

Diffuse Astrocytoma and Ollier's Disease

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Abstract

Several syndromes are associated with an increased incidence of intracranial tumors. Among these is enchondromatosis. It is a rare, nonhereditary condition. The common subtypes of enchondromatosis are Ollier's disease (OD) and Maffucci syndrome. It has been distinguished between them by the presence of vascular malformation and non-skeletal neoplasm in Maffucci syndrome. The emergence of malignant neoplasms, including gliomas is a well-recognized complication in Maffucci syndrome, but over the past few years there has been an increasing number of reported cases of patients with intracranial tumors and OD. In our case report we discuss a 23-year-old female recently diagnosed with World Health Organization (WHO) grade II diffuse astrocytoma and found to have OD.

Keywords: Ollier's disease; Maffucci syndrome; Gliomas; Diffuse astrocytoma; Dysembryonic neuroepithelial tumors; Gangliogliomas

Introduction

Malignant gliomas are tumors of glial origin of the central nervous system (CNS), exhibiting various degrees of differentiation [1]. Several syndromes are associated with an increased incidence of intracranial tumors. Among these is enchondromatosis. Enchondromas are common benign usually asymptomatic cartilaginous tumors [2, 3]. Enchondromatosis or Ollier's disease (OD, World Health Organization (WHO) terminology) [2] is defined by the presence multiple enchondromas and characterized by an asymmetric distribution of cartilaginous lesions that can be extremely variable. It is first described by Maffucci in 1881 in association with venous an-

giomas [4]. In 1899, Ollier described enchondromatosis in a patient with no evidence of vascular anomalies, known as OD [4]. The emergence of malignant neoplasms including gliomas is a well-recognized complication in Maffucci syndrome [2, 3, 5].

Case Report

A 23-year-old female presented at the clinic with 2 months' history of frontal mild pressure like headache that was managed by over the counter analgesia, and two episodes of mal seizure during sleep that last for 15 min. Neurological examination at time of presentation was normal. Upon physical examination, abnormal bony lesions were noticed in the left shoulder and left iliac bone.

Brain magnetic resonance imaging (MRI) showed three left frontal cortical based lesions which appeared hypointense on T1 weighted image (T1WI) and hyperintense on T2WI with mild mass effect without significant vasogenic edema. The largest lesion measured 5.6 × 5.4 × 4.3 cm, also showed inhomogeneity with cystic changes and modest enhancement after intravenous (IV) gadolinium administration. Also present was a tiny ring enhancing focus exhibiting restricted diffusion. The other two lesions had no enhancement nor diffusion restriction (Figs. 1, 2). In addition, a small complex sellar lesion with anterior enhancing component was demonstrated, it was extending into the suprasellar cistern and abutting the optic chiasm and the pre-chiasmatic portions of the optic nerves. Also noted was a cerebellar tonsillar ectopia (Fig. 3).

Computed tomography (CT) brain without contrast of the skull base demonstrated calcified small seller/suprasellar lesion, Chiari malformation type I and asymmetrical occipital condyles. The left enlarged condyle was radiolucent compared to the normal right condyle. She underwent left frontal craniotomy with the neuro-navigation guidance.

Hematoxylin and eosin-stained sections from the 2 × 2 cm soft and pinkish neuro- specimen showed infiltrative low-grade glioma with mixed morphology and microcytic foci. It was composed of uniform round to oval cells with fried egg appearance. There was neither evidence of mitotic activity, endothelial vascular proliferation nor necrosis (Figs. 4, 5). Immunohistochemical study was performed on paraffin embedded tissue revealed negative reaction with p53 antibody. Isocitrate dehydrogenase 1 (IDH1, mutantR132H) stain was negative too (Figs. 6, 7). *IDH1/2* pyrosequencing was showed positive result as *IDH1* codon 132 c.394C>T p. Arg132Cys (R132C) mutation was also detected. Cytogenetic study of

