UNIT 4 NEURODEGENERATIVE DISORDERS

Structure

4.0 OBJECTIVES

After completing this unit, you will be able to:

- identify the cardinal features of Parkinson's disease and differentiate Parkinson's disease from other parkinsonism;
- evaluate an elderly person with Parkinson's disease and plan its treatment schedule;
- identify other movement disorders in elderly and refer to specialist;
- diagnose and assess and evaluate neuropathies in elderly; and
- diagnose and evaluate neuro-muscular problems in elderly.

4.1 INTRODUCTION

Common neuropsychiatric disorders in the elderly are stroke, dementia, depression, Parkinson's disease and neuropathies etc. Vascular disorders, depression and dementia have already been covered in the preceding chapters. We shall now proceed to discuss disorders of movements, neuropathies and neuromuscular junctions in the elderly.

Neurological disorders in elderly are difficult to identify especially if they have insidious onset and are slowly progressive, because elderly being weak and frail attribute incapacity of disease to aging. Hence , special care must be taken to examine the elderly in detail to identify these disorders.

In this unit we will learn about Parkinson's disease, the commonest movement disorder in the

elderly, some other disorders which resemble Parkinson's disease superficially which are also known as parkinsonism. In addition, we will also learn about some not so common movement disorders, neuropathies and neuromuscular disorders in the elderly.

4.2 MOVEMENT DISORDERS IN ELDERLY

As you know movement disorders are a group of neurological diseases in which there is either occurrence of excessive abnormal movements or paucity and/ or slowness of normal movements in the absence of paralysis or weakness. These are therefore known as hyperkinetic and hypo-kinetic movement disorders respectively. The prototype of hypokinetic disorders is Parkinson's disease. Hyperkinetic movement disorders consist of tremor, chorea, dystonia, ballism, tics and myoclonus. Of the hyperkinetic disorders, common ones seen in elderly are essential tremor (ET) Huntington's disease (Huntingtons' chorea) and focal dystonias. The disease is caused by degeneration of pigmented neurons in substantia nigra resulting in diminished levels of dopamina in the brain.

4.2.1 Parkinson's Disease

Parkinson's disease was first described by James Parkinson in 1817. This is a disease of elderly and its prevalence increases from 1% in people over the age of 65 years to 5% in people over the age of 80 years. It occurs in all parts of the world and affects men and women equally. The disease has insidious onset and is slowly progressive leading to severe morbidity in advanced stage. The disease is caused by degeneration of pigmented neurons in substantia nigra resulting in diminished levels of dopamine in the brain.

Etiology

Though the etiology of the disease is not well known, there are some hypothesis as given below:

1) Accelerated aging
2) Environmental toxins
3) Genetic factors

Clinical Features

The cardinal clinical features are:

- Rest tremor at 4-6 Hz
- Bradykinesia or slowness of movements
- Rigidity, typically cogwheel type
- Postural instability which comes later on in the course of disease

Characteristically the disease starts asymmetrically with tremor in one hand which resembles "pill rolling" movements. This then spreads to involve leg on the same side followed by involvement of the opposite side.

Bradykinesia is characterized by slowness and paucity of all movements. It is manifested clinically as following :

1) "Masked facies" due to in-frequent blinking and infrequent change of facial expressions
2) Monotonous, soft voice
3) Drooping of saliva due to infrequent swallowing movements
4) Lack of postural adjustments
5) Absence of arm swing while walking
6) Dragging of feet while walking
7) Shuffling gait and festination

Rigidity is characterized by increased tone of all muscles. It may have cogwheel characteristics due to presence of tremors. This can be appreciated when the patients limbs are moved passively. Rigidity results in the following :

1) Stooped posture

2) Aches and pains in body

3) Stiffness of the body

Postural instability comes on later in the disease and results in frequent falls.

Other features like difficulty in walking, retropulsion in which there is tendency to run from walking to pace, retropulsion with tendency fall backwards and lateropulsion with tendency to fall side ways is also seen. Dementia, hallucinations and autonomic symptoms like postural hypotension, urinary incontinence and constipation may occur in advances disease. Eventually, the patient becomes rigid, helpless, incapacitated needing help for all self care activities.

Diagnosis

The diagnosis of Parkinson's disease is made on clinical grounds. There are no confirmatory tests. Insidious onset, slowly progressive disorder asymmetrical symptoms of tremor , rigidity and bradykinesia help in arriving at the diagnosis.Other conditions which cause parkinsonism should be excluded by thorough history and examination.

Differential Diagnosis

Parkinson's disease should be differentiated from a number of disorders which resemble Parkinson's disease and are collectively called parkinsonism. These disorders also occur in the elderly people. They are as follows:

1) Drug induced parkinsonism is caused by drugs such as reserpine and phenothiazines due to their action of blockade of dopaminergic transmission. This is characterized by symmetrical symptoms.

2) Post encephalitic parkinsonism was seen after Von economos' encephalitis. This disorder is also symmetrical and presence of tics and oculogyric crisis are common in this disorder.

3) Certain known causes like repeated head injury (in boxers), cerebral hypoxia, repeated cerebro vascular accidents and poisoning by manganese and carbon mono-oxide can also result in symmetrical parkinsonism.

