Brain tumors

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Chair of Neurosurgery

Epidemilogy

- There are approximately 385,000 deaths from cancer each year in the United States, of which 13 %, or 50.000, involve the central nervous system (CNS).

- Of these, 17 %, or 8500, are caused by primary brain tumors, 5000 of which are malignant gliomas.

Epidemilogy

- The results of an autopsy survey by Russell and Rubinstein suggest that 9.2 % of all tumors are in the brain and that 49 % of all primary brain tumors are gliomas.

- About 300 operations per year in Moldova.

Age

The average age of diagnosis for brain tumors is 57, and about 90% of primary brain tumors occur in adults, they can develop at all ages, usually peaking in two age groups:

- In adults between the ages of 55 and 65.
- In children between the ages of 3 and 12.

Classification

Neoplasms that affect brain tissue may be classified into three categories:

1. **Primary intraaxial tumors** (arise primarily from parenchymatous elements of the central nervous system (CNS) and account for approximately 50 percent of all intracranial tumors)
2. **Extraaxial nonparenchymatous tumors**, such as meningiomas
3. **Metastatic tumors**

Classification

Tumor locations are categorized in several ways:

- hemispheric
- specific lobes
- sites within specific lobes
- multiple lobes

- lobar versus nonlobar
- brainstem or thalamus or basal ganglia versus hemisphere
- deep versus superficial
- supratentorial versus infratentorial

WHO Histological Classification

- **I. Tumors of Neuroepithelial Tissue**
  - A. Astrocytic tumors
  - B. Oligodendroglial tumors
  - C. Ependymal tumors
  - D. Mixed gliomas
  - E. Choroid plexus tumors
  - F, Neuroepithelial tumors of uncertain origin
  - G. Neuronal and mixed neuronal-glial tumors
  - H. Pineal parenchymal tumors
  - I. Embryonal tumors

WHO Histological Classification

- **II. Tumors of Cranial and Spinal Nerves**
  - A. Schwannoma (Neurilemoma, Neurinoma)
  - B. Neuroflbroma
  - C. Malignant peripheral nerve sheath tumor (MPNST) (Neurogenic sarcoma, Anaplastic neurofibroma, "Malignant schwannoma")
- **III. Tumors of the Meninges**
  - A. Tumors of meningothelial cells
  - B. Mesenchymal, nonmeningothelial tumors
  - C. Primary melanocytic lesions
  - D. Tumors of uncertain histogenesis

WHO Histological Classification

- **IV. Lymphomas and Hemopoietic Neoplasms**
- **V. Germ Cell Tumors**
- **VI. Cysts and Tumor-like Lesions**
- **VII. Tumors of the Sellar Region**
- **VIII. Local Extensions from Regional Tumors**
- **IX. Metastatic Tumors**
- **X. Unclassified Tumors**

WHO malignancy classification

Four-category tumor grading system

- Grade I
  - Slow growing
  - Nonmalignant tumors
  - Patients have long-term survival
- Grade II
  - Relatively slow growing
  - Sometimes recur as higher grade tumors
  - May be nonmalignant or malignant
- Grade III
  - Malignant tumors
  - Often recur as higher grade tumors
- Grade IV
  - Highly malignant and aggressive

Etiology

Unknown as well as tumors of other localization

- Genetic factors
- Radiation
- Trauma
- Viral
- Ecology
- Hereditary
- Systemic diseases

Genetic Syndromes

Genetic syndromes associated with multiple CNS tumors are:

- Neurofibromatosis I (von Recklinghausen's Disease)
- Neurofibromatosis II (bilateral acoustic neurofibromatosis)
- Von Hippel-Lindau Disease
- Familial retinoblastoma

Symptoms

- General symptoms
  - The general symptoms of brain tumors are due to **increased intracranial pressure** (ICP), traction of the tumor, or brain herniations affecting pain-sensitive intracranial structures—the blood vessels, dura mater, and cranial nerves.
- Local symptoms
  - Depending on **localization** of the tumor
- Specific symptoms
  - Depending on **type and localization** of the tumor (ex. optic nerve gliomas, olfactive groove meningioma, pituitary adenoma etc.)

