Case Report

Bone scintigraphy in Ollier's disease: A rare case report

Shoukat H Khan, Tanveer A Rather, Parvaiz A Koul[1], Rumana Makhdoomi[2], Abdul Rashid Bhat[3], Dharmender Malik, Ram Manohar

Departments of Nuclear Medicine, [1]General Medicine, [2]Pathology, and [3]Neurosurgery, Sher-I-Kashmir Institute of Medical Sciences, Srinagar, Jammu and Kashmir, India

ABSTRACT

Ollier's disease is characterized by multiple skeletal enchondroma. There are published data regarding Ollier's disease being associated with vascular malformations and non-skeletal neoplasms. We report a case of Ollier's disease in a young male associated with osteochondroma, low grade glioma in the insular cortex of brain and Gilbert's syndrome. Technetium-99m methylene diphosphonate whole body bone scan is a sensitive investigation to ascertain the complete extent of skeletal involvement particularly the asymptomatic sites.

Keywords: Bone scan, glioma, Ollier's disease, osteochondroma, technetium-99m methylene diphosphonate

INTRODUCTION

Ollier's disease characterized by multiple skeletal enchondroma is a rare non-inherited disease of unknown etiology.[1] Majority of the skeletal enchondroma are present in the metaphyses and diaphyses of tubular limb bones.[1] The enchondroma particularly in hands and feet cause focal deformities that sometimes are complicated by pathological fractures, which may result in limb length discrepancies.[2-6] Maffuci's disease a close variant of Ollier's disease is characterized by soft-tissue hemangiomas and non-skeletal neoplasm in addition to multiple skeletal enchondroma.[7] The other subtypes of Ollier's disease like metachondromatosis, genochondromatosis, spondylochondrodysplasia, dysspondyloenchondromatosis and chierospondyloenchondromatosis are relatively rare.[1] Pathologically enchondroma result from a failure in the enchondral bone formation at the growth plates due to failure of terminal differentiation of growth plate chondrocytes.[8] High resolution computed tomography (CT) scan and magnetic resolution imaging (MRI) have documented additional non-skeletal neoplasm and vascular hemangiomas among patients of conventional Ollier's disease, which otherwise were categorized as de novo Maffuci's disease.[9] It is increasingly believed that Ollier disease, Maffuci's disease and other sub types are part of the spectrum of generalized enchondromatosis.[1]

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CASE REPORT

A 35-year-old male patient presented with 1 year history of intermittent headache and giddiness. This was sometimes associated with loss of consciousness and involuntary movements in hands. There was occasional loss of bowel and bladder control. In the past patient gave history of hard swellings in the right hand and lower legs from the age of 9 years. The swellings were biopsied and reported as enchondroma. On and off he sustained fractures in hand swellings after trivial trauma. They were managed conservatively with splints and analgesics. Patient had no other symptoms until 1 year back. There was no family history of similar illness. Systemic examination of the patient was unremarkable. Local examination revealed marked bony deformities with hard swellings in both the hands. Hard swellings were also palpable in the right fore arm and distal ends of both lower limbs. The laboratory profile revealed a normal hemogram, normal kidney function tests and normal serum electrolytes. The fasting blood sugar, serum uric acid, calcium and phosphorus were within the normal limits. Serial serum liver function tests revealed isolated elevation of bilirubin ranging from 2.51 mg/dL to 2.58 mg/dL. Total serum proteins were 6.50 g/dL with albumin fraction of 4.5 g/dL. The coagulogram parameters were within the normal limits. The electrocardiogram was normal. Abdominal ultra-sonogram revealed a Grade I prostatomegaly. X-ray examination showed lytic lesions

