PATHOLOGY OF THE NERVOUS SYSTEM

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I- Congenital anomalies

The earliest stage in brain development is the formation of the neural tube. Failure of a portion of the neural tube to close may lead to one of several malformations. Folate deficiency during the initial weeks of gestation is a risk factor.

1- Meningocele
- Sac-like meningeal out pouching through the vertebral arch and skull bone defect, it contains C.S.F.
- Common in the occipital region.

2- Encephalocele:
- Is similar condition, but the sac contains brain tissue.

3- Spina bifida:
- It is failure of closure of the caudal portion of the neural tube.
- There is bony defect in the neural arches of the vertebrae, commonly of lumbo-sacral region.
- It may be asymptomatic (spina bifida occulta) or associated with meningocele or meningomyelocele.

II- Vascular diseases

A- Inflamations:
- Syphilis, tuberculosis, PAN, S.L.E.

B- Degenerations:
- Particularly atheroma of extracerebral arteries at the base of brain and neck arteries.
- It manifests in elderly.

Complications:
1- Gradual ischaemia leads to senile cerebral atrophy.
2- Sudden ischaemia due to thrombosis on top leads to cerebral infarction.
3- Atherosclerotic aneurysm which may thrombose or rupture.
C- Cerebral aneurysms:

1- Congenital aneurysms (Berry aneurysms).
   - On the circle of Willis at both of the brain.
   - At points of bifurcation of the arteries.
   - Caused by congenital absence of the media.
   - It is sacular vary in size from 1/2 - 2cm.

2- Mycotic aneurysms:
   - Caused by main weakening of the wall of the artery by emboli of subacute bacterial endocarditis containing low virulent organisms.

3- Atherosclerotic aneurysm: In patient with atherosclerosis, - Fusiform aneurysms.

4- Traumatic arterial–venous aneurysms: penetrating injuries (bullet or stab wound) connect the carotid artery with the cavernous sinus, which become permanent with healing.

5- Intracerebral micro-aneurysms (Charcot- Buchard aneurysms)
   - Multiple, small, few mm. in size occur mostly in the basal ganglia inside the brain in essential hypertension

Effects of cerebral aneurysms:

1- Pressure on the surrounding nervous tissue when the aneurysm enlarges in size.

2- Rupture: Particularly with congenital and Mycotic types leading to fatal subarachnoid hemorrhage.

3- Thrombosis and calcifications: Causing ischaemic brain changes related to the affected vessels. (Infarction or brain atrophy)
**D) Intracranial hemorrhage:**

It may be meningeal or cerebral.

**I- Meningeal hemorrhage:**

*a- Extrudal hemorrhage*: (Epidural haematoma).

- It is due to rupture of the middle meningeal artery due to direct trauma with fracture of the parietal or temporal bone. Arterial blood accumulate between the dura and the skull bone. It leads to rapid progressive rise of ICP Pressing the brain.

*b- Subdural haemorrhage (haematoma).*

- It is due to trauma causing rupture of cerebral veins crossing the subdural space.
- Venous blood accumulate in the subdural pace, leading rise of I.C.P pressing the brain.

*c- Subaracraduroid hemorrhage:*

Is due to:

- Trauma or brain lacerations.
- Rupture of congenital or athrosclerotic aneurysms.
- Bleeding from angiomatous malformations as haemangioma.
- It cause increased I.C.P. and block the flow of C.S.F causing hydrocephalus.

**II- Cerebral haemorrhage:**

*a- Peticheal haemorrhage:*

Caused by:

- Repeated trauma as in boxers.
- Infections as encephalitis, meningitis and septicaema.
- Haemorrhagic blood diseases.

*b- Massive Intracerebral haemorrhage:*

It may be:

*a- Traumatic*: due to severe trauma with laceration of the brain and usually occurs on the opposite side of injury (contre -coup haemorrhage).
**b- Spontaneous:** Common and usually fatal, 50% related to hypertension.

Morphologically, haematoma expands the affected hemisphere and bulges its surface externally and shift the brain to the opposite side. Haemorrhage may dissect its way to the ventricular system or subarachnoid space.

Healing occur within months if patient survive. Macrophages remove the clot then fibrillary gliosis forms containing haemosiderin laden macrophages.