4) Syndrome of Parkinsonism

   - Progressive supranuclear palsy (Steele-Richardson-Olszewski Syndrome) is characterized by parkinsonian features along with rigidity of neck, walking difficulty and frequent falls early in the course of disease with disturbance of ocular motility.
   - Multiple system atrophy (MSA) is characterized by symmetrical parkinsonian features along with pyramidal, cerebellar, autonomic and mental disturbance in various combinations.

Management

Prudent management of a patient of Parkinson's disease requires: (a) patient education, (b) assessment of deficit, (c) assessment of patients requirement, (d) physiotherapy, (e) positive attitude, (f) drugs and (g) surgery

a) Patient education : Patient is told about the nature of illness, need for regular treatment and what to expect in future.

b) Assessment of deficit is done to prescribe the correct treatment

c) Assessment of patients requirement : The treatment is different if the patient is the sole bread earner, if his job requires high degree of physical activity, if the patient is in show business or if the patient is retired.

d) Physiotherapy is helpful in reducing rigidity and aches and pains and keeps the patient agile.

e) Positive attitude help the patient cope up with his disabilities.

f) Drugs : Following drugs are used in the treatment of Parkinson's disease.

   1) Levodopa: Levodopa is the gold standard in the treatment of Parkinson's disease. It restores the dopamine level in the brain. It is usually combined with peripheral dopa-decarboxylase inhibitor to prevent conversion of levodopa to dopamine outside the brain, thus reducing the dose of levodopa and the side effects of levodopa. The combination is available in the ratio of 4:1 of levodopa and carbidopa (100+25mg) or 10:1 ratio(100+10mg, 250+25mg). The dose and timing of

medication is adjusted according to the needs of the individual patient.

2) Anticholinergic drugs are helpful in controlling tremors. Care should be taken while prescribing anticholinergic drugs because they can cause confusion, hallucinations, narrow angle glaucoma and urinary retention. Usual dose is 2-4 mg/day.

3) Amantadine has mild antiparkinsonian action and acts by releasing dopamine from presynaptic terminals. Usual dose is 100-300 mg/day.It can cause ankle edema in small number of patients.

4) Dopamine agonists: A large number of drugs act directly on dopamine receptors. There are two major types of dopamine agonists: ergot derivatives e.g. bromocriptine, cabergoline, lisuride and non-ergot derivatives such as pramipexole and ropinirole. Dopamine agonists can be started alone in early Parkinson's disease or used in combination with levodopa. Dopamine agonists should be started in low dose and the dose should slowly built up. It is important to start dopamine agonists in young PD patients because the side effects of long term use of levodopa can thus be avoided.

5) Monoamine oxidase- B inhibitors are a group of drugs which prevent catabolism and reuptake of dopamine. Therefore, they are useful in the treatment of Parkinson's disease (eg. selegiline).

6) Catechol O-methyl transferase inhibitors: These also act by preventing catabolism of dopamine (e.g. tolcapone, entacapone).

g) Surgery : Though modern treatment is very successful, patients with advanced Parkinson's disease may have complications of advanced disease and long term levodopa therapy such as motor fluctuations, hallucinations and psychosis. Neurosurgical treatment can be undertaken under these circumstances. Essentially, three types of surgeries are done: ablative type in which a discrete lesion is made in any of specified areas of brain. The other types of surgery are deep brain stimulation in which thalamus or globus pallidus or sub thalamic nucleus is stimulated. The third type of surgery is the transplantation surgery in which adrenal medullary tissue or fetal mesenchymal tissue is transplanted in the brain of PD patient.

Indications of surgery in Parkinson's disease are:

1) Advanced Parkinson's disease

2) Severe dyskinesias, hallucinations and motor fluctuations.

3) Absence of dementia, life threatening concurrent illness, and postural disturbance.

Check Your Progress 1

1) Define Hypokinetic disorder and name one prototype.

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2) Describe cardinal features of Parkinson's disease.

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3) Name drugs used in treatment of Parkinson's disease.

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4) Which are drugs used in controlling tremors?

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5) What are indications of surgery?

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4.2.2 Huntington's Disease (Huntington's Chorea)

After learning of Hypokinetic disorder, now we will discuss Hyperkinetic movement disorder. Huntington's disease was described by George Huntington in 1872 in New York, USA. The disease is caused by a genetic disorder which results in expansion of trinucloetide CAG on chromosome 9. This results in production of an abnormal protein called Huntingtin. The disease has an autosomal dominant mode of inheritance and therefore 50% of children of an affected parent are at risk of developing this disease.

Clinical Features

Both sexes are equally affected. The usual age of onset is 5th decade, but can affect older and younger people. A phenomenon of anticipation is seen in families of Huntington's disease. This means that if a child inherits the disease from father, the age of onset in the child is much younger. This is due to larger expansion of CAG repeats in the offspring. Such a phenomenon is not seen when the disease is inherited from mother. Main clinical features consist of chorea which may manifest as frequent grimacing, irregular, arrythmic bizarre movements of limbs, irregular respiration and abnormal gait. Associated with chorea there is some rigidity and slowness of activity. Dementia is one of the main features of clinical picture and is slowly progressive. Most patients also have depression. The disease runs a slowly progressive course and death usually occurs due to inter-current infection and rarely by suicide.

