

# Hepatic Adenomatosis in Aicardi Syndrome: A Clinical Report and Review of The Literature

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## Case Report

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# Abstract

Aicardi Syndrome is a rare X-linked dominant genetic disorder characterized by callosal agenesis, generalized seizures, chorioretinal lacunae and vertebral anomalies. Uncommon neoplasms have been previously observed in affected patients. We describe the case of a 19-year-old woman with Aicardi Syndrome developing multiple giant mass lesions in the liver. Histopathology revealed hepatic adenomas.

## Introduction

Jean Aicardi in 1965 described a syndrome of spasms in flexion, callosal agenesis and ocular abnormalities [1]. In the following years other findings were identified, in particular porencephalia, facial asymmetry and vertebral dysplasia [2]. Aicardi Syndrome (AS) is an X-linked dominant genetic disorder, observed almost exclusively in female patients, being lethal in males; rare XXY male cases have been described [3]. Extensive genetic studies have been performed but the mutation has not yet been identified [4]. Some reports describe rare neoplasms complicating with AS [5, 6]; here we report the case of a young AS woman developing multiple giant liver adenomas.

## Case Description

A 19-year-old woman was referred to our center due to abdominal pain and US finding of multiple large mass lesions in the liver. The patient had a known diagnosis of AS, with severe scoliosis, agenesis of the corpus callosum (Fig. 1), central chorioretinal lacunae (round depigmented areas in the retina), spasms and mental retardation. Her regular anticonvulsant medications were Felbamate and Rufinamide; four years before, because of severe pelvic pain occurring during each menstrual period, she had started estrogen-progestin oral therapy (ethinylestradiol/drospirenone). When the woman presented to our attention she complained new onset of severe abdominal pain in the upper abdomen; US revealed large liver lesions (maximum diameter 13 cm), irregularly hypoechoic, with hyperechoic foci and diffused in both lobes. At physical examination the liver was markedly enlarged. Significant serum laboratory tests results were: hemoglobin 10 g/dL, bilirubin 1.2 mg/dL, AST 16 U/L, ALT 56 U/L and alpha fetoprotein level 1.1 ng/mL. No serologic markers of viral hepatitis were present. Abdominal CT confirmed multiple solid liver masses, with spherical shape, pseudocapsule appearance, early contrast enhancement and inhomogeneous washout. The biggest lesion was located in the right lobe with diameter of 13 cm; it presented both fluid areas and spontaneously hyperdense foci, suggesting necrosis and hemorrhagic phenomena (Fig. 2). Percutaneous liver biopsy of the largest mass was performed, with US guide and under local anesthesia (Fig. 3). Histopathological sample revealed typical hepatic adenoma. After multidisciplinary discussion, because of the high number of large lesions, no surgical therapy was performed; the estrogen-progestin therapy was stopped. At three months follow-up reduction in size of all the lesions was observed, with resolution of abdominal discomfort.

## Discussion

Our patient presented typical characteristics of Aicardi Syndrome (AS): callosal agenesis, generalized seizures, chorioretinal lacunae and vertebral anomalies [2, 7]. Moreover, she developed multiple hepatic adenomas. These rare benign liver tumors arise in noncirrhotic liver; they occur predominantly in young women who take oral contraceptives or other steroid medications [8]; the annual incidence is 3 per 100,000 in women who have used oral contraceptives over years [9]. A small part of patients have multiple lesions; >3 lesions is defined liver adenomatosis [8]. Its development is associated with some genetic syndromes, in particular glycogen storage diseases [10]. The risk of adenoma malignant transformation is supposed to be 5–6%, but it is difficult to distinguish between adenoma and well-differentiated hepatocellular carcinoma both in imaging and histopathologically; because of its rarity, the natural history of adenoma-carcinoma progression is still unclear [11].

Among previously reported patients with AS, increased incidence of rare neoplasms was observed: choroid plexus papilloma, teratoma, embryonal carcinoma and angiosarcoma [12, 13, 6]; Tanaka et al. in 1985 described a case of young AS girl with hepatoblastoma [5]. Our patient presented with multiple large liver adenomas developed after four years of estrogen-progestin therapy, a relatively limited period of time. This may suggest a genetic tendency in AS woman to develop liver neoplasms, making oral contraceptive therapy contraindicated. Further studies are necessary to confirm and understand the tendency to develop tumors in AS patients.

