# Gaucher disease

**Introduction:** Gaucher disease (GD) is a lysosomal storage disorder caused by multiple genetic mutations leading to deficiency of lysosomal enzyme β- glucocerebrosidase. It is an autosomal recessive disease characterised by mutation in chromosome 1q, N370S and L444P being the most common (95%). The function of glucocerebrosidase is to breakdown substrate glucocerebroside into glucose and ceramide. Failure of this enzyme leads to accumulation of substrate in lysosomes affecting macrophages. These abnormal macrophages are called Gaucher cells and they typically show a wrinkled tissue paper appearance under light microscopy. This phenotypical change is associated with changes in cell surface receptors leading to expression of inflammatory mediators like IL 1 β, IL-6, TNF Alpha etc. Accumulation of glucocerebroside is majorly seen is liver spleen and bone marrow. The prevalence of the disease is approximately 1 in 1 lakh with a higher preponderance in Ashkenazi Jews (1 in 855). Residual enzyme activity provides protection to the nervous system, however skeletal and visceral abnormalities are obvious. A Gaucher-like disease can also occur due to a mutation affecting the protein saposine-C which is required for the optimal activity of β- glucocerebrosidase. The pathophysiology of most lesions in GD is unknown but the dysregulation of calcium homeostasis is associated with neurological manifestations. The presence of N370S mutation is considered to be protective against neurological symptoms except for Parkinson like syndromes (1).

**Clinical and radiological presentations:** The disease mainly exists in 3 types, type 1 being the most common (99%) and type 2 seen most rarely. The age of onset in type 1 ranges from early childhood to late adulthood and the clinical spectrum ranges from asymptomatic to multiorgan dysfunction and death. Type 2 is rarest but the most severe form characterised by neurodegeneration and extreme visceral involvement. The age of onset on type 2 GD is 3-6 months and death usually occur in the first 2 years of life. Type 3 is generally considered as an intermediate between type 1 and type 2, with neurological involvement occurring later in life and with decreased severity (2).

70-100% patients of type 1 and type 3 GD have skeletal manifestations and they are the reasons for seeking a physician consult early on in the natural history of disease. The pathophysiology of skeletal manifestations is unknown. However, infiltration of the bone marrow by Gaucher cells leads to decrease in the number of osteoprogenitor cells and therefore Osteopenia. This is associated with an increased risk of fractures. Infiltration by

Gaucher cells can also decrease Osteoclastic activity thereby affecting bone remodelling and decreased fracture healing potential. This in turn affects the blood vessels causing ischemia and osteonecrosis. Anaemia, Splenectomy and male gender are risk factors for osteonecrosis (3). Bone infarcts can occur at multiple sites in the body (4,5).

Skeletal manifestations include:

1)Chronic bone pain

2)Decrease in bone mineral density

3) Increased risk of fractures

4) Bone crisis (Acute episodes of bone pain)

5) Increased risk of infections

6) Osteonecrosis (43% in patients with GD)

Radiological features include:

1. Endosteal erosion of long bones
2. Fractures – Vertebral and Lower limb
3. Erlenmeyer flask deformity

(Similar radiographic picture may also be seen in Sickle cell disease and hemoglobinopathies)

Plain Radiography shows the above features. A low intensity signal in both T1 and T2 sequences can be seen on an MRI. Technetium-$99^{m}$ bone scan findings show increased uptake in bony lesions of GD patients but it shows decreased uptake in the regions of bony infarcts. The above-mentioned skeletal symptoms and radiological picture in association with multiorgan involvement like hepatosplenomegaly and Parkinsonism like syndrome should raise the suspicion of a metabolic disorder. The evidence on bone turnover in GD is conflicting. Blood reports show cytopenia and abnormal Liver function tests. A bone biopsy can be performed to establish the diagnosis of GD. The presence of Gaucher cells is not pathognomic as pseudo Gaucher cells are seen in diseases like leukaemia and myeloma. Enzyme activity testing done to assess β glucocerebrosidase activity in peripheral blood leucocytes is considered diagnostic (Less than 15% of mean activity). Genetic testing is helpful in detecting the mutations involved.

**Treatment:** Treatment of GD in the earlier days included only palliative care. In 1991, human placenta extracted enzyme was introduced. This enzyme replacement therapy (ERT) helped to improve various blood and clinical parameters in GD patients. Patients who started ERT within 2years of initial diagnosis have lesser incidence of osteonecrosis (6). Skeletal manifestations like fractures, osteonecrosis and deformities require surgery in the form of stabilization and joint replacement.

**References:**


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**IOA Clinical record format (Google questionnaires format)**

| | Preoperative | Postoperative | | | |
|---|---|---|---|---|---|
| | | 3m | 6m | 12m | 5yrs |
| Demography<br>Age, sex<br>Occupation<br>Address | | | | | |
| Clinical details<br>Age at the time of diagnosis<br>Pain, swelling, tenderness, ROM etc.<br>Bone(s) involved<br>Patient Consent taken? | | | | | |
| Radiographic findings (upload image) | | | | | |
| MRI/CT<br>(upload images)<br>Any other Imaging | | | | | |
| Histopathology | | | | | |
| Treatment details | | | | | |
| Medications (dose, duration) | | | | | |
| Surgery details | | | | | |
| Radiation therapy details | | | | | |
| Follow up (recurrence/complications/sec surgery etc.) | | | | | |