Differential Diagnosis

A large number of disorders resemble Huntington's disease superficially. They are:

1) **Sydenhams' chorea:** this occurs in children and young adults and is associated with rheumatic fever and rheumatic heart disease.

2) Overdose of levodopa in Parkinson's disesae can resemble Huntington's disease, but careful history will help in establishing time sequence of symptoms and arrive at correct diagnosis.

3) **Drug induced chorea:** Drugs such as phenothiazines, lithium, rarely carbamazepine and phenytoin can result in choreiform movements and may persist for some months even after the incriminating drugs are discontinued.

4) Rarely, elderly people can have chorea due to infarction of discrete areas in brain like caudate nucleus. Chorea due to infarction affects one half of the body and is not generalized.

Investigations

1) Clinical history and examination are most important in the diagnosis

2) CT scan: which will show atrophy of caudate nucleus and dilatation of frontal horn of lateral ventricles.

3) Genetic tests: This is now available and can show CAG expansion on chromosome 9.

Treatment

- No treatment is available which can halt the progress of the disease
- Drugs like butyrophenones (haloperidol) and phenothiazines can suppress chorea.
- For depression tricyclic antidepressants can be used.

Check Your Progress 2

1) Huntingtons disease belong to which group of disorder?

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2) What are cardinal features of this disease?

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3) Which are the investigations needed to confirm the diagnosis?

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4) Which are the drugs used in suppressing the chorea?

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4.2.3 Essential Tremor

Essential tremor is a common hereditary disorder. It may occur at any age but is also seen in elderly and is then called senile tremors.

Clinical Features

The disorder runs in families. The tremor is typically more marked in holding posture like holding a cup of tea etc. Hence it is called postural tremor. It has very fast frequency (8-12 Hz). It is suppressed by alcohol consumption. Neurological examination does not show any other abnormalities and all investigations are also normal.

It may be necessary to differentiate it from thyrotoxic tremor or tremors due to drugs such as lithium, sodium valproate and adrenergic agents like salbutamol etc.

Treatment

- Tremors respond very well to adrenergic – blocking agents (propranalol) 20-40 mg three times a day.
- Primidone in small doses (i.e. 50mg) at times is also effective in suppressing tremors.

4.2.4 Dystonias

Dystonias are abnormal involuntary contractions of muscles resulting in twisting and torsion of the affected body part. They may be associated with tremors and sometimes with myoclonus. Though generalized dystonias affecting the whole body is common in children, focal dystonias involving a localized part of the body is common in older people.

Focal dystonias can involve face (cranial dystonia or Meige's syndrome), neck (spasmodic torticollis), arm (writers' cramp) or larynx (spasmodic dysphonia). Meige's syndrome is characterized by abnormal dystonic movements of face. It could be localized to eyes (blepharospasm) and jaw muscles (oro-mandibular dystonia). This is the commonest type of dystonia in the elderly. Spasmodic torticollis results in twisting and turning of the neck to one side with pain. Writer's cramp are characterized by abnormal posture, cramping and pain in hand, forearm and arm during writing and other specific acts with hands like typing, using hand tools or musical instruments or while eating or counting currency notes.

Treatment

1) Treatment is difficult
2) Use of anticholinergic agents like trihexyphenidyl is helpful.
3) Benzodiazepines like lorazepam is helpful in some patients.
4) Dopamine antagonists (haloperidol) or dopamine receptor blocking agents (tetrabenazine) can be used cautiously in the treatment of focal dystonia.
5) Recently, injection with botulinum toxin has been used for treatment of focal dystonias with good results. The effect lasts 10-12 weeks and needs to be repeated.

Check Your Progress 3

1) Classify dystonia.

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2) What is the commonest cause of focal dystonia?

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4.3 NEUROPATHIES IN ELDERLY

After description of movement disorder, we will now aprised you of disorder of peripheral nerve. Peripheral neuropathy is a general term meaning disorder of peripheral nerves due to any cause. Some of the causes of peripheral neuropathy in the elderly are same as those in younger people and some are special for the elderly. The clinical diagnosis of peripheral neuropathy is made on the basis of a history of tingling and numbness in distal parts of feet and hands, weakness and wasting of distal part of limbs manifest by foot drop, slipping of foot-wear from feet while walking and difficulty in using fingers for activities like buttoning shirt, holding small things, screwing ear –rings etc. On examination, the patients may have graded sensory impairment, which means the most distal parts will have maximum deficit and as one moves proximally the impairment will become less, in a "stocking and glove" distribution. The weakness and wasting is in distal distribution and deep tendon jerks will be absent or diminished. The patient may have difficulty walking on heel and may slap the floor with feet while walking as foot drop becomes more apparent. When loss of proprioceptive sensation is prominent ataxia may be out of proportion to weakness and the patient may also complain of a feeling of "walking on cotton wool" even when he walks on hard surface. Sometimes there is disturbance of autonomic functions in the form of diminished distal sweating and swelling of feet. The skin may also show evidence of trophic changes in long-standing cases.

Though this is the typical description of peripheral neuropathy, you should also be aware of variations like mono-neuritis multiplex, in which individual nerves are affected and predominantly proximal type of disorder as occurs in acute demyelinating polyneuropathy (AIDP or Gullian Barre syndrome) may sometimes occur. The diagnosis of peripheral neuropathy also requires ascertainment of the cause of neuropathy in addition to confirming the diagnosis of neuropathy.