## Declarations

### Compliance with Ethical Standards

**Funding.** This study was not supported by any funding.

**Conflict of interest.** The Authors declare that they have no conflict of interest.

**Ethical Approval.** All procedures performed were in accordance with the ethical standards of the Institutional Research Committee and with the 1964 Helsinki Declaration and its later amendments.

**Informed Consent.** Informed consent was obtained from the Patients.

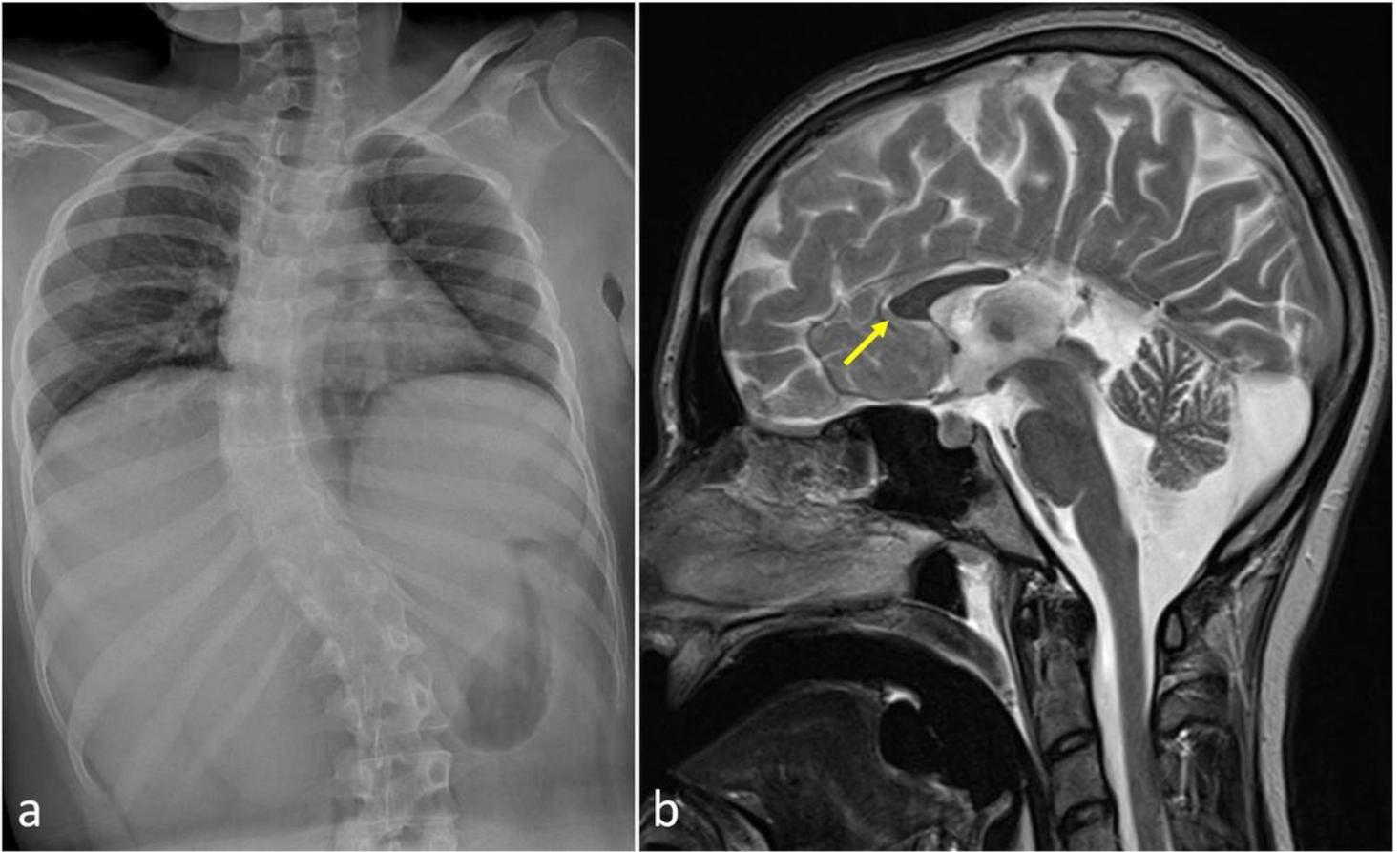
**Consent for Publication.** Consent for publication was obtained for the Patients' data