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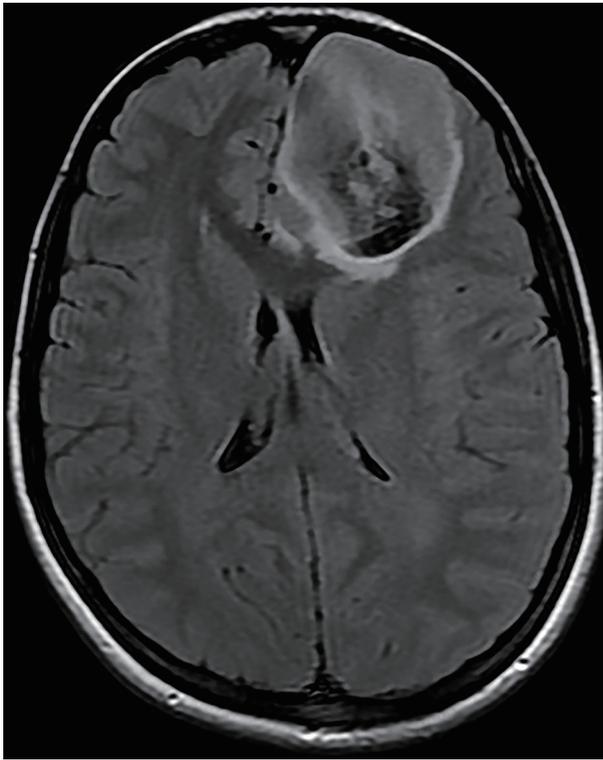


Figure 1. Brain MRI shows three left frontal cortical based lesions which appear hyperintense on T2 weighted image with mild mass effect but without significant vasogenic edema. The largest lesion shows inhomogeneity with cystic changes and modest enhancement after IV gadolinium administration with tiny ring enhancing focus which shows restricted diffusion. MRI: magnetic resonance imaging; IV: intravenous.

1p19q revealed intact 1p36 19q13 which confirmed diffuse astrocytoma, WHO grade II diagnosis.

X-ray of the pelvis showed ill-defined mixed lytic and

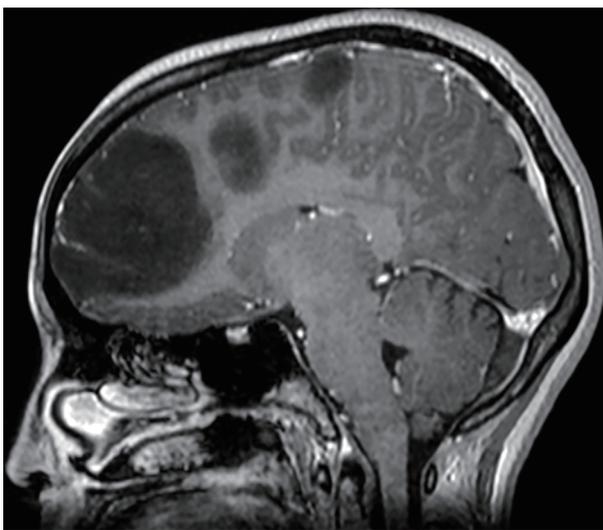


Figure 2. Brain MRI shows three left frontal cortical based lesions which appear hypointense on T1 weighted image. MRI: magnetic resonance imaging.



Figure 3. Brain MRI shows a small complex sellar lesion with anterior enhancing component. It is extending into the suprasellar cistern. MRI: magnetic resonance imaging.

sclerotic lesions with chondroid matrix irregularity and bony destruction affecting mainly the left iliac bone, to a lesser extent the left inferior pubic ramus and the iliac side of the right sacroiliac (SI) joint. No periosteal reaction nor pathological fracture was present.

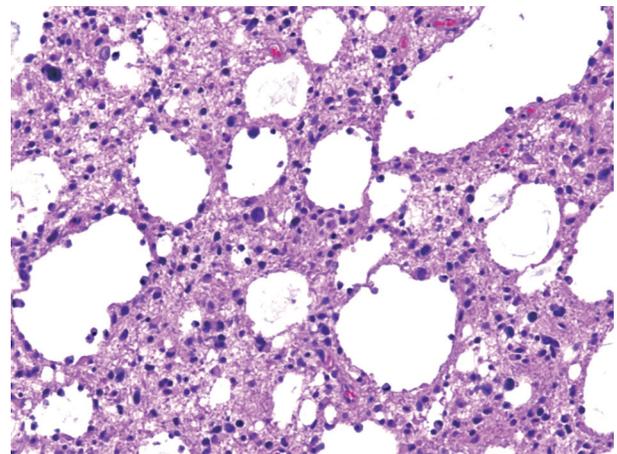


Figure 4. Histopathological examination of the diffuse astrocytoma specimen at intermediate power (x 20) shows an infiltrative growth pattern and microcytic changes.