**Prognosis**
- 40% die related to increased ICP, in survivors, relative good function retained.

**E- Cerebral infarction:**
Causes: complete sudden local arterial occlusion from.
- (1) Thrombosis on top of atheromatous arteries or aneurysm.
- (2) Embolism come from detached thrombus from left side of the heart in patient with mitral stenosis or mural thrombus on myocardial infarction.

**N.E:**
1- The common site is the middle cerebral artery branches supplying basal ganglia and internal capsule.
2- It is pale infarction
   - After 6 hours: pale, opaque and dry.
   - After 12 hours: Slight soft, swollen homogenous with loss of differentiation between grey and white matter.
   - After 48 hours: Liquefactive necrosis occur with cyst containing creamy yellow fluid.
   - After months, healing by gliosis, small infarcts are replaced by gliosis while large infarcts are surrounded by gliosis.

**M/E:**
- Softening of brain tissue with phagocytosis of fragmented tissue by microglia
- Astrocytic proliferation replace the area of small infarction or form cyst wall around big infarcts.

**Prognosis:**
Massive infarction may by fatal due to increased I.C.P.
III- Hydrocephalus

Def:- accumulation of excessive CSF within the ventricular system with pressure atrophy of the brain tissue.

Causes:

1- Increased C.S.F secretion: from choroid due to chorioiditis or choroid plexus papilloma.

2- Obstruction of C.S.F flow:
   a- Congenital causes: Narrowing of the foran of ventricles or aqueduct of Sylvius.
   Arnold- chiary malformation: This is downward displacement (herniation) of the cerebellum or into the foramen magnum with block of forami
   b- Acquired causes:
      I- Post- meningitis adhesions, or haemorrhage, block Foramina of 4th ventricle.
      II- Subarachnoid hemorrhage in brain stem.
      III- Space occupying lesion as brain tumour or abscess.

3- Defective C.S.F absorption: Through arachnoid villi, and may be due to:
   a- Congenital Causes: Agenesis, aplasia or hypoplasia of the arachnoid villi
   b- Acquired Causes:
      I- Obliteration of vault subarachnoid space by an expanded space occupying lesion forcing the brain up against the skull.
      1I- Fibrosis of arachnoid villi after meningitis or subarachnoid hemorrhage
      1II- Thrombosis of superior sagittal sinus.

Types of hydrocephalus:
1- Communicating hydrocephalus: The ventricles communicate with the subarachnoid space
2- Non- communicating hydrocephalus: The obstruction is intraventricular in the 4th ventricle.
Pathological features:

1- Permanent dilation of the ventricular systems proximal to the site of obstruction. The dilatation is generalized in cases of increased production and decreased absorption of C.S.F.

2- Raised ventricular C.S.F pressure increases fluid accumulation in periventricular white matter (interstitial oedema).

3- Pressure atrophy of brain tissue.

4- Skull changes.
   a- In children: It yield under increasing cranial I.C.P
      - Bones are thinned
      - Sutures are separated

   b- In adults:
      - Head does not enlarges (sutures and fontanels are closed)
      - Skull bone show varying degrees of convolutional markings.

   In cases of brain substance atrophy in old or infarcts or due to removal of part of the brain there is compensatory increase in volume but not pressure of C.S.F. and compensatory dilation of the ventricles or subarachnoid space.
IV- Infections

A- Bacterial infections

1- Acute pyogenic meningitis:

Definition: Acute suppurative inflammation of the meninges

Organisms:
In neonates, the causative organisms are Escherichia coli and the group B streptococci
In children and old ages, the causative organisms are Hemophilus influenza, Streptococcus pneumoniae
In adolescent and adult, the causative organisms are Neisseria meningitides.

N/E:

1- The leptomeninges:
Are hyperaemic, thick opaque, tense
The subarachnoid space is filled with yellow pus more apparent at the base of the brain and on frontal and parietal regions. The spinal leptomeninges are involved.

2- The brain is swollen, oedematous and meningeal vessels are dilated and congested.

3- The ventricles are moderately dilated, contain turbid C.S.F. As ependymal lining is rough (choroiditis and ependymitis).

Microscopically:
- The subarachnoid space contains excess neutrophils and pus cells, with some histiocytes within variable amounts of fibrin network.
- Meningeal vessels are dilated and congested.
- Brain underneath show oedema and cellular degeneration.