Address for correspondence:
Dr. Shoukat H Khan, Department of Nuclear Medicine, Sher-I-Kashmir Institute of Medical Sciences, Srinagar - 190 011, Jammu and Kashmir, India. E-mail: drshkhan199@yahoo.co.in

with sclerosed margins in the metacarpals and phalanges of both hands [Figure 1]. Similar lesions were noted in both the tibia and fibula [Figure 2]. There were two exostosis (osteochondroma) one each at the medial aspects of upper ends of both the tibia [Figure 3]. X-ray skull was reported to be normal. In order to see the extent of skeletal involvement patient underwent a whole body technetium-99m methylene diphosphonate scan on a dual head gamma camera fitted with a low-energy all-purpose collimator. The bone scan revealed multiple foci of intense tracer uptake in sternum, right humerus, right radius, right ulna, right hand, right femur, right tibia, right fibula, left hand, left femur, left tibia, left foot [Figure 4]. The lesions predominantly involved the tubular limb bones sparing the axial skeleton. Bone scan revealed extra sites of involvement at right humerus, sternum and both femoral shafts. Bone scan appearance was reported to be consistent with multiple enchondroma seen in Ollier's disease. A non-contrast CT head showed a well-defined hypo-dense lesion with no evidence of perilesional edema in left insular cortex. MRI revealed a well-defined lesion with no perilesional edema in left insular area that was hypo-intense on T1-W image [Figure 5] and hyper-intense on T2-W image and flair sequences [Figure 6]. Radiological features suggested a glioma in the region of left insular cortex. There was moderate enhancement on contrast imaging. At surgery a grayish mass was seen in the left insular area of brain, which on histo-pathological examination was reported as low grade astrocytoma. A final diagnosis of Ollier's disease associated with osteochondroma, Gilbert's syndrome and insular glioma of brain was made.

DISCUSSION

Ollier's disease is mostly encountered in childhood, affecting both sexes equally. The estimated prevalence of the disease is 1/100,000.[1] There is large variability with respect to number, size, location, age of onset and the requirement of treatment. The multiple enchondroma are usually distributed unilaterally and may involve the entire skeleton, although skull and vertebral bodies are rarely involved.[1] Malignant transformation into secondary chondrosarcoma of some enchondroma may occur in 5-50% of patients.[1] Association of Ollier's disease with intracranial glioma though rare has been reported in literature. On review of the literature, we came across 19 patients of Ollier's disease with associated intracranial glioma. Majority of the glioma are low grade astrocytoma. Frontal lobe is the most favored site in 50% of patients followed by brain stem.[2] Most patients have a single intracranial glioma however in 31.5% of patients' multiple intracranial glioma have been reported. Our patient had a single glioma in left insular cortex, which has not been reported in the literature so far. Patients with Ollier disease are treated for their skeletal lesions on a case to case basis with procedures like splinting of the fractures and sometimes curettage and bone grafting.[10] The lesions grow slowly until skeletal maturity. Ollier's disease is probably a syndromic entity of multiple enchondroma with associated vascular malformations, non-skeletal neoplasm like brain glioma and metabolic disorders like Gilbert's syndrome. It may also have additional skeletal lesions of cartilaginous cells like osteochondroma. Abnormalities in signaling pathways that regulate growth and parathyroid hormone 1 receptor (PTH1R) mutations have been reported in ~10% of Ollier's disease patients. Recently identical gene IDH1 mutations have been

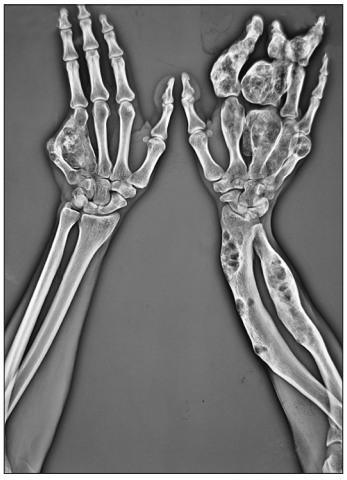

Figure 1: X-rays antero-posterior of both hands showing lytic lesions with sclerosed margins (enchondroma) in the metacarpals and phalanges of both the hands