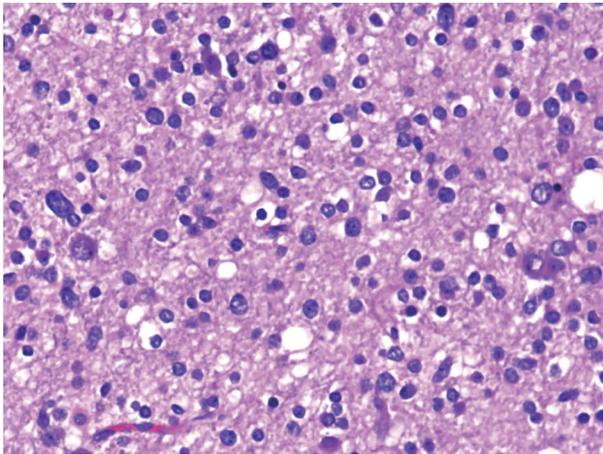


Figure 5. Histopathological examination of the diffuse astrocytoma specimen at high power ($\times 40$) show a tumor cells have a more round and uniform appearance with microcytic changes.

Ill-defined mixed lytic and sclerotic lesion at the proximal metadiaphyseal region of the left humerus was also demonstrated, causing cortical distraction. Lamellated and Codman periosteal reaction were noted as well as a wide zone of transition. Dorsal and radial bowing of the radius with exaggerated radial inoculation, dislocation of the proximal radial head, shortening and bowing of the ulna were all suggesting Madelung's deformity. Proximal fourth and fifth phalanges also showed lytic lesions. These features were suggestive of polyostotic enchondromatosis (OD) (Fig. 8).

Enhanced chest CT showed left upper lobe few nonspecific subpleural nodules. There was an intraluminal filling defect in the inferior division of the right lower lobe pulmonary artery. Also, there were multiple osseous expansile lesions with popcorn type calcification. No evidence of metastasis (Fig. 9).

CT scan-guided biopsy of the left iliac bone lesion confirmed the benign cartilaginous proliferation, consistent with chondroma. It is negative for malignancy and inflammation. Patient was discharged and was followed up with oncology

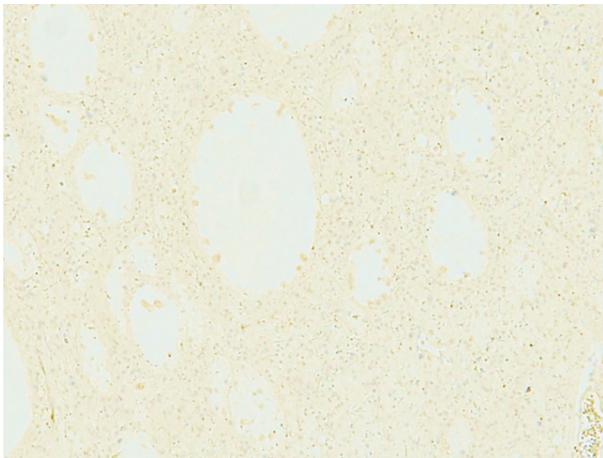


Figure 6. Negative immunohistochemical staining for IDH1. IDH1: isocitrate dehydrogenase 1.

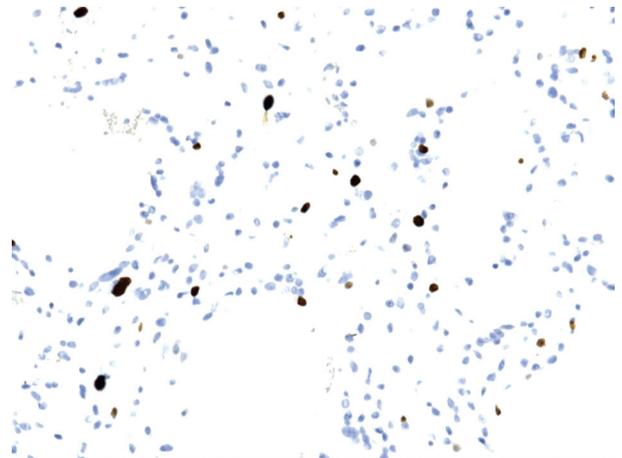


Figure 7. Ki67 immunohistochemical staining shows from low to focally moderate (up to 6-8%).

department and genetics.

