

# Management Dilemma of a Neuropathic Knee in a Known Case of Larsen Syndrome: A Case Report

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## Learning Point of the Article:

Meticulous clinical examination and a high index of suspicion is required to diagnose and manage rare cases.

## Abstract

**Introduction:** Larsen syndrome (LS) is a rare genetic disorder affecting mainly the connective tissues. It is characterized by characteristic facial anomalies, cervical kyphosis, cardiorespiratory disorders, and multiple joint dislocations. We present a case of a 15-year-old male with unstable neuropathic knee joint instability in a known case of LS. The paucity of literature on the management of this rare condition puts an orthopedician in dilemma regarding the optimal treatment.

**Case Report:** A 15-year-old male, known case of LS, presented to our outpatient department with pain and instability in the right knee for 2 years. Clinically, the patient was having syndromic facies. The diagnosis of LS was confirmed on gene mapping. The right knee was swollen with medial joint line tenderness and restricted flexion. The patient had coronal plane valgus instability. The hypertrophied synovium eroded the articular surface. The radiograph of knee was suggestive of neuropathic arthropathy in fragmentation stage.

**Conclusion:** Orthopedician should be aware of such rare entity with its bony and soft-tissue manifestations. Neuropathic knee is not an absolute contraindication to total knee replacement, especially with advanced prosthesis. Primary arthrodesis to be considered in young adults with instability.

**Keywords:** Larsen syndrome, knee instability, triple arthrodesis, atlantoaxial fusion.

## Introduction

Larsen syndrome (LS) is a genetic disorder of autosomal dominant or autosomal recessive inheritance, affecting mainly the connective tissues, with an incidence of 1:1,000,000 [1]. LS is a rare disorder caused by mutations in FLNB gene located on chromosome 3p14.3 and carbohydrate sulfotransferase 3 deficiency [2]. Autosomal dominant is usually linked to mutation in FLNB gene which encodes filamin B protein and autosomal recessive is linked with carbohydrate sulfotransferase 3 deficiency. Most of the variants are inherited in an autosomal dominant fashion [3].

The disease is characterized by characteristic facial anomalies

(prominence of forehead, hypertelorism, and depressed nasal bridge), spinal anomalies (cervical kyphosis and scoliosis), tracheomalacia, cleft palate, hearing loss, cardiac disorders, clubfoot, and multiple joint dislocations of knee, hip, and elbow [3]. The most common skeletal abnormality reported are spinal anomalies and instability of the knee joint [4]. The knee of LS patient is prone to progressive destruction of bone associated with peripheral neuropathy, traditionally described as neuropathic arthropathy of the knee [5]. The clinical presentation includes warm and swollen knee with instability. The radiographs show rapid and progressive resorption of bones [5]. The paucity of literature regarding the management of

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**Figure 1:** Typical facies of Larsen syndrome.



**Figure 2:** Radiograph showing C1-C2 fusion.



**Figure 3:** Clinical picture showing diffuse swelling of the right knee.

unstable neuropathic knee in a known case of LS poses management dilemma for the orthopedic surgeon. Various non-operative management includes pharmacological therapy, casting, and bracing. The operative management includes external fixator, fusion, and arthroplasty [6]. Considering the rarity of LS and its orthopedic manifestation, the existing literature regarding the optimal operative management is very rare and evidence for best treatment with long-term follow-up is limited.

**Case Report**

A 15-year-old male presented with limp for 2 years. Clinically, the patient (Fig. 1) was having typical facies (flat forehead, depressed nasal bridge, hypertelorism, flat midface, bilateral clinodactyly, and spatulate fingertips). Parents were normal with no complaints. The pregnancy was complicated by oligohydramnios starting at 18 weeks of gestational age and continuing throughout the pregnancy. The patient was born as a

preterm, premature breech delivery at 30 weeks with birth weight 1600 g. The patient did not cry after birth, had hyaline membrane disease and hyperbilirubinemia (5.2 mg/dl) at birth for which he received surfactant and phototherapy respectively and was admitted in NICU for 13 days. He underwent karyotyping on day 17 based on his skeletal and respiratory abnormality, which turned out to be normal. On genetic mapping, the diagnosis of LS was confirmed. Ultrasonography (abdomen and pelvis) suggests moderately dilated left renal pelvis. Cardiac echo was normal. The patient was diagnosed to have bilateral developmental dysplasia of hip, a month after birth for which both hips were immobilized in hip spica for 3 months. The child was able to ambulate without any support by 15 months of age. At 5 years, the patient complained of neck pain without any neurological deficit. On clinicoradiological examination, atlantoaxial instability was confirmed for which atlantoaxial fusion done (Fig. 2). Post-operative outcome was uneventful with resolution of symptoms.