4.3.1 Causes of Peripheral Neuropathy in Elderly

There are many causes of peripheral neuropathies in the elderly. These have been listed in Table 4.1. However, there are some which are more frequently encounter in the elderly. These are described below.

Gullian Barre Syndrome

Though AIDP (Gullian Barre Syndrome) occurs generally in young people, when it affects elderly, the prognosis is poorer. It is characterized by acute to subacute (upto 6 weeks) onset of weakness especially of the proximal group of muscles resulting in difficulty in getting up from squatting position and difficulty in raising arm above the shoulder level. Sensory involvement is minimum or rare. The disease progresses rapidly and can cause weakness of facial muscles, bulbar muscles resulting in difficulty in speech and swallowing and weakness of respiratory muscles.

Diabetic Neuropathy

It is common among patients of diabetes mellitus of long duration with poor diabetic control. Though diabetic patients can have many types of polyneuropathies, the commonest is distal symmetrical chronic sensory type of neuropathy associated with pain, tingling and numbness of feet and absent ankle jerks. Other types of neuropathies in diabetes mellitus are chronic distal symmetrical sensory-motor neuropathy, diabetic mononeuritis multiplex, acute or subacute proximal motor neuropathy, chronic proximal motor neuropathy and trunkal neuropathy etc.

Table 4.1: Causes of Peripheral Neuropathies in Elderly

• Acute demyelinating polyneuropathy (AIDP or Gullian Barre Syndrome)
• Metabolic causes
• Diabetic neuropathy
• Ureamic neuropathy
• Vitamin B_{12} deficiency
• Toxic causes
• Alcoholic neuropathy
• Drugs (antitubercular, anti-neoplastic, gold)
• Heavy metals (arsenic, lead)
• Cancers
• Predominantly axonal type
• Predominantly demyelinating type
• Infection
• Leprosy
• AIDS neuropathy
• Gammopathies
• Monoclonal
• Macroglobulineamia
• Cryoglobulineamia

Polyneuropathy

Polyneuropathy associated with cancers is common in elderly. It may occur as a manifestation of para-neoplastic syndrome or may be due to the drugs used in the treatment of the cancer. Common cancers associated with peripheral neuro-pathies are oat cell carcinoma of lung, breast carcinoma, lymphomas including Hodgkin's, multiple myeloma, solitary plasma cytoma and ploycythemia vera. The peripheral neuropathy with cancers is usually mild, sensory and is of both axonal and demyelinating type.

Drug induced Neuropathies

They are generally axonal and less often demyelinating, more often sensory or sensory-motor and of chronic type.

Leprous Neuropathy

Leprous neuropathy in elderly has the same pattern as in the younger people. It can manifest as mono-neuritis multiplex involving ulnar nerves or small cutaneous nerves with hypopigmented, atrophic and hypesthetic skin patches and thickened nerves especially dosal cervical nerve, ulnar nerve, median nerve or lateral popleteal nerve. Rarely, leprous neuropathy can present as distal symmetrical predominantly sensory neuropathy with thickened nerves and painless, non-healing ulcers on feet.

Association of neuropathies and dysproteineamia is common and can occur with monoclonal gammapathies (IgA, IgM and IgG), multiple myeloma, solitary (osteosclerotic or osteolytic) myeloma or cryoglobulineamia. They are severe, chronic, usually sensory and do not reverse with treatment except in the case of solitary osteosclerotic type which responds very well to surgical or radiotherapy of primary lesion.

4.3.2 Investigation of Peripheral Neuropathy

Before proceeding to investigate a patient of peripheral neuropathy complete history of any systemic illness (e.g. diabetes mellitus), systemic malignancy (weight loss, blood in sputum, post menopausal bleeding etc), bone pain, exposure to drugs for medical or non-medical reasons, exposure to toxins (e.g. organophosphorus insecticides, pesticides), exposure to intoxicants (arsenic, lead etc.) and antecedent illness (such as upper respiratory infection, dog bite, other infections etc.) should be obtained. Systemic examination should be thorough and should include examination for aneamia, jaundice, breast lump, prostate enlargement, chest examination, Mees' lines on nail (arsenic neuropathy), blue line on gums (lead poisoning), state of nourishment, skin changes, bony tenderness, nerve thickening etc. Besides, this

investigations include are:-

1) Complete blood count, heamoglobin, ESR, smear examination for type of anaemia.

2) Blood sugar examination

3) X-ray chest

4) Serum protein electrophoresis

5) Electrodiagnostic test (nerve conduction studies and electro-myogram). This will confirm the diagnosis of peripheral neuropathy and distinguish between demyelination or axonopathy as the dominant type of neuropathy.

4.3.3 Treatment

Treatment of peripheral neuropathy is aimed at treating the underlying cause, providing physical aids and physiotherapy. In case tingling and painful dysesthesia causes discomfort some treatment can be given to alleviate them.

Treatment of Cause

1) Diabetes mellitus if present should be controlled.

2) If peripheral neurpathy is due to drugs and toxins they should be identified and withdrawn

3) In case of malignancy they should be treated surgically or by radiotherapy.

4) Neuropathies due to dysprotienemia respond very well to plasmapheresis.