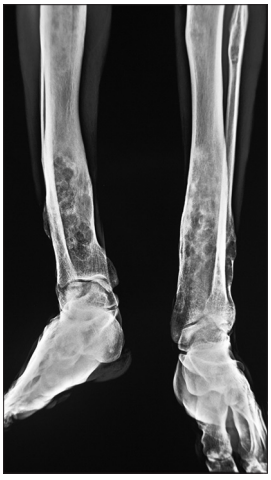

Figure 2: X-rays showing lytic lesions (enchondroma) in the regions of growth plates and adjoining regions of both the tibia and fibula

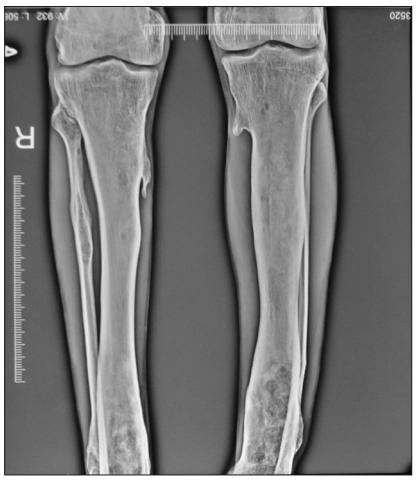

Figure 3: X-rays showing two exostosis (osteochondroma) one each at the medial aspects of upper ends of both the tibia