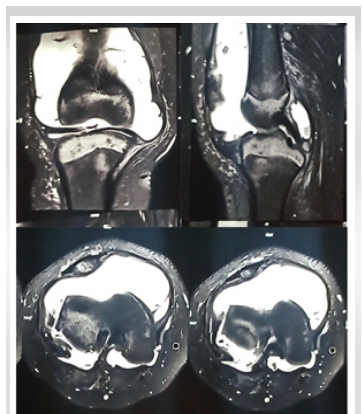
At 14 years of age, the patient presented with a limp. The right



**Figure 4:** Clinical picture showing restricted flexion of the right knee



**Figure 5:** Clinical picture showing coronal plane valgus instability.



**Figure 6:** MRI showing diffuse synovitis.



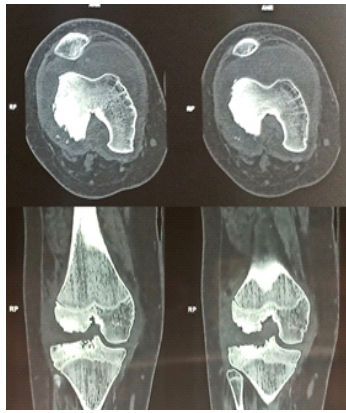


Figure 7: CT showing cortical erosion.



Figure 8: Radiograph showing triple arthrodesis.

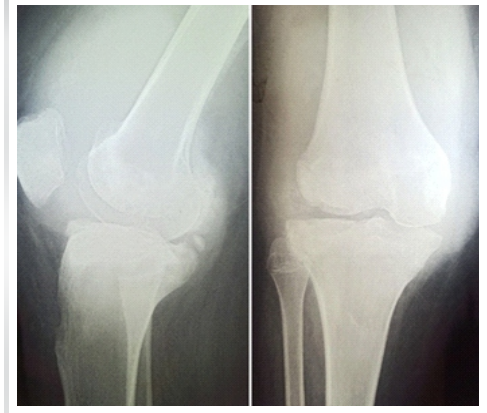


Figure 9: Radiograph showing right neuropathic knee in chronic fragmentation stage.

knee was having diffuse swelling with medial knee joint line tenderness (Fig. 3). The knee having restricted flexion up to 80° with decreased sensation over the anterolateral aspect (Fig. 4). The patient had coronal plane valgus instability which has significantly progressed over a period of past 1 year (Fig. 5). The synovium was hypertrophied (Fig. 6) which was eroding the articular surface (Fig. 7). The patient also had triple arthrodesis performed in the ipsilateral foot (Fig. 8). Spine, bilateral sacroiliac joint, bilateral hip, and left knee examinations were normal. The distal pulses were equally palpable on both sides. Radiographs showed reduction in medial joint space with knee in a chronic fragmentation stage (Fig. 9). The clinicoradiological finding of the joint was similar to the neuropathic arthropathy.

### Discussion

LS is a rare genetic disorder with a frequency of 1:250,000 [7]. LS is characterized by ligamentous laxity, leading to multiple joint dislocations, characteristic facial features, and cervical instability [8]. Hip and knee joints are most commonly affected [9]. The exact pathogenesis of neuropathic knee is sparsely understood. Few theories have been described in the literature. The neurovascular theory (French theory), given by Charcot, states that damage to neurons and an autonomic dysfunction result in vasodilation and activation of cytokines. The activated cytokines with increased blood flow causes osteoclast mediated resorption of bones [10]. The neurotraumatic theory (German theory), given by Virchow, suggests repetitive microtrauma in an insensitive joint leads to recurrent effusions, ligamentous laxity leading to instability, and finally osteochondral damage [11]. The neuropathic knee in a known case of LS is extremely rare (1:10,000,000) and so is the treatment options. Various treatment options reported in PubMed are discussed below.