5) Neuropathy due to vitamin B12 deficiency responds very well to intramuscular infection of vitamin B12 in doses of 1000µgm every day for a week, then every week for 4 weeks and thereafter once in three months.

6) Demyelinating neuropathies respond to oral steroids.

Treatment of Painful Dysesthesia

- Anti-epileptic drugs e.g. carbamazepine (200mg 2or 3 times in a day) or diphenyl hydantoin (5-7mg/kg/day)
- Amitryptalline (10-25mg/day) at night
- Gabapentine (300 – 900mg/day) in divided doses
- Capsain ointment locally. The problem with Capsain is that for initial 2 weeks there is increase in burning paraesthesiae.

Physical Aids and Physiotherapy

- In case of severe foot drop special shoes with toe-lifting springs should be advised
- Physiotherapy helps in building up paralysed and weak muscles.
- Ataxia due to disturbance of joint and position sensation can be treated by gait training.

Check Your Progress 4

1) What are the cardinal features of peripheral neuropathy?

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2) What are the common causes of peripheral neuropathy inthe elderly?

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3) How to investigate a case of Peripheral neuropathy in the elderly?

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4.4 DISORDERS OF MUSCLES IN ELDERLY

After nerve involvement, we will concentrate on muscle disorder, that are Disorders of muscles are called myopathies (myo=muscle, pathy = disease). The myopathies are characterized by slowly progressive muscle weakness involving specific muscle groups. In majority of myopathies, the proximal groups of muscles are predominantly affected resulting in difficulty in getting up from squatting position, difficulty in walking causing waddling gait and difficulty in combing hair. Myotonic disorders, in addition, display presence of myotonia in which the muscles relax very slowly after forceful contraction. This can be elicited clinically by asking the patient to clench the first tightly and then asking the patient to open the fist quickly or by tapping the muscle with knee hammer which will leave a dimple on the muscle. There are no sensory symptoms or paraesthesiae, no fasciculations and the deep tendon jerks are preserved (except when the muscle is very severely wasted).

4.4.1 Causes of Myopathies

There are several causes of myopathies: genetically determined (muscular dystrophies), endocrine/metabolic, toxic, inflammatory, disorders of muscle energy metabolism, disorders of lipid metabolism and paraneoplastic myopathies. Among those listed above only a few types of myopathies are seen in the elderly which are presented in Table 4.2.

Table 4.2: Common Types of Myopathies in Elderly

- Muscular dystrophies
  - — Fascioscapulohumeral dystrophy
  - — Myotonic dystrophy
  - — Scapuloperoneal dystrophy
  - — Oculopharyngeal dystrophy
  - — Distal dystrophy
- Inflammatory/Infective myopathy
  - — Polymyositis
  - — Dermatomyositis
  - — AIDS
- Metabolic/endocrine myopathies
  - — Thyroid
  - — Parathyroid
  - — Other endocrine disorders
- Toxic myopathy
  - — Clofibrate Cholesterol lowering drug
  - — Perhexilene (Angina)
  - — Corticoid
  - — D-Penicillamine
  - — Chloroquine
  - — Labetalol/propranolol etc.

We shall now discuss briefly the more common types of myopathies seen in elderly.

Facioscapulohumeral type of muscular dystrophy is inherited as autosomal dominant disorder with onset in 3rd or 4th decade. Both sexes are equally affected. Since this disease causes minimal disability and does not affect longevity, elderly patients with this disease may be seen. As the name implies there is weakness and wasting of facial muscles (food sticking in the vestibule of month, liquids drooping from the angle of month, inability to whistle), shoulder

and arm muscles (winging of scapula, difficulty in raising arm above shoulder level). Foot drop also occurs due to weakness of peroneal muscles.

Myotonic dystrophy is also an autosomal dominant disorder. The disease starts in 2nd or 3rd decade, but due to its mild nature older individuals are also seen with this disease. Weakness initially involves eyelids, neck muscles and distal muscles of limbs. Myotonia can be demonstrated in affected muscles. Other characteristic features in these patients are: characteristic droopy face, cataract, wasting of sternocleido-mastoid, gonadal atrophy and intellectual impairment. Cardiac abnormality in the form of rhythm disturbance occurs in some patients. The disease is transmitted by mutation on chromosome 19q.

Scapuloperoneal dystrophy is characterized by foot drop and winging of scapulae. It presents in 3rd-5th decade.

Oculopharyngeal dystrophy is characterized by slowly progressive ptosis and limitation of eye movements. The pupils are spared. Patients do not complain of diplopia because the disease is symmetrical. It usually presents in 5th or 6th decade. Involvement of pharyngeal muscles occurs later with dysphagia.

Distal muscular dystrophy is very rare. It causes weakness and wasting of hands and feet quite like neuropathy but there is no sensory impairment and deep tendon jerks are normal.

Poly myositis/dermatomyositis: This is a form of inflammatory myopathy of unknown etiology. In polymyositis (PM) skin is spared whereas in dermatomyositis (DM) skin is also involved. It is caused by autoimmune mechanism. Five groups of PM/DM are identified. They are primary idiopathic PM, primary idiopathic DM, PM/DM associated with neoplasia, childhood PM/DM and PM/DM associated with other connective tissue disorder.

