

## OSTEOPETROSIS - A SURVEY OF 17 CASES

*Mumtaz Khan Burki, Mehr Dil Khan Wazir & Iftikhar Qayum*

*This is a retrospective survey of 17 children with osteopetrosis admitted in paediatrics ward from 1990 to 1995. Their clinical data, radiographs, laboratory data & histories were analyzed. All of them were male with age range from 1 month to 5 years. 80% of patients had a history of parental consanguinity. All of them had moderate to severe anaemia and failure to thrive as their presenting symptoms. Other predominant associated features were stuffy nose with depressed nasal bridge (95%), hepatosplenomegaly (90%) and increase in size of head (80%). Neurological complications such as visual loss (80%) and deafness (40%) were also observed. Not a single fracture was observed.*

*The diagnosis of osteopetrosis was made by chance, radiologically. Treatment in all patients was symptomatic. No curative treatment was available. Mortality was high due to repeated infections and bleeding. The possibility of a new subtype of malignant recessive osteopetrosis is discussed.*

### INTRODUCTION

Osteopetrosis is an inherited skeletal condition characterized by increased bone radiodensity<sup>1</sup> as a result of impaired bone resorption due to osteoclastic dysfunction<sup>2</sup>. There are three clinical groups<sup>3,4</sup>:

1. Infantile malignant autosomal recessive (fatal).
2. Intermediate autosomal recessive (non-fatal).
3. Autosomal dominant or adult type.

It is a rare skeletal disease with incidence of 1:500,000 in North American population<sup>3</sup> and 1:20,000 in the Caucasian races<sup>5</sup>. Though myelophthisic anaemia is a major presenting symptom, patients may manifest with any infection, such as upper and lower respiratory tract infections, gastroenteritis, septicemia and meningitis. Other symptoms may include failure to thrive, distention of abdomen, hydrocephalus, progressive visual loss and deafness<sup>1,4</sup>.

The diagnosis of osteopetrosis is confirmed by increased radiodensity on skeletal radiographs. Orthopaedic problems such as

fracture of bones is the commonest symptom in autosomal dominant or adult type<sup>4</sup>. Light and Electron Microscopic morphology of trabecular bone reveals apparently inactive osteoclasts with little or no involvement in bone resorptive activity. These cells also show different morphologic features, such as loss of ruffled borders and clear zones found in normal bone osteoclasts. The number of osteoclasts is markedly increased, in contrast to osteoblasts, bone lining cells and marrow stromal cells, which are markedly decreased in most patients<sup>6,7</sup>.

There is no specific treatment for osteopetrosis except supportive measures such as blood transfusions for correction of anaemia and antibiotics for treating presenting infections. The only curative treatment is allogenic bone marrow transplantation which is highly expensive and only available in particular centres<sup>8</sup>. Recent approaches using high doses of Vit D, Parathormone, interferon gamma and macrophage colony stimulating factor have caused improvement of the bony pathology and provided further insights into the underlying mechanisms of osteopetrosis.<sup>9,10,11</sup>

---

From: Women & Children Hospital & Ayub Medical College, Abbottabad

**DR MUMTAZ KHAN BURKI**, Assistant Professor, Department of Paediatrics.

**PROF MEHR DIL KHAN WAZIR**, Head, Department of Paediatrics.

**DR IFTIKHAR QAYUM**, Senior Lecturer, Department of Pathology, Ayub Medical College.

Corresponding Author: **DR M K BURKI**.

## MATERIALS AND METHODS

A total of 17 cases (ages 1 month to 5 years) were included in the study. The detailed history, clinical data and skeletal radiographs were observed. Serological tests and bone marrow biopsy were done. The following laboratory tests were performed:

1. Blood complete picture, Blood *CIS*.
2. Hb electrophoresis.
3. Serum calcium, phosphate, alkaline phosphatase.
4. Bone marrow aspiration.
5. Whole body skeletal surveys.
6. Urine & Stool R/E.