Increased intracranial pressure

ICP may be caused by:

- the tumor mass,
- associated cerebral edema,
- obstruction of cerebrospinal fluid (CSF) pathways,
- obstruction of the venous system draining the brain,
- obstruction of the cerebrospinal fluid-absorbing mechanisms.

General symptoms

Headache

- Headache may be a generalized sign of increased intracranial pressure, or it may localize to the site of the tumor.
- It is usually described as a chronic deep pain rather than the superficial or bandlike sensation of a tension headache.
- The headache caused by generalized increase in intracranial pressure usually occurs on a daily basis and **is especially prominent in the morning upon awaking from sleep.**
- The headache secondary to increased ICP is usually **associated with papilledema**. In children, the headache **is frequently associated with morning vomiting without nausea**.
- At times, the headache localizes to the side or the area of the tumor. This most often occurs when there is local invasion of dura or bone by the tumor. Gentle tapping of the scalp may aggravate the headache or identify a sensitive area.

General symptoms

Vomiting

- Vomiting is frequently seen in patients with increased ICP from a brain tumor.
- It **often occurs with headache**, and a vomiting episode may actually relieve the headache.
- Vomiting is a particularly common symptom in children with posterior fossa brain tumors and is usually described as projectile vomiting.
- It usually **occurs in the morning upon** arising and is not associated with nausea.

General symptoms

Behavior

- Subtle, gradual change in personality and behavior, irritability, somnolence, or lethargy.
- These symptoms are seen very early in frontal lobe tumors or as a sign of increased intracranial pressure from a posterior fossa tumor causing hydrocephalus.
- In children, there may be deterioration in school performance.
- These symptoms often go unrecognized for weeks or months and are usually more apparent retrospectively upon development of other neurological symptoms.

General symptoms

Double vision

- Diplopia is frequently a symptom of **bilateral sixth nerve palsies**.
- If the palsies are indeed bilateral, there is no localizing value to the diplopia as it is a sign of generalized increased ICP.

General symptoms

Seizures

- Generalized seizures comprise the **initial symptom in about 15 percent of patients** with brain tumors, and occur sometime during the illness in about 30 percent of patients with brain tumors.
- Whether a tumor will produce seizures depends largely on its location and growth characteristics.
- The patients with a tumor **in or near the sensorimotor cortex** are more likely to have a seizure than patients with a tumor in a frontal or temporal pole.
- **Focal and/or Jacksonian seizures** are often associated with a cerebral tumor.
- A brain tumor should be strongly suspected in any new seizure disorder occurring in an adult.

Local symptoms
Frontal lobe

- **The symptoms of frontal lobe dysfunction include**
  - personality change,
  - new-onset focal and major-motor seizures,
  - motor deficits, and loss of micturition control.
- **The signs of frontal lobe dysfunction include**
  - decline in intellect and memory,
  - aberrant behavior,
  - paraparesis or hemiparesis,
  - grasp reflexes (e.g., palmomental),
  - Broca's or motor aphasia if the dominant frontal lobe is involved (left hemisphere in right-handed patients).

    Motor aphasia implies an inability to speak but with understanding of instructions.

Local symptoms
Parietal lobe

- **Symptoms of parietal lobe dysfunction are:**
  - sensory loss, sensory inattention or even focal sensory seizures
  - aphasia or apraxia depending upon the dominant or nondominant hemispheres affected,
  - visual field defects,
  - attention hemianopsias,
  - and visual agnosia.
- **Other classical signs are:**
  - agraphesthesia, or inability to appreciate numbers written on the skin;
  - astereognisis, or underestimating the size of objects;
  - abarosthesia, or a disturbance in perception of difference in weight.