This disorder is more common in women (2:1). The disease usually runs a subacute or chronic course, but rarely may start acutely. Pain in muscles is seen in about 10-15% patients and is more common if the disease occurs acutely. Muscles affected are proximal group of muscles of pelvic and shoulder girdle resulting in difficulty in getting up from floor and combing hair. Weakness of pharyngeal muscles, neck muscles and respiratory muscles is common. Ocular muscles are never affected. In DM skin changes in the form of diffuse or localized erythema, scaling and maculo-papular eruption are common. Classical rash is lilac coloured (heliotrope) rash around eye-lid, bridge of nose and cheek (butterfly distribution). Vasculitis and calcification of skin is more common in children. Evidence of other collagen vascular diseases like systemic lupus erythematosus (SLE), rheumatoid arthritis and polyarteritis nodosa occurs in about 20% of cases. Though the deep tendon jerks are preserved normally in majority of patients, its absence suggests involvement of peripheral nerves. This is commonly seen in patients with malignancy. Patients with malignancy usually have DM and are elderly men. Common malignancies associated with PM/DM are lung, breast, ovary, gastrointestinal and myeloproliferative and may be detected up to 2 years after the onset of PM/DM. Involvement of heart is common (30%) and is in the form of ECG changes or even myo-cardial ischeamia.

Myositis in AIDS is common and occurs in all stages of disease.

Several metabolic and endocrine disorders can lead to muscle weakness esp. of the proximal group. These are hypothyroidism, thyrotoxicosis hyper-and hypo-parathyroidism, adrenal disorders, pituitary disorders and diabetes mellitus. Hypothyroidism is associated with painful, aching enlarged muscles esp. calves (Hoffmann's syndrome) and thyrotoxicosis commonly involves proximal muscles and extra-ocular muscles with exophthalmos.

A large number of drugs and toxins cause myopathies. These are generally reversible after stopping the incriminating agent.

4.4.2 Investigations

The primary investigations are done to confirm a myopathy and secondary tests are done to identify the cause and assess involvement of other organs.

Primary tests include:

1) Serum creatinine kinase (CK) It is elevated in almost all disorders of muscles. They are increased to very high levels in disorders with active muscle degeneration like Duchenne muscular dystrophy (up to 200 times normal) and PM(Poliomyositis) (up to 20 times normal), whereas in endocrine myopathy it may be elevated only mildly. Other enzymes like aldolase, lactic dehydrogenase, SGOT and SGPT are also elevated.

2) Electromyography (EMG) is useful in deciding if muscle weakness and wasting is due to primary muscle disease (myopathic) or due to disease of nerve or anterior horn cells (neurogenic). The myopathic pattern shows small potentials with normal phases and complete recruitment of motor units on forced contraction. On the other hand neurogenic pattern consists of high amplitude potentials with increased number of phases and incomplete recruitment of motor units on forceful contraction. In addition, the nerve conduction studies are normal in disorders of muscles and are impaired in disorders of nerves.

3) Muscle biopsy is useful in confirming the diagnosis and can also show presence of muscle necrosis with presence of inflammatory cells in PM/DM.

Secondary tests include:

- History of exposure to drugs and intoxicants
- Heamogram with ESR
- Renal and liver function tests
- Thyroid, adrenal and other endocrine function tests if indicated
- Serum electrolytes
- ECG, X ray chest
- Tests for collagen vascular disease
- In case malignancy is suspected, screening for malignancy may be done

4.4.3 Treatment

1) No specific treatment is available for muscular dystrophies

2) In the distal and scapuloperoneal muscular dystrophy with foot drop, toe lifting shoes can be prescribed.

3) Myopathies due to endocrine disturbance respond to treatment of the incriminating disorder.

4) Myopathies due to drugs and toxins also respond to withdrawl of the incriminating agent.

5) Myotonia in patients with myotonic dystrophy can cause problem. This can be treated with diphenyl hydantoin, quinine or procainamide.

6) Treatment of PM/DM consists of treating the cause (collagen vascular disease, malignancy). In idiopathic cases steroids (1-2mg/kg/day) can be given. If response is inadequate azathioprine (2.5-3.5mg/kg/day) can be given. Other drugs used are cyclophosphamide and methotraxate. In case the disease is rapidly progressive intravenous immunoglobulins and plasmapheresis can be given.

7) Physiotherapy is important in the long-term management of all types of patients.

Check Your Progress 5

1) What are the main features of myopathies?

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2) What are the common causes of myopathies in elderly?

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3) How to investigate a case of myopathy in elderly?

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4.5 DISORDERS OF NEUROMUSCULAR JUNCTION IN ELDERLY

Lastly, you will be aprised of disorder of neuromuscular junction, you know that Neuromuscular junctions (NMJ) are areas in the muscle where a peripheral nerve makes contact with the muscle at the synapse. The terminal part of the nerve at the NMJ is termed as pre-synaptic and the part of the muscle as post synaptic. The neurotransmitter liberated when a nerve impulse reaches the NMJ is acetyl-choline (Ach). There are two main disorders affecting the NMJ, namely myasthenia gravis (MG) and Lambert-Eaton myasthenic syndrome (LEMS). In MG the defect is post-synaptic and there are antibodies against the Ach receptor on the post-synaptic membrane with eventual destruction of the synapse. In LEMS on the other hand the defect is pre-synaptic and essentially consists of reduction of Ach at the pre-synaptic membrane.