The treatment given was blood transfusions for correction of anaemia and appropriate antibiotics for treating infections. Steroid therapy (for 3 weeks) was given to two patients with thrombocytopenia.

## RESULTS

There were 17 patients, all of them were male and majority of patients were under one year of age. The youngest patient was 1 month old and oldest 5 years (Table 1). 80% patients were having parental consanguinity.

TABLE 1: CLINICAL DATA REGARDING AGE AND PERCENTAGE OF PATIENTS

Clinical Features	Ages	%Ages
Anaemia	All ages	100
failure to thrive	All ages	100
Stuffy nose	1 mo -1 year	90
Hepatosplenomegaly	After 1 month	90
Thrombocytopenia	1 year - 5 year	80
Hydrocephalus	After 1 month	80
Visual loss	After 1 month	80
Hearing loss	After infancy	60
fracture bones	Upto 5 years	-



Fig.1 2 years old osteopetrotic child with depressed bridge of nose, poor dentition, mild hydrocephalus, hepato-splenomegaly & anaemia.

All patients were moderately to severely anaemic and underweight (Fig 1). They had normal serum values of calcium and phosphate but alkaline phosphatase was raised in majority of patients. Bone marrow aspiration was done in 2 patients, one was normal and the other was difficult to aspirate, hi majority of cases, parents did not allow for aspiration of bone marrow. In all cases, increased radiodensity of skeletal radiographs was observed which was the only- diagnostic criteria for this disease (Fig 2).



fig 2. Skeletal radiograph of an osteopetrotic child

X-ray chest and long bones showed increased radiodensity; "bone in bone" appearance and transverse striations at metaphyseal ends of long bones 1,4 were seen in 2 patients (ages 3 & 5 years) (Fig 3).

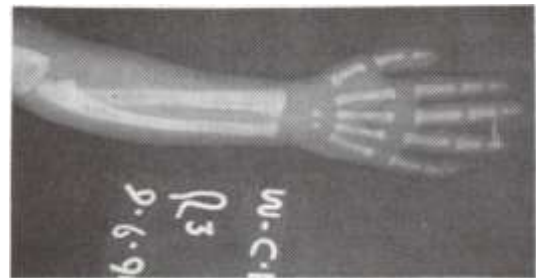


Fig.3. Transverse striations and bone-in-bone' appearance of bones of forearm and hand in an osteopetrotic child.

Increased radiodensity of the base of the skull was found in 60% of patients (Fig 4). Fracture of bone was not found in a single patient.



Fig. 4 X-Ray skull of an osteopetrotic child.

Osteopetrosis is not an X-linked disorder, but in our study it was noticed that all patients were male. Treatment given was symptomatic, e.g. blood transfusions for anaemia and antibiotics for infections. Only patients who developed thrombocytopenia were given steroids for 3 weeks and the response was satisfactory, with improvement in their blood picture.

Mortality was very high in majority of patients due to repeated infections and non-availability of curative treatment such as bone marrow transplant.

## DISCUSSION

Our survey may be highlighting a different pattern or type of osteopetrosis. In addition to the common presenting features, such as anaemia, failure to thrive and hepatosplenomegaly, we noticed that stuffy nose with breathing difficulty was also a very common symptom. Orthopaedic problems such as fracture of long bones was not seen in even a single patient in our study. Similarly, all cases were males; majority (80%) of them had parental consanguinity, which makes one suspicious of an X-linked mode of inheritance.

In different literatures and textbooks, osteopetrosis is considered as a somatic hereditary disorder. A study similar to ours, of 19 cases of osteopetrosis in Saudi Arabia over a 5 years' period was made<sup>12</sup> and they had male to female ratio of 6:13. Sonta-Jakimezky-D<sup>13</sup> in 1993 reported a case of osteopetrosis, a boy of 13 years presented with three fractures of femur. The reason might be that fractures are more common

in older children having autosomal dominant or adult type of osteopetrosis<sup>14</sup> while in our study the oldest patient was 5 years old with autosomal recessive inheritance, in which fracture of bone is less common. Despite the fact that our patients appeared to be in malignant recessive osteopetrosis, with radiographic features described as for cases presenting with fractures, remarkably none had any bony problems. This may indicate a new subtype of malignant recessive osteopetrosis with minimal or no serious bone involvement, but with hematologic and immunologic abnormalities accounting for most deaths due to infections.