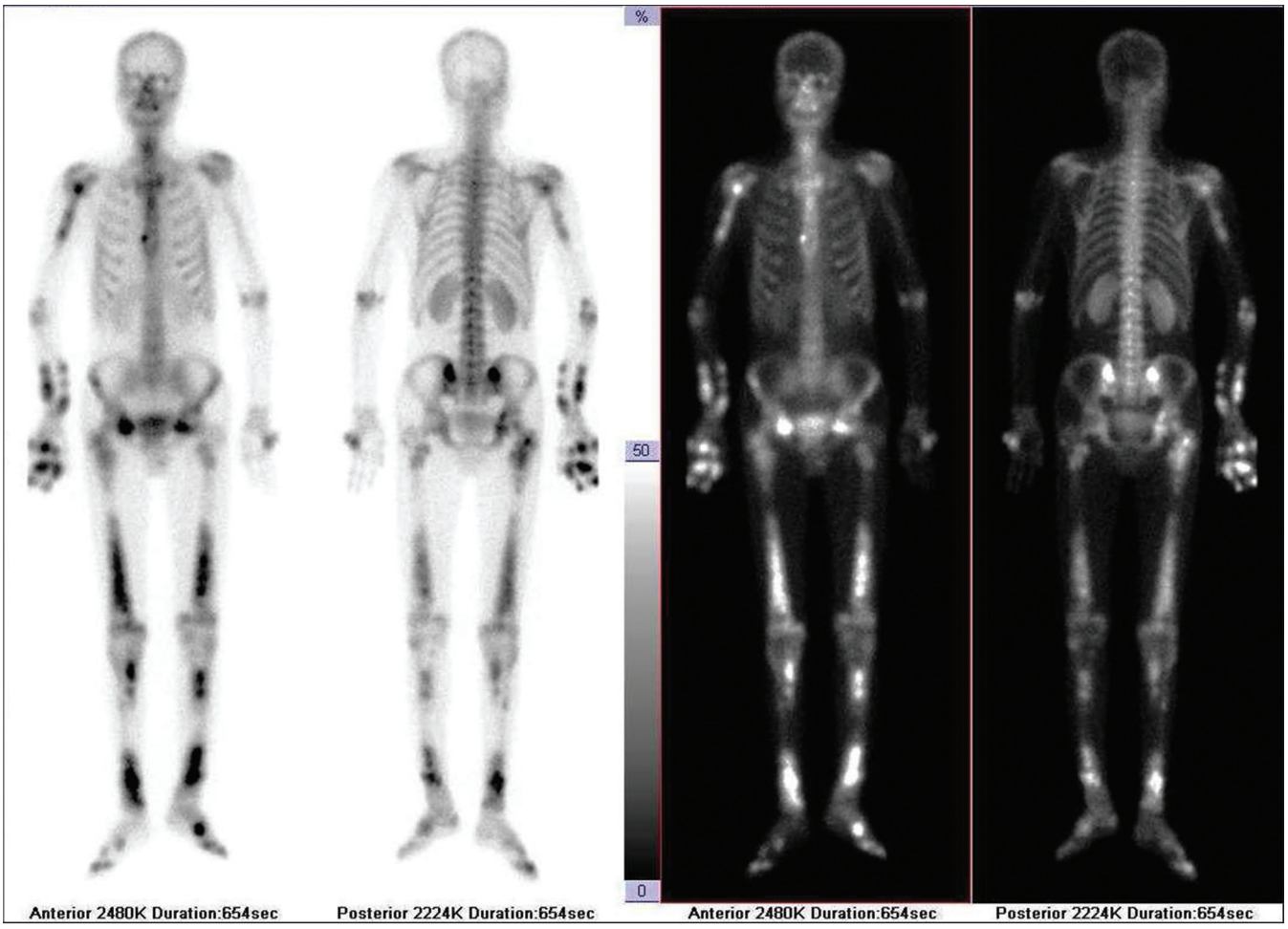

Figure 4: Technetium-99m methylene diphosphonatewhole body bone scan showing multiple foci of intense tracer uptake in the skeleton suggesting extensive enchondromatosis

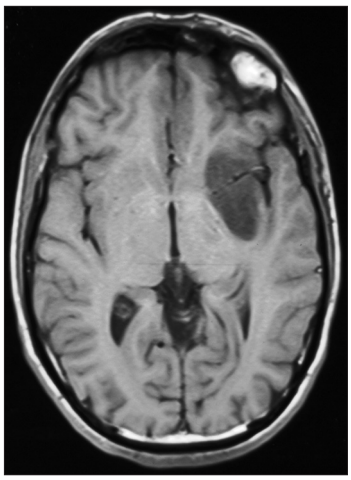

Figure 5: Magnetic resonance imaging revealed a well-defined lesion with no peri-lesional edema in left insular area that was hypo-intense on T1-W image

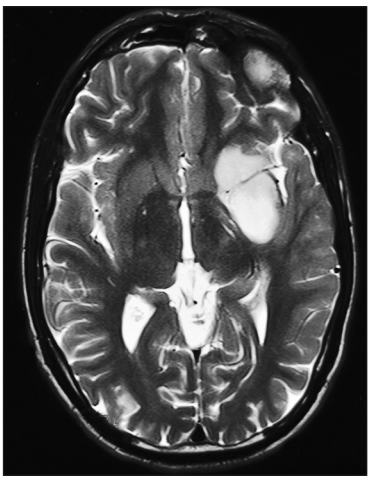

Figure 6: Magnetic resonance imaging revealed a well-defined lesion with no peri-lesional edema in left insular area that was hyper-intense on T2-W image

reported in patients of low grade astrocytoma and among patients with single and multiple enchondroma speculating a common link between patients of glioma and Ollier's disease.[2] Another common link involving enchondroma and glioma in patients of Ollier's disease are mutations in parathyroid hormone related peptide parathyroid hormone related peptide Type-1 receptor (PTHR1).[2] The peripheral skeletal enchondroma in patients of Ollier's disease are amenable to possible profiling for IDH1 and PTHR1 mutations to identify a subset of patients who are likely to develop intracranial glioma necessitating a supervised

follow-up. Exostosin-1 germ line mutation among patients of multiple osteochondroma resulting in deregulated cartilaginous cells of growth plate has been reported.[11] Patients of Gilbert's syndrome have alteration in the promoter sequence for the gene of enzyme uridyldiphosphonate glucuronylphosphotransferase resulting in its reduced expression.[12] Presence of a genetic link at molecular level through signaling pathways among associated lesions in Ollier's disease is a matter of open debate and research. Ollier's disease may eventually turn out to be a complex syndrome than an isolated skeletal disorder of multiple enchondromatosis.

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