4.5.1 Myasthenia Gravis

As mentioned earlier Myasthenie gravis (MG) is a pre-synaptic disorder of NMJ and results in easy fatiguability of muscles along with weakness, which particularly affects the proximal group of muscles, ocular muscles and bulbar muscles. It is an auto-immune disorder with antibodies against ACH receptors are present.

Clinical Features

Though MG affects younger people, a small number of people older than 50 years are also affected. Usually it affects men in later life i.e. in 50's and 60's. A large number of these patients have thymoma. The clinical picture is characterized by easy fatigability and weakness. The disease runs a fluctuating course with diurnal variations and remissions and relapses. The muscles affected are ocular and eye lid muscles causing ptosis and diplopia which is seen in about 85% of patients. Facial muscles and bulbar muscles may be affected giving rise to abnormal facial expression, difficulty in chewing, nasal quality of speech, nasal regurgitation of fluids and dysphagia. Involvement of limb muscles starts from proximal group but becomes generalized when severe. Weakness of respiratory muscles causes dyspnoea and requires use of assisted ventilation.

Investigations

1) Neostigmine or Ediophonium test. After assessing the patient, neostigmine (15mg) IM or edrophonium (1mg) IV is given and patient is evaluated for reversal of weakness at frequent intervals.

2) Electrodiagnostic test is done by stimulating a peripheral nerve (median or ulnar nerve) repeatedly at 3-5Hz and recording the action potentials. In myasthenic patient there is reduction in amplitude of the potential by more than 10-15%. This test is called repetitive nerve stimulation test and the response is called decremental response.

3) Ach receptor antibody can be estimated in serum. It is present in about 80% MG patients. It may be present in only 50% patients when MG is confined to ocular muscles.

4) Xray chest or CT scan of chest should be done to look for thymoma, thymic enlargement or lung carcinoma.

5) Attempt should be made to look for other auto-immune disorders.

Treatment

Treatment of MG can be divided in two main groups:

a) Symptomatic therapy

b) Therapy to induce remission

Symptomatic therapy is achieved by use of neostigmine (15mg) one to four or five times a day orally or pyridostigmine (60mg) one to four times a day orally. The dose can be increased or decreased according to the need of the patient.

For induction of remission several measures are used. They are: thymectomy, steroids (prednisolone 1-2mg/kg body weight /day), azathioprine (2-3mg/kg body weight/day), cyclosporine, plasmapheresis and intravenous immunoglobulin.

4.5.2 Lambert-Eaton Myasthenic Syndrome (LEMS)

This is a pre-synaptic disorder of the NMJ. It is a rare disorder and is generally associated with malignancy, commonly small cell carcinoma of lungs. This is also an autoimmune disorder in which the antibodies are directed against the calcium channels of motor nerves. The disorder resembles myasthenia gravis as patients with LEMS have diplopia, ptosis and proximal muscle weakness. But patients with LEMS have absent deep tendon reflexes, autonomic changes such as dry month and increment response on repetitive nerve stimulation test.

Response to treatment is poor and consists of immunosuppression by drugs and plasma pheresis.

Essentially, there are two types of movement disorders; the hypo-kinetic rigid syndromes and hyper-kinetic syndromes. Parkinson's disease (PD) is the commonest type of hypo-kinetic rigid syndrome in the elderly. PD is characterized by rest tremor, rigidity, bradykinesia and postural instability. PD should be differentiated from Steele Richardson-Oszwalski syndrome, drug induce parkinsonism, multiple system atrophy and parkinsonism due to repeated head injury. Apart from Parkinsonism other movement disorders in elderly are essential tremors and focal dystonias. Among focal dystonias, cranial dystonia (Meige's syndrome) is the commonest disorder.

Peripheral neuropathy is a disorder of peripheral nerves and is characterized by sensory impairment, weakness and wasting and loss of deep tendon jerks in the distal parts of the body. Rarely, it can affect a single nerve or several discrete nerves, in that case it is called mono-neuritis multiplex. It is caused by a large number of factors, some of which are also seen in younger people. Evaluation of an elderly patient with peripheral neuropathy requires confirmation of diagnosis and investigating for the extent of involvement and the cause of neuropathy especially metabolic causes and malignancy. Specific treatment is available for some causes of neuropathy.

Check Your Progress 6

1) Name the disorders of neuromuscular junction.

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2) What is the cause of Myasthemia gravis (MG)?

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3) What is the cause of Lambert-Eaton myasthenic syndrome (LEMS)?

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4) How to investigate a case of Myasthemia gravis (MG) in the elderly?

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4.6 LET US SUM UP

The disorders of muscles are collectively called myopathies. Generally, myopathies involve the proximal group of muscles. Though a large majority of myopathies occur in children and young adults, a small number have their onset in 4-5th decade. Due to the benign nature of these disorders they are slowly progressive and are compatible with longer life and therefore can be observed even in the elderly. Apart from a limited number of muscular dystrophies, muscle disorders commonly seen in elderly are polymyositis/dermatomyositis, metabolic/ endocirne myopathies and rarely toxic myopathies.

Disorders of neuromuscular junction can affect either at the pre-synaptic level as in LEMS or at the post synaptic level as in MG. Of the two disorders, MG is commoner. MG is characterized by fluctuating weakness with remissions and relapses. In both the disorders ocular, bulbar, neck, proximal limb muscles and respiratory muscles are affected in varied combination. LEMS is characterized by involvement of autonomic nervous system and therefore these patients may also complain of dryness of mouth and absent deep tendon jerks.