Local symptoms
Temporal lobe

- **Symptoms of temporal lobe disease include**
  - temporal lobe epilepsy or complex-partial seizures, with an aura of auditory, visual, smell, taste, and visceral sensations,
  - unilateral temporal lobe lesions, specifically involving the hippocampal gyrus, rarely cause significant memory impairment,
  - bilateral lesions cause the syndrome of Korsakoff's psychosis - inability to learn or establish new memories, together with confabulation and psychotic behavior.
  - bilateral lesions can also produce the classic Kluver-Bucy syndrome, an amnestic syndrome with apathy, placidity, hypersexuality, and psychic blindness or visual agnosia.
  - the patient with uncal herniation may present with acute third nerve dysfunction and hemiparesis due to compression of the nerve and cerebral peduncle.

Local symptoms
Occipital lobe

- **The symptoms of occipital lobe dysfunction include**
  - seizures preceded by visual hallucinations (e.g., flashing lights and colors, visual field deficits, and visual agnosia), especially if the dominant hemisphere is involved.
- **The signs of occipital lobe dysfunction are**
  - a classical contralateral, congruous homonymous hemianopsia, with macular sparing,
  - alexia, or inability to read,
  - visual agnosia, or inability to recognize objects.

Local symptoms
Cerebellum

- **The classical signs and symptoms of cerebellar lesions**
  - Lesions affecting the midline structures, particularly the vermis often cause severe gait and truncal ataxia, making it impossible for the patient to stand or sit unsupported.
  - Lesions in the lingula may cause trochlear nerve (IV) dysfunction, or they may extend into the superior cerebellar peduncle ipsilaterally and cause tremor of the ipsilateral arm.
  - Vertigo and vomiting in addition to the ataxia.
  - It should also obstruct the aqueduct, fourth ventricle, or the CSF pathways causing headache, papilledema, and vomiting from increased intracranial pressure secondary to obstructive hydrocephalus.
  - Nystagmus is usually found with involvement of the flocculonodular lobe and the fastigial nucleus (vestibular connections).
  - Lastly, cerebellar speech, or scanning dysmetric speech is a thick, slow, plodding, slurred speech, "marble-mouth," a uniquely cerebellar disorder.

Optic Nerve Gliomas

Symptoms and Signs

The clinical presentation depends on whether the tumor is in the orbit or is located intracranially.

Intraorbital gliomas present with painless proptosis, which may be the only sign, especially in infants. The most common initial symptom is loss of vision.

The visual field: the defects may be dense or mild, quadrantic, hemianoptic, or irregular.

Medulloblastomas

Symptoms and Signs

Patients with a medulloblastoma usually present with some variation of the clinical triad of headache, vomiting, and ataxia.

The patient usually presents with midline cerebellar signs.

Children frequently have morning projectile vomiting without nausea, secondary to obstructive hydrocephalus.

The child will gradually become ataxic.

As the tumor invades the cerebellum, localizing symptoms such as loss of coordination will develop.

As the brainstem is involved by direct or indirect pressure or invasion, there will be long-tract signs and cranial nerve deficits.

Papillomas of the Choroid Plexus

Symptoms and Signs

Generally, the tumor produces symptoms and signs of increased ICP. In infants and young children, choroid plexus papillomas present with a clinical picture of hydrocephalus, vomiting, irritability, squint, and enlarging head.

The rapid and sudden onset of hydrocephalus and the presence of papilledema are two features that distinguish hydrocephalus due to a choroid plexus papilloma from nontumor hydrocephalus.

Pineal Tumors

Symptoms and Signs

Three phases in the clinical progression of these tumors.

- Headaches, with or without vomiting, characterized the first phase.
- The second phase was characterized by blurred vision, diplopia, change in mental outlook, ataxia. dizziness, drowsiness, and the development of the Parinaud syndrome.
- In the third phase, papilledema. marked weakness, and varying degrees of spasticity appeared.