### Immobilization

Limited or non-weight-bearing mobilization during the early fragmentation stage helps in pain control and joint stability, leading to improvement in mobility. The various modalities for immobilization include restrained orthosis, orthotic walker shoes, and total contact casting. Immobilization halts the process of bone resorption and leads to remineralization. This option is generally considered for those who are medically comorbid to undergo operative intervention or in a young patient to slow down the disease process. There are no studies which advocate long-term immobilization to be beneficial in the management of neuropathic arthropathy.

### Pharmacological Management

The pathophysiology behind neuropathic knee includes interleukin-1, tumor necrosis factor- $\alpha$ , and RANKL. Hence, the goal of treatment includes inhibition of these inflammatory markers and osteoclast activity. These drugs are most efficient in the active fragmentation stage. As per the studies, bisphosphonates, calcitonin, and calcitonin combined with oral calcium caused significant reduction in the bone turnover markers. However, there are no studies available which highlights the efficacy of pharmacological drugs on long-term outcomes.

### Arthroplasty

Arthroplasty in recent day literature is considered the best modality to correct deformity and to improve mobility in knee pathologies. However, neuropathic knee poses certain challenges for arthroplasty which are inherent. The challenges include fixed deformities, limited bone stock, ligamentous laxity, abnormal vasculature and neurology, high infectivity rate, and residual post-operative instability. The intraoperative challenges include soft-tissue balancing and the choice of implant. Few surgeons prefer high constrained prosthesis with longer stems while others prefer cemented hinged prosthesis

with or without metaphyseal augments. The largest series in the treatment of neuropathic knee is of Parvizi et al. [12]. He managed 40 cases of neuropathic knee with total knee replacement. He used hinged prosthesis with long stems augmented by metal wedges or bone grafts. In a mean follow-up of 7.9 years, there was a failure rate of 15%. The causes of failure include aseptic loosening, implant exchange to correct instability, infection, and periprosthetic fracture. In another study, Kim et al. managed 19 cases with cemented, condylar, and constrained prosthesis in a known case of neuropathic knee [13]. At mean follow-up of 5.2 years, 16% of patients had aseptic loosening whereas 31% of patients had to undergo arthrodesis. Most authors consider total knee arthroplasty as an absolute contraindication for neuropathic knees. However, with newer implants and augments, few studies have shown satisfactory results.

### Arthrodesis

Arthrodesis since past is the best surgical option available with a surgeon for painless and stable knee in neuropathic cases. The various modalities available for arthrodesis include external fixator, plate constructs, and an intramedullary nail. Contraindications for knee arthrodesis include contralateral hip or knee arthrodesis and ipsilateral advanced arthritis of hip and ankle. Gasse et al. managed 15 cases of neuropathic knee with double frame fixator with 100% of patients having solid fusion [14]. There are many case reports where neuropathic knee was conserved by other modes such as hexapod fixators, plate constructs, or intramedullary nail. The usual complications after the total knee arthroplasty are limited by primary arthrodesis.

The literature on neuropathic knee complicated by instability of LS is extremely rare. A detailed review of PubMed revealed only

three cases of LS who were managed by operative intervention. Klien et al. treated a case of anterior instability of knee in a 3-year-old child, a known case of LS with a hexapod fixator [15]. After a follow-up of 4 years, the patient had a knee range of 110°. Muller et al. presented a case of a 59-year-old female with bilateral congenital knee dislocation in a known case of LS. They gradually distracted the knee with an external fixator followed by constrained total knee prosthesis [16]. The case was free of any complications in a follow-up period of 2 years. Mustafa et al. managed a 31-year-old male, a case of chronic luxation of the right knee with primary arthrodesis [17]. The patient was satisfied with the clinical result after a period of 2 years with no complications reported.

### Conclusion

Despite LS being a congenital deformity, orthopedicians should be aware of its bony and soft-tissue manifestations. Neuropathic knee is not an absolute contraindication to total knee replacement, especially with better designed constrained, hinged prosthesis with long stems. Although knee arthroplasty is the preferred modality of treatment in various knee pathologies, primary arthrodesis to be considered in young population with instability considering the complications associated and revision rates after total knee arthroplasty. Paucity of existing literature and lack of long-term studies result in failure of consensus on optimal treatment of neuropathic knee in a known case of LS. Treatment should be individualized.

### Clinical Message

Arthrodesis to be considered over arthroplasty in syndromic, early-onset neuropathic knee.

**Declaration of patient consent:** The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given the consent for his/ her images and other clinical information to be reported in the journal. The patient understands that his/ her names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

**Conflict of interest:** Nil

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