An intriguing possibility exists, which warrants further studies on our patients. This is that in a way similar to the classification of autosomal dominant osteopetrosis into two further types by Bollerslev<sup>15</sup>, there may exist two types of autosomal recessive osteopetrosis, one type (Type I) with almost no fractures, the other (Type II) with bone fractures quite common.

No specific treatment for our osteopetrosis patients could be established, except symptomatic measures. Mortality was very high in our cases because of severe anaemia, bleeding, repeated infection and non-availability of curative treatment such as BMT.

## REFERENCES

1. Shapiro F. Osteopetrosis. Current clinical considerations. *Clin Orthop*, Sep (294) 1993; 34-44.
2. Cook PF & Moore SG. Case report 746: Osteopetrosis. *Skeletal Radiol*, 1992; 21(6): 396-8.
3. Colonia AM, Chaimberg CG, Yoshinari NH, et al. Osteopetrosis: report of 2 cases and review of the literature. *Rev Hosp Clin Fac Med Sao Paulo*, Sep-Oct 1993; 48(5): 242-7.
4. Bejaoui M, Baraket M, Lakhoua R, et al. Recessive osteopetrosis. Identification of a form of medium severity. *Arch Fr Pediatr*, Aug-Sep 1992; 49(7): 627-31.
5. Dahl N, Holmgren G, Holmberg S & Ersmark S. Fracture patterns in malignant osteopetrosis (Albers - Schonberg disease). *Arch Orth Trauma Surg*, 1992; 111(2): 121-3.
6. Helfrich MH, Aronson DC, Everts V, et al. Morphologic features of bone in human osteopetrosis. *Bone*, 1991; 12(6): 411-9.
7. Bollerslev J, Marks SC Jr, Pockwinse S, et al. Ultrastructural investigations of bone resorptive cells in two types of autosomal dominant osteopetrosis. *Bone*, Nov-Dec 1993; 14(6): 865-9.

8. Gerritsen EJ, Vossen JM, Van-Loo IH, et al. Autosomal recessive osteopetrosis: variability of findings at diagnosis and during the natural course. *Pediatrics*, Feb 1994; 93(2): 247-53.
9. Schneider GB, Relfson M & Langman CB. Effects of 1,25-dihydroxyvitamin D3 on bone resorption and natural immunity in osteopetrotic (ia) rats. *J Bone Miner Res*, Apr 1994; 9(4): 585-91.
10. Key LL Jr & Ries WL. Osteopetrosis. The pharmaco-physiologic basis of therapy. *Clin Orthop*, Sep (294) 1993; 85-9.
11. Philippart C, Tzehoval E, Moricard Y, et al. Immune cell defects affect bone remodeling in osteopetrotic op/op mice. *Bone Miner*, Dec 1993; 23(3): 317-32.
12. Abdel-Al YK, Shabani IS, Lubani MM, et al. Autosomal recessive osteopetrosis in Arab children. *Ann Trop Pediatr*, 1994; 14(1): 59- 64.
13. Sonta-Jakimczyk D & Gawlicki W. Osteopetrosis in a 16-year-old boy. *Wiad Lek*, Jul 1993; 46(13-14): 528-30.
14. el-Tawil T & Stoker DJ. Benign osteopetrosis: a review of 42 cases showing two different patterns. *Skeletal Radiol*, Nov 1993; 22(8): 587-93.
15. Bollerslev J & Mosekilde L. Autosomal dominant osteopetrosis. *Clin Orthop*, Sep (294) 1993; 45-51.