Discussion

There have been 25 reported cases in the literature including our patient since 1979 (Table 1) [4, 6-9].

A retrospective analysis of these cases showed the age of the patients ranged from four to 55. The majority were males in their second decade of life. This is similar to the observations of Bathla et al and Hori et al [4, 8].

Nine of the 25 cases were of a high grade. One case was reported as astrocytoma with no further grading. There was one reported case of oligodendroglioma and four cases with oligoastrocytoma [4]. Our case is representing the twelfth low grade astrocytoma associated with OD [4, 7].

Over the past few years OD patients seem to have an increased risk for the development of non-skeletal malignancies,

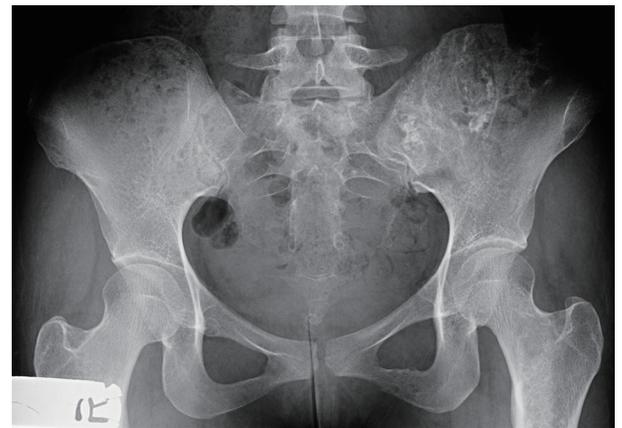


Figure 8. X-ray of the pelvis (AP view) shows ill-defined mixed lytic and sclerotic lesions with chondroid matrix, irregularity and bony destruction affecting mainly the left iliac bone and to a lesser extent the left inferior pubic ramus and the iliac side of the right SI joint. No periosteal reaction nor pathological fracture. AP: anteroposterior; SI: sacroiliac.

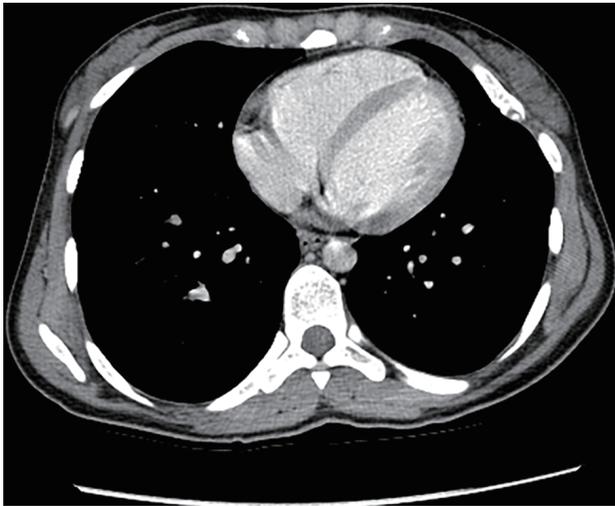


Figure 9. Enhanced chest CT (axial view) shows few nonspecific sub-pleural nodules in the left upper lobe. There are multiple osseous expansile lesions with popcorn type calcification. CT: computed tomography.

especially intracranial tumors of glial origin [6, 9]. Our patient along with the previously reported cases points to the association between OD and glial tumors. Our patient along with the previously reported cases points to the association between OD and glial tumors.

Actually, the morphology of the brain tumor in our case was that of oligodendroglioma with infiltrative nature, microcysts formation and fried egg appearance. However, the immunohistochemical study for IDH1 (mutant R132H) was negative, in such cases and according to the WHO of the CNS tumors 2016, it should be cytogenetically studied for both *IDH-1/2* and 1p19q to reach to the definitive diagnosis [10].

