### Introduction

Mucolipidosis II and Type III are rare lysosomal storage disorders caused by absent or diminished alpha/beta-hexosaminidase activity respectively. The resulting defective mannose phosphorylation affects transport of lysosomal hydrolases into the lysosome, severe mutations of both alpha/beta of GNPTAB encoding a and beta subunits of alpha/beta-hexosaminidase result in MLII and MLIIA and heterozygous missense mutations are associated with familial persistent stuttering.

### Table 1: Clinical profile and laboratory investigations in 9 patients with Mucolipidosis II and III

<table>
<thead>
<tr>
<th>Patient Case</th>
<th>7m</th>
<th>2ydm</th>
<th>4y</th>
</tr>
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<tbody>
<tr>
<td>Age at diagnosis</td>
<td>5m</td>
<td>2ydm</td>
<td>4y</td>
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<tr>
<td>Birth weight at term</td>
<td>&lt; 2.5kgs</td>
<td>&lt; 2.5kgs</td>
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<td>Growth below the 3rd centile for all parameters with negligible increase beyond 2yrs age. Global developmental delay was seen in all with major motor and cognitive impairment.</td>
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<td>Dysmorphic features, radiological and biochemical studies and mutation spectrum in nine cases</td>
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<td>Type III</td>
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<td>Type II</td>
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### Discussion

- Dysmorphic features, radiological and biochemical studies and mutation spectrum in nine cases (5 females and 4 males) of MLII and III from one centre studied over a 6yr period are described here. Parental consanguinity was present in 6/9 (73%) families and two affected sibs were from one family. Age at diagnosis ranged from 5m to 5½ y. Perinatal skeletal abnormalities were described in two.
- Birth weight at term was < 2.5kgs in all. Growth was below the 3rd centile for all parameters with negligible increase beyond 2yrs age. Global developmental delay was seen in all with major motor and cognitive impairment. Respiratory problems were present in 7/9 ranging from snoring, stridor and recurrent infections to progressive respiratory failure and three died of severe respiratory failure between 2y and 4yfs.
- Facial features present universally included coarse face, periodontal fullness, epicanthic folds, flat nasal bridge, triangular nasal tip, full lips, delayed or abnormal dentition and gingival hypertrophy. Progressive clawing of hands with restricted movements was seen in all nine. Three older children (6½ y by 12½ y/8m) had a milder phenotype and all of these had craniosynostosis and bilateral carpal tunnel syndrome.
- Inguinal hernia, light coloured hair and irides and multiple mongoloid patches were seen in two patients each. One of these patients had persistent popular lesions on lip mucosa, presumed to be seborrhoeic dermatitis, which was described in only one of the three remaining.
- Full skeletal survey was done in all with typical dysostosis multiplex and osteopenia.
- Plasma enzymes (a Mannosidase, a Fucoidase and b Hexosaminidase) were elevated to 40 fold in all tested.
- Echocardiography was abnormal in 6/9 with mitral regurgitation being the commonest defect.
- Corneal clouding was seen in 6/9 with ocular albinism (1), temporal pallor (1) and normal fundus in 7/9.
- Abnormal neuro-imaging was noted in 2/9 cases.
- Results of GNPTAB and GNPTG gene sequencing were available in six cases. Recurrent common mutations in Exons 17 and 18 of GNPTAB gene were noted in cases 1, 2, 4 and 6 (Table 1). A novel homozygous insertion was seen in Exon 7 of GNPTG gene in cases 7 and 8 (both sibs). Functional studies to further delineate this novel mutation have been planned.

### References


### Images

**Image 1:** Corneal clouding was seen in 6/9 with ocular albinism (1), temporal pallor (1) and normal fundus in 7/9.

**Image 2:** Echocardiography was abnormal in 6/9 with mitral regurgitation being the commonest defect.

**Image 3:** Plasma enzymes (α Mannosidase, α Fucoidase and β Hexosaminidase) were elevated to 40 fold in all tested.

**Image 4:** Full skeletal survey was done in all with typical dysostosis multiplex and osteopenia.