Parinaud's syndrome is considered to be a pathognomonic sign of tumors in this area of the brain. In this syndrome, the pupils usually are largely dilated and react poorly to light, and there is paralysis of upward gaze.

MENINGIOMAS

- Sagittal Sinus and Falx Meningiomas
- Convexity Meningiomas
- Sphenoid Ridge Meningiomas
- Olfactory Groove Meningiomas
- Suprasellar Meningiomas
- Optic Nerve Meningiomas
- Posterior Fossa Meningiomas
- Lateral and Third Ventricle Meningiomas

ACOUSTIC NEUROMAS

Symptoms and Signs

Auditory symptoms are the earliest and most striking symptoms and appear in the form of tinnitus and progressive loss of hearing. **Tinnitus** usually precedes **dizziness**. Vestibular symptoms are less pronounced and consist of mild persistent episodes of objective or subjective vertigo.

The tumor may become extremely large before **seventh cranial nerve symptoms** appear.

As the tumor grows out of the porus acousticus and into the cerebellopontine angle, the **fifth cranial nerve** or the descending tract of the fifth nerve in the brainstem becomes compressed by direct pressure on the brainstem, producing numbness of the ipsilateral face.

As the tumor enlarges, compression of the adjacent cerebellar hemisphere or the cerebellar peduncle produces **ataxia, vertigo, and dysmetria** of the ipsilateral extremities. Initial gait ataxia may progress to a tendency to fall to the side of the tumor. **Nystagmus** toward the side of the lesion develops.

Further increase in size displaces the **brainstem**, as well as **cranial nerves IX, X, and XI**. There may be difficulty in swallowing and talking, with slurred or nasal speech.

The dislocation of the pons may cause **obstruction of the fourth ventricle**, or the tumor may grow upward through the incisura of the tentorium, obstructing the flow of spinal fluid and leading to increased pressure secondary to **hydrocephalus**. This will cause headaches and vomiting.

As the tumor becomes larger, a **sensorineural hearing loss** can be documented by audiometry and absent caloric responses on the affected side.

CRANIOPHARYNGIOMAS

Symptoms and Signs

Children with a craniopharyngioma usually present with headaches, vomiting, or visual loss, and psychological changes. Diabetes insipidus is rare.

Adults usually present with endocrinological disturbances and visual field defects. Examination may reveal visual field defects and often bitemporal hemianopsia.

About 30 percent of children are found to have papilledema. Small stature is noted in children.

Adults will have endocrine disturbances such as amenorrhea or loss of libido.

Pituitary tumors

Functional pituitary tumors

- adrenocorticotropic hormone – Cushing's disease (hypertension, purple striae on flanks, amenorrhea, hyperpigmentation, weight gain, osteoporosis)
- prolactine – amenorrhea-galactorrhea syndrome
- growth hormone – acromegaly in adults, gigantism in children

Mass effect of pituitary tumors

- optic chiasm – bitemporal hemianopsia
- pituitary gland – hypothyroidism, hypoadrenalism, hypogonadism, diabetes insipidus
- cavernous sinus – cranial neuropathies (III, IV, V, VI), occlusion of the sinus

Life−Threatening Syndromes

Symptoms of brain tumors that indicate an emergency condition requiring prompt intervention include the following:

- Pupil dilation.
- A fixed gaze.
- Paralysis on one or both sides of the body.
- Blindness or defective vision in one eye.

The *Karnofsky scale* is an objective measurement of functional ability in patients with CNS neoplasm.

