Case Report

Multiple enchondromatosis (Ollier's disease) with two primary brain tumors

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ABSTRACT

A rare case of multiple enchondromatosis associated with 2 primary brain tumors is reported. A 21-year-old female who has diagnosed as Ollier's disease at the age of 9-years was admitted to the hospital with complaint of diplopia and progressive right upper and lower limb weakness. Magnetic resonance imaging of the brain depicted 2 intra-axial mass lesions. Stereotactic biopsy showed low grade fibrillary astrocytoma in both lesions. This report emphasizes that patients with Ollier's disease are at a higher risk for primary brain tumors than has been previously recognized.

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Multiple enchondromatosis (Ollier's Disease) is a rare nonhereditary disease of unknown pathogenesis, characterized by multiple persistent asymmetrically distributed intra osseous unossified cartilaginous masses in the metaphyses and diaphyses of bones which may lead to growth distortion with secondary shortening and deformity of the limbs. Sarcomatous transformation of the enchondromas may occur. Three forms of multiple enchondromatosis (ME) have been described. Ollier's disease is usually confined to bone manifestations with unilateral predominance and no associated soft tissue hemangiomas.[1,2] Maffucci's syndrome is another rare form of multiple enchondromatosis. It consists of chondromatosis, angiomatosis and sometimes dyschromic lesions.[3] Kast's disease is a very rare variant associated with cutaneous manifestations like vitiligo and pigmented nevi.[4] Among patients with ME those with Ollier's disease are considered to be at a lower risk for developing sarcomatous transformation of enchondromas and non sarcomatous (non skeletal) malignancies than those with Maffucci syndrome.[5] This paper reports a new case of Ollier's disease with 2 primary brain tumors, one in the right parasagittal frontal lobe and one diffusely infiltrating the brain stem. It therefore suggests that patients with Ollier's disease are at a higher risk for primary brain tumors than has been previously recognized and along with previously reported cases it suggests that Ollier's disease and Maffucci syndrome may be spectrum of the same disease process.

Case Report. A 21-year-old female patient presented with a 5-month history of progressive right upper and lower limb weakness and 2-month history of diplopia provoked by left lateral gaze with disappearance of the diplopia upon left eye closure. The patient was a known case of ME (Ollier's disease) since she was 9-years-old. Skeletal survey was carried out upon admission, which revealed multiple bony lesions typical for enchondromas in both hands **(Figure 1)**, right proximal humerus, right iliac bone right scapula and left anterior 6th rib. Physical examination disclosed multiple deformities in both hands and proximal right upper limb related to bony lesions (enchondromas). Dermatological examination

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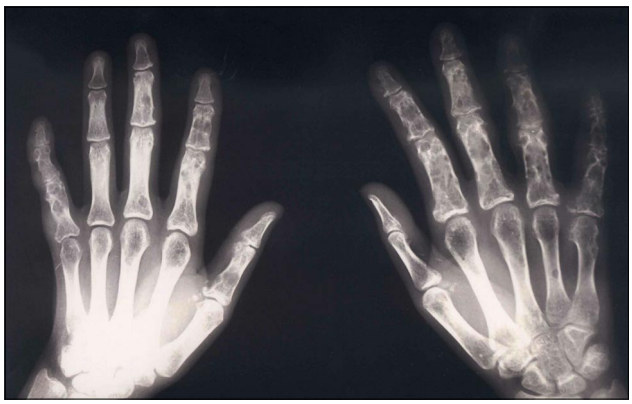

Figure 1 - Radiograph of both hands showing multiple bilateral enchondromas.