1p19q codeletion is an important diagnostic cytogenetic tool differentiating diffuse astrocytoma from oligodendroglioma, 1p19q is normal in the former and codeleted in oligodendroglioma regardless of the grade. This rule is only applied to adult oligodendroglioma. Oligodendroglioma of adult patients exhibit mutation of *IDH1/2*, 1p36 and 19q13 codeletion, and intact *ATRX* while the pediatric oligodendroglioma have normal 1p19q and *IDH1/2* with intact *ATRX*.

IDH1/2 is mutated in most of diffuse astrocytoma, regardless of the grade, distinguishes astrocytoma with a more fa-

Table 1. Twenty-Five Reported Cases in the Literature Including Our Patient Since 1979

Studies	Case year	Age/gender	Histology
Bathla et al, 2012 [4]	1979	26/NS	Grade II oligoastrocytoma
Bathla et al, 2012 [4]	1987	38/M	Astrocytoma
Bathla et al, 2012 [4]	1987	29/M	Anaplastic astrocytoma
Bathla et al, 2012 [4]	1988	34/M	Grade II astrocytoma
Bathla et al, 2012 [4]	1990	24/M	Low grade astrocytoma
Bathla et al, 2012 [4]	1991	29/F	High grade astrocytoma
Bathla et al, 2012 [4]	1994	23/M	Anaplastic astrocytoma
Bathla et al, 2012 [4]	1994	25/M	Oligodendroglioma
Bathla et al, 2012 [4]	1994	46/M	Oligoastrocytoma
Bathla et al, 2012 [4]	1998	28/M	Low grade astrocytoma
Bathla et al, 2012 [4]	1999	16/M	Diffuse brainstem (astrocytoma?)
Bathla et al, 2012 [4]	1999	23/F	pons involvement (astrocytoma?)
Bathla et al, 2012 [4]	1999	28/?	Low grade astrocytoma?
Bathla et al, 2012 [4]	2002	7/F	Low grade astrocytoma
Bathla et al, 2012 [4]	2004	21/F	Low grade fibrillary astrocytoma
Bathla et al, 2012 [4]	2006	28/F	Anaplastic mixed oligoastrocytoma
Bathla et al, 2012 [4]	2008	14/M	Anaplastic astrocytoma.
Bathla et al, 2012 [4]	2009	6/F	Glioblastoma multiforme
Hori et al, 2010 [8]	2010	4/M	Anaplastic astrocytoma
Bathla et al, 2012 [4]	2010	19/M	Grade III anaplastic astrocytoma
Bathla et al, 2012 [4]	2012	16/M	Grade II glioma
Khan et al, 2013 [7]	2013	35/M	Low grade astrocytoma
Rebecca et al, 2016 [6]	2016	26/M	Anaplastic oligodendroglioma
Gajavelli et al, 2016 [9]	2016	55/F	Anaplastic astrocytoma
Present study	2020	23/F	Grade II astrocytoma

favorable course from IDH-wild type tumors which have a less favorable course [10].

In diffuse glioma cases of adults with unavailability of immunohistochemical ATRX and IDH1/2 antibodies as in our situation, 1p19q is first tested. If the tumor harbors 1p19q codeletion, no need to test for *IDH1/2* as it should be mutated in adult oligodendroglioma. Only the cases with normal 1p19q, i.e., astrocytoma diagnosis molecular study for *IDH1/2* should be requested.

Conclusions

OD carries a high risk of skeletal and extra-skeletal malignancy specially brain tumor. Our case we present OD with IDH-mutant diffuse astrocytoma. The previous literatures show that patients with OD develop gliomas at a relatively younger age and there is a high rate of multifocality [4, 5]. In addition, common locations are frontal lobe and brainstem.

Acknowledgments

None to declare.

Financial Disclosure

None to declare.

Conflict of Interest

The authors declare that they have no conflict of interest.

Informed Consent

The patient has signed the informed consent.

Author Contributions

Assem Al Rumeh and Toleen Shaikh wrote the whole manuscript and provided the clinical information. Ahmad Lari did

the surgery and provided the notes. Abdullah Muharib provided the radiology images with explanation of each image. Wafaa Al Shakweer reviewed the manuscript.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

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