THE KARNOFSKY SCALE

100 Normal - no evidence of disease
90 Minor symptoms - able to carry on normal activity
80 Some symptoms - normal activity with effort
70 Unable to carry on normal activity - cares for self
60 Cares for most needs - requires occasional assistance
50 Requires considerable assistance
40 Disabled
30 Severely disabled
20 Active supportive treatment needed - very sick
10 Moribund

Diagnostic Tools – Physical Exam

Neurological examination

- eye movements
- vision
- hearing
- reflexes
- balance and coordination
- sense of smell and touch
- abstract thinking
- memory

Diagnostic Tools

- Computerized tomography (CT) scan
- Magnetic resonance imaging (MRI)
- Positron emission tomography (PET)
- Single photon emission computed tomography (SPECT)
- Angiography

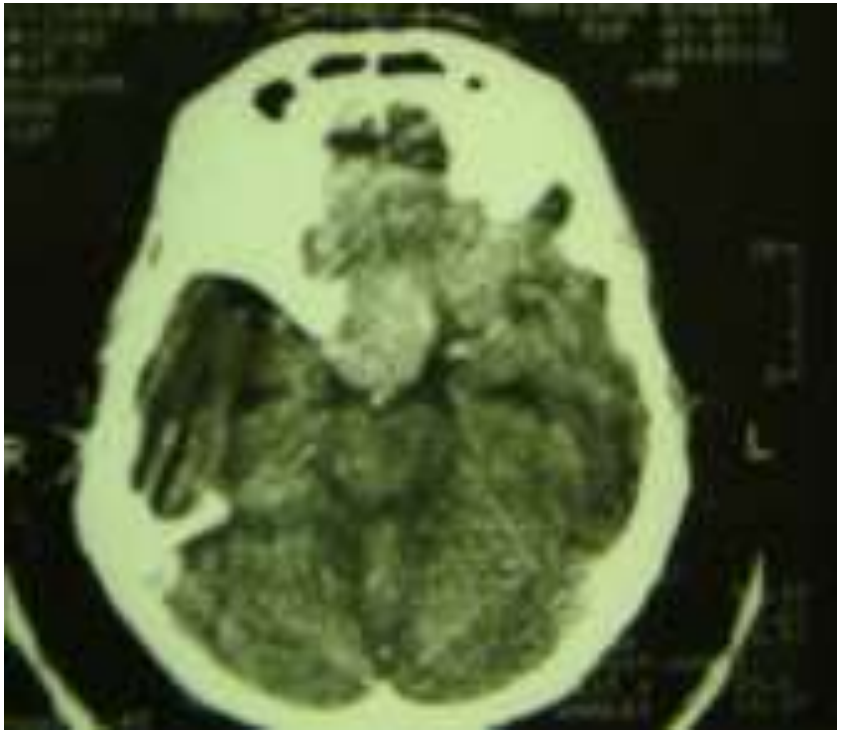
Diagnostic Tools

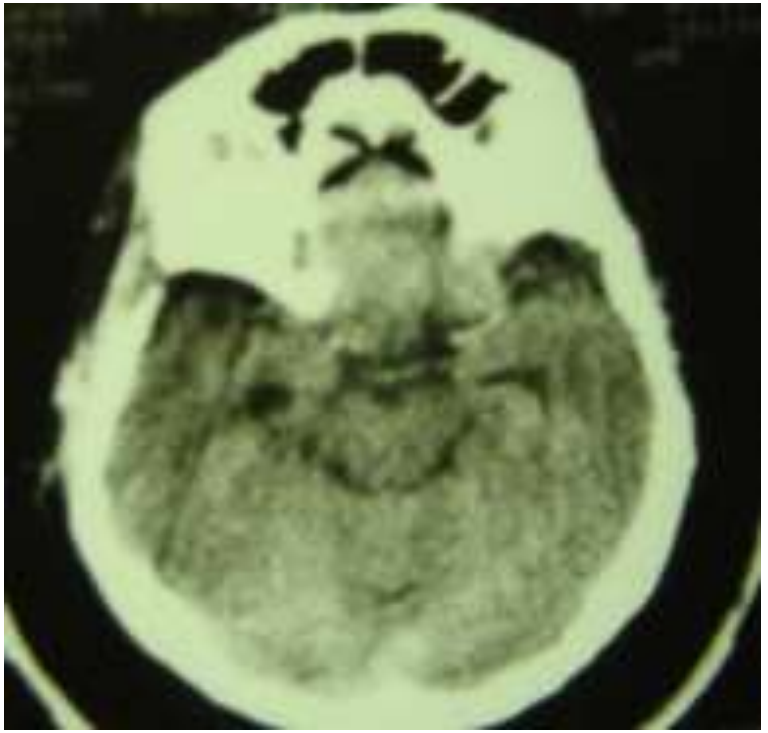
- Laboratory tests
  - Audiometry
  - Electroencephalogram (EEG)
  - Endocrine evaluation
  - Evoked potentials
  - Lumbar puncture
  - Myelogram
  - Perimetry