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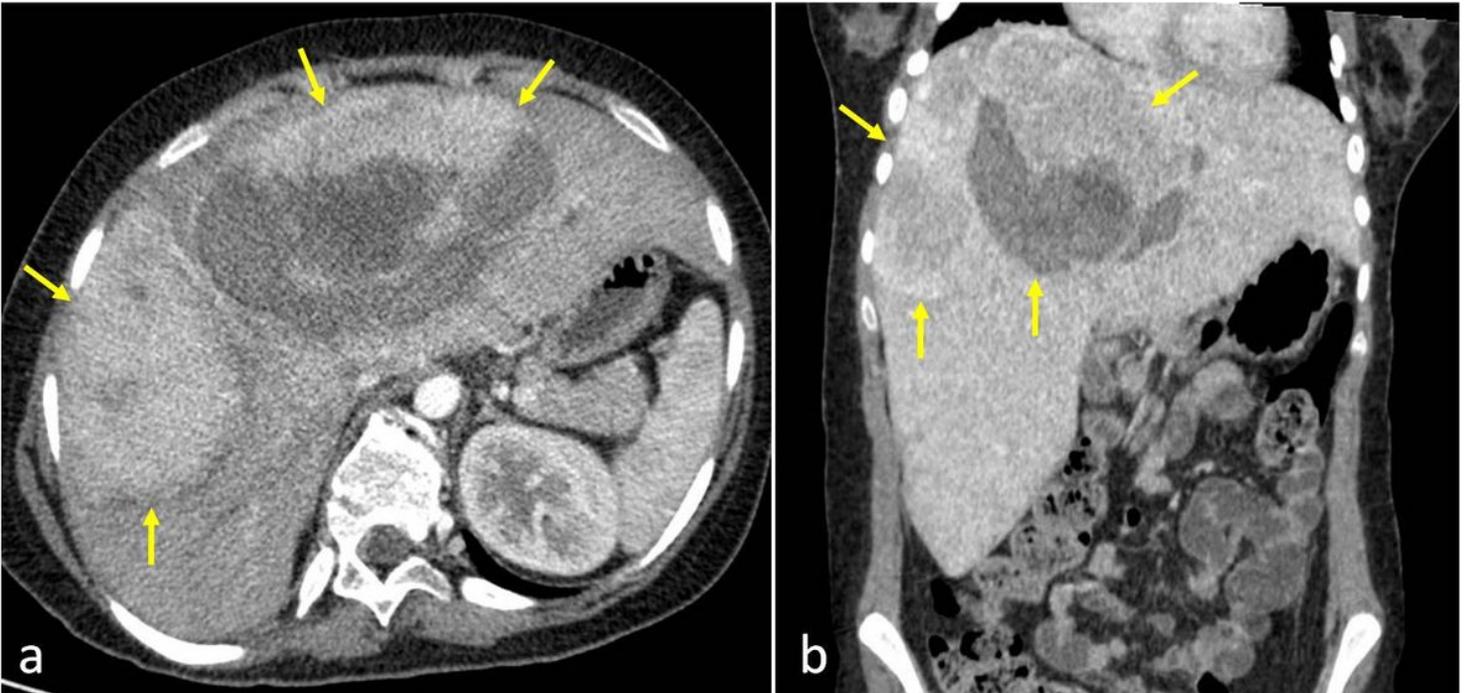
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## Figures



**Figure 1**

a. Spine x-ray of 19-year-old woman with Aicardi Syndrome shows severe scoliosis; some dorsal vertebrae are fused together. b. Sagittal T2-weighted MR image reveals agenesis of the corpus callosum; only the rostrum and genu are partially visible (arrow). The cisterna magna is enlarged.



## Figure 2

Contrast-enhanced abdominal CT, arterial phase (a) and portal-venous phase (b). Multiple large solid liver lesions are depicted (arrows); they present early inhomogeneous contrast enhancement, with fluid areas and spontaneously hyperdense foci, signs of necrosis and hemorrhagic phenomena.



## Figure 3

Ultrasonography image; the largest lesion is well visible, irregularly hypoechoic with hyperechoic foci and pseudocapsule appearance. Percutaneous biopsy was performed under local anesthesia.