C.S.F. Changes:
Taken by lumbar puncture show increased pressure, abundant neurophils, elevated protein, and reduced glucose.
Complication of pyogenic meningitis:

increased intracranial pressure.
a- Pressure of the exudates on the cranial nerves cause nerve paresis especially 3,4,6.
b- Extension of infection to the under lying brain tissue causing meningo- encephalitis and small brain infarcts.
c- Peripheral spread of infection produce subdural abscess and sinus thrombophlebitis.
d- Meningococcol speticaemia may occur when big number of meningocci reach the blood. This can cause bilateral suprarenal hemorrhage and acute suprrenal failure (water- house Friedricksen syndrome).
e- Fibrous adhesions between meningeal layers and between these and the brain compress the cranial nerves , (nerve paresis) and block the c.s.f circulation causing Hydrocephalus.

Prognosis: Untreated cases are usually fatal.

2- Brain abscess

Causative organism: Pyogenic bacteria, (strept. and staph.)

Methods of infection:
a- Direct implantation: Opened (compound) skull fracture.
b- Local extension:
  - Mastoiditis or otitis media lead to cerebellar or temporal lobe cerebral abscess.
  - Frontal' sinusitis produces frontal lobe abscess. Small veins are suggested to transmit infection.
c- Hematogenous spread:
  - Emboli from cardiac vegetations of acute bacterial endocarditis.
  - Intrathoracic suppuration by vertebral system of veins producing frontal lobe abscess.

Pathological features:
a- **Acute abscess:**
- Brain tissue is softened, with cavity filled with pus, surrounded by area of congestion and has irregular shreedy lining. It changes to chronic.

b- **Chronic abscess:**
- Develops after 3-6 weeks
- Has fibrous wall of fibrogliosis and the lining is smooth.

**Microscopically:** There is central necrosis surrounded by neovascularization, oedema fibrous tissue capsule and gliosis.

**Complications:**

a- Direct spread produces suppurative encephalitis, subdural abscess, sinus thrombophlebitis and extradural abscess.

b- Rupture into ventricular system (ventriculitis) or subarachnoid space producing meningitis.

**Chronic Specific infections:**
1- Tuberculosis.
2- Syphilis.

**B- Viral infections**

C.N.S can be attacked by many different viruses which have some common features,

1 - There is generalized viraemia which in a proportion of cases is followed by localization in the C.N.S

2- The virus multiply within the nerve cells causing either Nissel degeneration and many inclusion bodies (virus particles)

3- There is hyperemia and mononuclear cell inflammatory response inform of lymphocytes plasma cells and microglia. Nerve cell necrosis, which are removed by microglia (neuronophagia)

4- Healing occur by glial scar (gliosis).

**Type of viral infection:**

I/-Acute viral leptomeningitis (lymphocytic):

Mild meningitis with C.S.F containing excess mature lymphocytes. Occur in association with encephalitis or as a complication of other viral infections as mumps. It produce no complications
2- Viral encephalitis

*a- Herpes simplex type 1:*

Causes:

- Encephalitis affecting children and young adults. The infection is necrotizing and often hemorrhagic encephalitis in the severely affected regions.

- Acute viral infection of sensory nerve ganglia, its nerve and its area of supply (skin or mucous membrane) - It produce redness and vesicles which ulcerate without scar. Primary infection may be followed by secondary attacks on lowering of resistance.

*b- Herpes Simplex Virus Type 2:*

HSV-2 also affects the nervous system and usually manifests in adults as a meningitis. Disseminated severe encephalitis occurs in many neonates born by vaginal delivery to women with active primary HSV genital infections.

*c- Herpes Zoster:*

Varicella-zoster virus (VZV) causes chickenpox during its primary infection, latent infection occur in neurons of dorsal root ganglia of lower cervical and upper thoracic and Gasserian ganglia (Fifth nerve).

Reactivation in adults causes the virus to traverse along the sensory nerves to skin and manifests as a painful, vesicular skin eruption in the distribution of one or a few dermatomes (shingles). This is usually a self-limited process, but there may be a persistent pain syndrome in the affected region (post-herpetic neuralgia).