4.7 KEY WORDS

Acetylcholine : This is a substance liberated at the synapse to transmit impulse.

Neuromuscular junction : Area where peripheral nerve makes contact with the muscle at the synapse.

Polymyositis : Inflammation of muscle involve a specific group of muscle.

4.8 ANSWERS TO CHECK YOUR PROGRESS

Check Your Progress 1

1) Slowness of normal movements in the absence of paralysis or weakness is known as Hypokinesia and Prototype is Parkinson's disease.

2) The cardinal symptoms of Parkinson's disease are: rest tremor, rigidity, bradykinesia and postural instability

3) Drugs used in treatment of Parkinson's disease are levodopa, combination of levodopa and calidopa.

4) Anticholinegic drugs are used in controlling the tremors and sometimes cause confusion, hallucination, urinary retention and glaucoma.

5) Indications for surgery in parkinson's disease are:-

   a) Advanced Parkinson's disease.

   b) Severe dyskinesis as hallucination and Motor fluctuation.

   c) Absence of dementia, life threating concurrent illness and postural disturances.

Check Your Progress 2

1) Huntingtons disease belongs to hyperkinetic movement disorder group.

2) Chorea, rigidity, slowness of activity and dementia are the cardinal features of the disease.

3) Besides clinical history and physical examination, CT Scan head and Genetic test to show CAG expansion on chromosome 9, are the investigations required to confirm the diagnosis.

4) Drugs used to suppress chorea are haloperidol and phenothiazines.

Check Your Progress 3

1) Dystonias can be classified as:

   a) Generalised dystonia

   b) Focal dystonia

   — Cranial dystonia

   — Cervical dystonia (spasmodic torticollis)

   — Spasmodic dysphonia

   — Writer's cramp

2) The commonest cause of dystonia in the elderly is Meige's syndrome or cranial dystonia.

Check Your Progress 4

1) Cardinal features of peripheral neuropathy are:

   i) "Glove and stocking" type of sensory impairment

ii) Distal numbness and paraesthesiae

iii) Distal wasting and weakness with foot drop

iv) Diminished or absent deep tendon jerks

v) Trophic changes of skin (in chronic cases)

2) Common causes of peripheral neuropathy in elderly are:

i) Metabolic

ii) Toxic/drug induced

iii) Associated with cancers

iv) Associated with gammopathies

v) AIDP

vi) Leprosy

3) Investigations of a case of peripheral neuropathy in elderly are as given below:

i) Complete blood count, ESR

ii) Smear for RBC morphology

iii) Blood sugar

iv) X-ray chest

v) Serum protein electrophoresis

vi) Serum B12 level

vii) Examination of breast, prostate, pelvis

viii) Ultrasound abdomen, pelvis

ix) Stool for occult blood

x) Nerve conduction studies and EMG

Check Your Progress 5

1) The main features of myopathies are

i) Pure motor disorder

ii) Weakness and wasting of muscles

iii) Most often proximal group of muscles are affected. Specific groups of muscles are affected, some are spared.

iv) Presence of muscle hypertrophy in some disorders (eg. Duchenne muscular dystrophy, hypothyroid myopathy).

v) Presence of myotonia in myotonic dystrophies

vi) Deep tendon jerks are preserved

vii) Features of causative factors may be available on history or examination.

2) Common causes of myopathies in elderly are:

i) Muscular dystrophies

— Fascioscapulonumeral

— Myotonic Dystrophy

— Scapuloperoneal

— Oculopharyngeal

— Distal muscular dystrophy

ii) Metabolic myopathy

iii) Polymyositis/dermatomyositis

iv) Toxic myopathies

3) Investigation of a case of peripheral neuropathy in elderly involves the following:

   i) Pedigree chart and examination of family members if affected

   ii) Serum CK, aldolase

   iii) EMG

   iv) Muscle Biopsy

   v) Complete heamogram, ESR

   vi) Thyroid function tests

   vii) X ray chest

   viii) ECG

   ix) Examination of breast, pelvis, prostate examination especially in patients with dermatomyositis

   x) Ultrasound abdomen and pelvis in patients with DM

Check Your Progress 6

1) The disorders of NMJ are myasthenia gravis and Lambert Eaton myasthenic syndrome.

2) Myasthenia gravis is an autoimmune disorder in which antibodies are formed against the acetyl choline receptors on the post synaptic membrane resulting in destruction of the post synaptic membrane.

3) LEMS is caused by antibodies against calcium channels in the presynaptic membrane which help in release of acetyl choline. Due to this there is reduction in the release of acetylcholine at the nerve terminal when an impulse arises.

4) Following investigations should be done in a case of MG in the elderly

   i) Prostigmine/Edrophonium test to prove improvement in weakness with prostigmine/edrophonium injection.

   ii) Repetitive nerve stimulation test to prove presence of abnormal fatiguability.

   iii) X-ray chest or CT scan chest to look for thymic hyperplasia, thymoma, lung malignancy.

   Thyroid function tests, because of common association between both hypo-and hyper-thyroid state with MG and control of myasthenic symptoms with control of thyroid status.