indicated by arrowhead) are well seen on MRI (C and D) but poorly delineated on ultrasound (A and B).**

postnatally with TSC. Our analysis found a soft tissue mass in the right ventricle on antenatal ultrasound which correlated with SEGA on postnatal MRI. This finding was not captured in the initial ultrasound report. There are only 3 previously reported cases in the literature of antenatal detection of brain lesions associated with TSC by ultrasound though these cases are prospective [5]. In all 3 cases, mass lesions in the head of the caudate in keeping with SEGA were detected [5].

At this time, there are no reports of sensitivity of neurosonography for the antenatal detection of intracranial abnormalities associated with TSC, however, our case suggests that antenatal ultrasound could be used as a screening modality for the detection of TSC in utero. With supportive evidence and ongoing trials for the prophylactic treatment of patients with TSC prior to the onset of seizures, it is important to determine routine screening methods for the prenatal diagnosis of TSC.

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