In immunosuppressed patients, acute herpes zoster encephalitis can occur.

*d- Acute anterior poliomyelitis*

Acute viral infection usually of the anterior horn cells caused by Poliovirus which is an enterovirus transmitted by ingestion of contaminated foods and drinks, Incubation periods 1-3 weeks

*Stage of diseases:*

- Intestinal stage 5 days
- Viraemia stage 5 days
- Neural stage at which the virus attaches the anterior horn cells of the spinal cord (rarely brain stem)

*Pathological features:*

*N/E:*

Affect the cervical and lumbar enlargements of the cord, which become swollen with hyperaemia of leptomeninges. Cut section show swollen gray matter of anterior horn.
**M/E:**
Degeneration and necrosis of anterior horn cells (groups or separate cells). Perivascular cellular infiltrate of lymphocytes, plasma cells and polymorphs and microglia cells that engulf dead nerve cells at late stage

**Fate:**
- Healing by gliosis is followed by
  I- Degeneration and thinning of the related peripheral nerves
  II- Neuropathic muscular atrophy and replacement by fibrofatty tissue of the related muscles.

- Sever forms of poliomyelitis, associated with ascending infection to involve the brain stem with paralysis of respiratory center which may end fatal, (polioencephalitis or bulbar poliomyelitis)

**e- Rabies**
Rabies is a severe encephalitis caused by Rabies virus transmitted to human through bites of rabid animals, then spread along the peripheral nerves to the C.N.S. the incubation period depends on the distance between the wound and the brain.

**Site of affection:**
- Posterior root ganglia, posterior horn of spinal cord, medulla, hypothalamus, hippocampus and cerebellum

**N/E:** - Swelling and hyperemia of the affected tissue

**M/E:**
- Diffuse encephalomyelitis, Swelling and necrosis, vascular dilation, perivascular infiltration by plasma cells and lymphocytes
- Infected cells contain intracytoplasmic acidophilic bodies called Negri bodies more in hippocampus and cerebellum

**Clinically:**
- Hydrophobia and aerophobia caused by spasm of larynx and Pharynx. --- usually fatal.

**f- AIDS:**
- C.N.S. is commonly affected in HIV infected patients. It can cause:
  1- Aseptic meningitis.
  2- Subacute encephalitis of cerebral and cerebellar hemispheres and in severe cases the brain stem and spinal cord causing AIDS-dementia complex.
  3- Help opportunistic infections as fungal and toxoplasma.
  4- Complicated by tumours as cereberal lymphoma.
V- INTRACRANIAL TUMOURS

A- Tumors of neuroepithelial tissues:

1- Gliomas

Are the commonest primary C.N.S tumors, they are:

a) Astrocytoma:
- Tumors of astrocytes are the commonest glioma.

Site:
- Cerebellum of children.
- Cerebrum of adults.

N/E:
- Soft grey mass with ill-defined outline. The cut surface shows areas of cystic degeneration.
- In high grade forms it shows necrosis and haemorrhages.

M/E:
- Neoplastic Astrocytes, branched cells with fibrillary background it may be of variable grades of differentiation.

a) Pilocytic astrocytoma --- grade I
- Mildly cellular, formed of mature astrocytes within excess fibrillary back ground, cells are bipalor with stroma of eosinophilic elongated and coma shaped fibers (Rosenthal fibers).

b) Gemistocytic astrocytoma --- grade (II)
Large astrocytes with excess cytoplasm and eccentric nuclei

c) Anaplastic astrocytoma---- grade (III):
Formed of pleomorphic less mature astrocytes with excess mitosis. Without necrosis

d) Glioblastoma Multiforme ----- grade IV
Formed of primitive astrocytes with marked Pleomorphism, Giant cells, mitosis, nerosis, vascular endothelial proliferation in glomeruloid manner.

b- Oligodendrogioma:
- From oligodendroglia cells of cerebrum.
- Middle age.
N/E: Localized, pink, Firm with cyst formations and calcification.

M/E: Rounded cells, with uniform swollen nuclei and clear cytoplasm with focal of calcification.

c- **Ependymoma:**
- Children and young adults
- From ependymal cells lining the ventricles, commonly the 4th ventricle and Lower part of the spinal cord

N/E: Fleshy vascular mass.