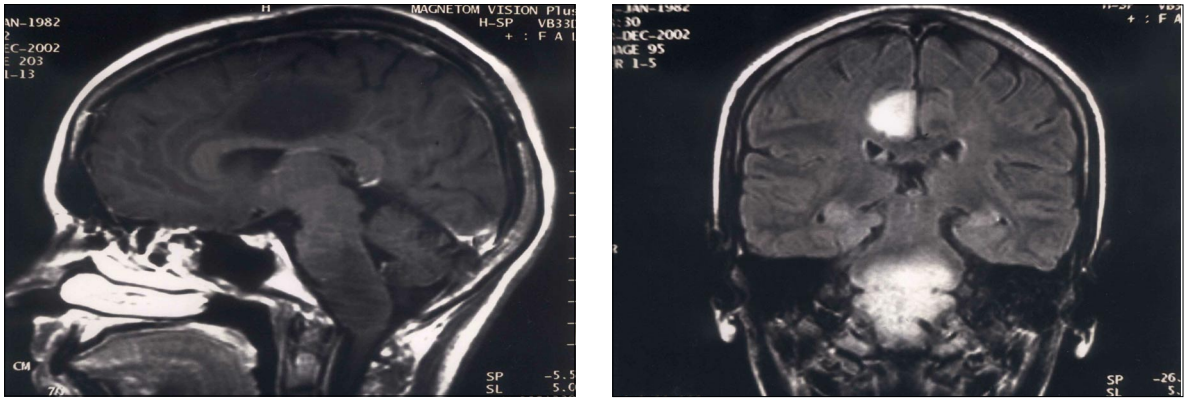

Figure 2 - Magnetic resonace imaging of the brain. **(a)** Sagittal T1 weighted magnetic resonance imaging of the brain with gadolinium contrast medium demonstrates 2 non enhanced hypointense mass lesions located in the right parasagittal frontal lobe and in the brain stem. **(b)** Coronal FLAIR magnetic resonace image showing the 2 above mentioned lesions with a hyperintense signal.

showed no evidence of hemangiomas or other cutaneous manifestations. Neurological examination revealed left abducent nerve palsy, reduced power (3/5) in both right upper and lower limbs, bilateral brisk reflexes and babiniski sign on the right side, no sensory loss. Visual acuity and color vision were normal. Brain magnetic resonance imagine (MRI) demonstrated 2 intra-axial mass lesions; one in the right parasagittal frontal lobe and one diffusely infiltrating the brain stem. Both lesions were homogenously hypointense on T1 (**Figure 2a**); hyperintense on T2 and on Fluid Attenuation Inversion Recovery (FLAIR) weighted images (**Figure 2b**). No enhancement exhibited in both lesions after the intravenous injection of gadopentetate dimeglumine. Magnetic resonance imaging interpretation strongly suggested low grade gliomas. Computerized tomography guided stereotactic biopsy was carried out and several biopsies from both lesions were obtained. These showed increased cellularity, pleomorphic nuclei and associated microcyst formation supporting the diagnosis of low grade fibrillary astrocytoma. No mitotic figures were detected, and there was no evidence of vascular proliferation or necrosis. The MIB-1 showed a proliferative index of less than 3%.

Discussion. Multiple enchondromatosis can usually be diagnosed by clinical and radiological findings; sometimes pathological confirmation is required. Clinically it manifests as gross bony deformities due to intra osseous metaphyseal and diaphyseal cartilaginous masses. Shortening of the extremities with resulting limb length discrepancies may also occur.[6] The lesions are usually painless unless associated with pathological fracture or superimposed trauma. Deforming and symptomatic lesions are usually treated by curettage or en bloc excision. Radiologically, the lesions appear as a rounded or oval centrally located intraosseous

lucencies commonly associated with matrix calcifications. They may symmetrically or asymmetrically expand the bone. Bowing and shortening of the bone may also be seen. Small bones of the hands and feet are most common sites followed by long bones of the upper and lower limbs. Iliac crest is the most common flat bone site.[7] Malignant transformation of the enchondroma into chondrosarcomas, osteosarcomas and fibrosarcoma is a well known complication with estimates of incidence vary widely between 10-50% in Maffucci syndrome,[8] which is also associated with a high rate of extra skeletal malignancies including intracranial gliomas, leukemias, ovarian, pancreatic and hepatocellular carcinomas[9] as well as some benign lesions like adrenal and pituitary adenomas, ovarian cysts and uterine polyps.[10] Ollier's disease on the other hand is only rarely associated with sarcomatous degeneration of the enchondromas or other systemic neoplasms.[11] This has always been considered as a key difference between Ollier's disease and Maffucci syndrome, however, the development of 2 primary brain tumors in this case, along with several reports in the literature that showed increasing evidence of gliomas in patients with Ollier's disease made this distinction debatable, and support the concept of 2 variants of the same disease with predisposition to development of tumors from various germ layers.[12,13] Fourteen cases of ME associated with intracranial gliomas (including this case) have been described in the literature. Frappaz et al[3] reviewed 10 cases in the literature in which Ollier's disease was associated with gliomas. The pathology was distributed between low grade astrocytomas (3 cases), high grade astrocytoma (3 cases), and low grade gliomas (4 cases). Three cases out of the 10 were located in the posterior Fossa, with only one case of diffuse brain stem involvement. Two cases showed multicentric localizations. Van Nielen and De Jong[14] presented a case of Ollier's disease with 2 intracerebral low grade gliomas located deep in the temporal lobe and in the pons cerebri extending caudally in the brain stem. To the best of my knowledge, the present case is the fourth patient reported in the literature with Ollier's disease and multicentric low-grade gliomas, and the only one with simultaneous supratentorial glioma involving the right parasagittal frontal lobe, and infratentorial glioma diffusely infiltrating the brain stem. This case and other cases reported in the literature support the observation that presence of primary brain tumors is not confined to patients with Maffucci syndrome but also occur in patients with Ollier's disease. It also supports a continuum between these 2 disease entities and suggests that clinicians must be aware of the need for long term surveillance in patients affected by these conditions.

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