M/E: (a) Elongated cells arranged perivascular in pseudorosettes, commonest
(b) Papillary type.

2- **Embryonal tumors (Medulloblastoma)**
- Common childhood brain tumor
- At the roof of 4th ventricle 19

N/E:
Fleshy soft grey mass projections in the 4th ventricle may penetrate the brain to reach the subarachnoid space (trans-coelomic spread)

M/E:
Small dark stained cells arranged in rosettes.

N.B:
Similar nerve cell tumors are:
- Retinoblastoma from retina
- Neuroblastoma of from sympathetic nervous system

3- **Tumors of Meninges:**

a- **Meningothelial tumors (Meningioma)**
- In adults.
- Originates from the endothelial cells of the arachnoid villi commonly in relation to superior sagittal sinus.

N/E:
Rounded firm capsulated tumor attached externally to the dura and imbedded in the brain tissue internally.
- Cut surface: greyish white and often show whorly appearance.
- Older tumors slow secondary changes as bone, cartilage and fat (metaplastic changes)

**M/E:**

Formed of spindle shaped cells arranged in concentric layers with calcifications in the center (Psammoma bodies).

**N.B:** It is more common female and some tumours have estrogen receptors so it grows rapidly during pregnancy.

- It may turn malignant.

b- Mesenchynal (non meningotheial tumors):
  - Lipoma.
  - Angiolipoma
  - Vascular tumors
  - Haemangioblastoma: Benign tumor arises in cerebellum.
  - Cavernous haemangioma

4- Tumours of peripheral nerves

1- Neurilemmoma or schwannoma:
  - A benign tumour originating from schwann cells.

**N/E:**

- The commonest is acoustic neuroma of 8th cranial nerve at the base of the brain (cerebello- pontine angle)
- Solitary mass, capsulated, firm round or fusiform with the related nerve at one side
- Cut surface is grey white and may show cysts

**M/E:**
Spindles shaped cells arranged in bundles, with rod-shaped nuclei side by side in palisade manner with reticular and collagen fibers in between.

### 2- Neurofibroma:

**N/E:**
Fusiform mass through which the nerve pass Firm grey uncapsulated

**M/E:**
Spindle shaped cells in bundles with fibrous stroma and neurofibres.

### 3- Multiple neurofibromatosis.
(Von-Reckling-Hausen disease of nerves).

Hereditary autosomal dominant hamartoma consists of:
- Multiple neurofibromas of cutaneous nerves.
- Cafe au lait skin patches of skin hyperpigmentation.
- Localized or diffuse overgrowth from of fibrous tissue of overlying skin (Elephantiasis neuromatosa).

**Prognosis:**
Malignant transformation is common than in schwannoma. (10%).

### 3- Neurofibrosarcoma:
Most cases complicate multiple neurofibromatasis, than solitary neurofibroma or schwannoma.
- Microscopically as fibrosarcoma

**Other tumors:**

### 1- Choroid plexus tumors:
- Choroid plexus papilloma.
- Choroid plexus carcinoma.
2- Pineal body tumors
   a- Pinealoma
   b- Pineoblastoma
3- Hemopoietic tumors:
4- Germ cell tumors: as germinoma
5- Tumors of seller region: Craniopharyngioma.
6- Metastatic tumors:
   - They represent 30% of brain tumors
   - Majority are carcinomas.
   - Occur mostly in older people.
   - They reach the C.N.S. through arteries or vertebral system of veins.
   - Common sources: carcinomas of lungs breast, kidney and leukaemias

N/E:
- Multiple nodules of variable size in the cerebrum at junction of grey and white matter with oedema around
- The nodules show haemorrhage, necrosis and cyst formation

M/E:
As primary tumor and in relation to blood vessels.

Effect of intracranial tumors:

1- Local effects:
   - Manifestation of compression of the affected site followed by others due to destruction and loss of function such as hemiplegia
1- Hydrocephalous.
2- Increased intracranial tension composed by increased intracranial contents by:
   - Tumor mass
   - Cerebral oedema due to compression of the veins by tumour obstruction of C.S.F. pathway.

Manifestations:
   - Headache
   - Papilloedma (blurring of vision) oedema of optic disc due to compression of retinal veins.
   - Brain herniation.