Diagnostic Tools

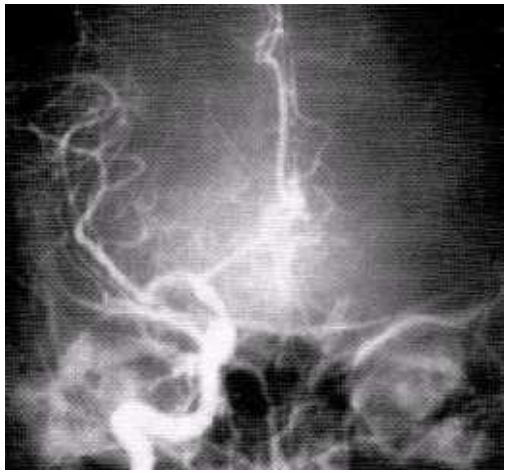
- Needle biopsy
  - Needle inserted through a burr hole and tissue extracted for tissue diagnosis
- Stereotactic biopsy
  - Computer used to guided needle biopsy to extract tissue

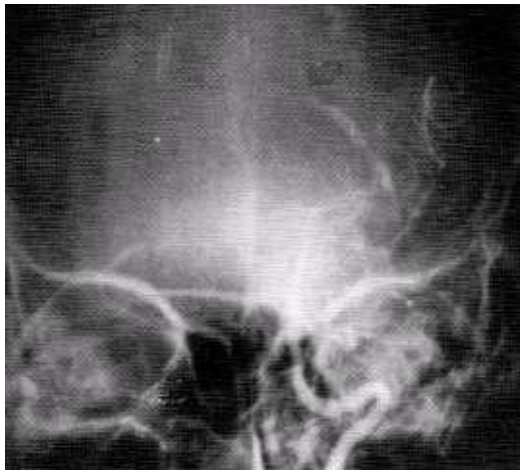
CT-scan

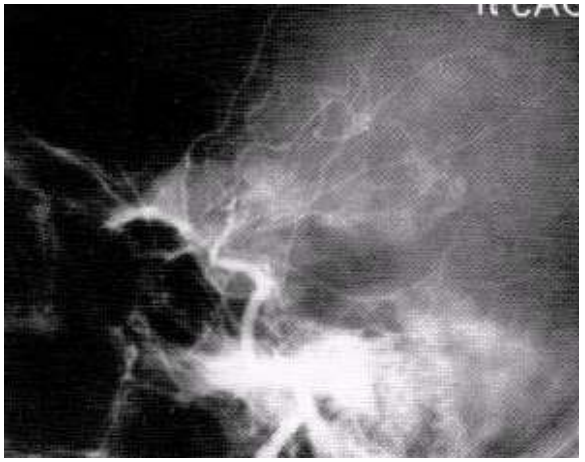


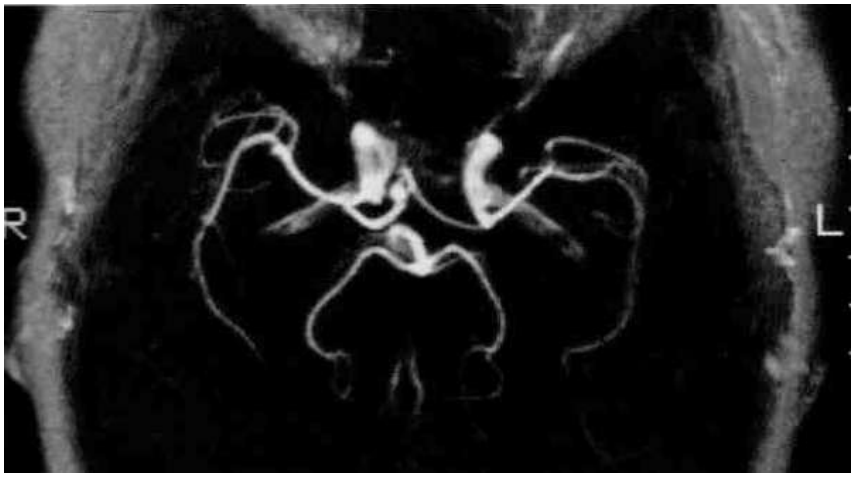


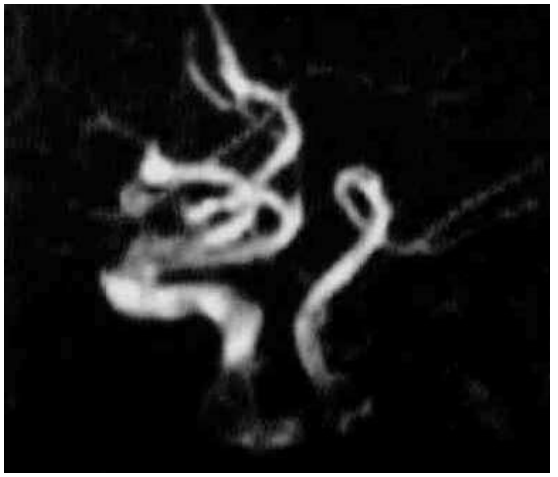
Angiography



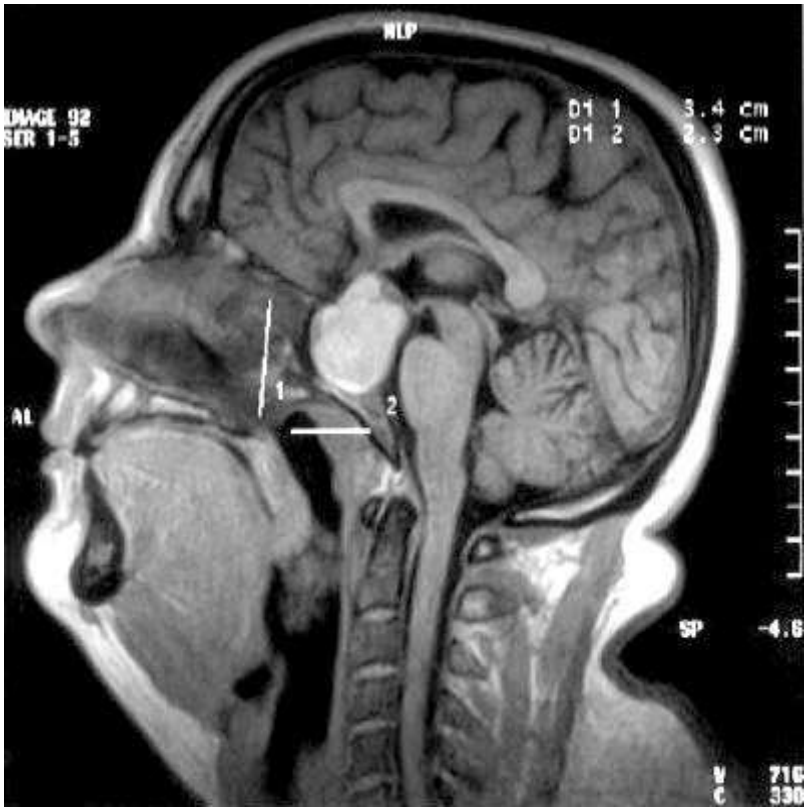


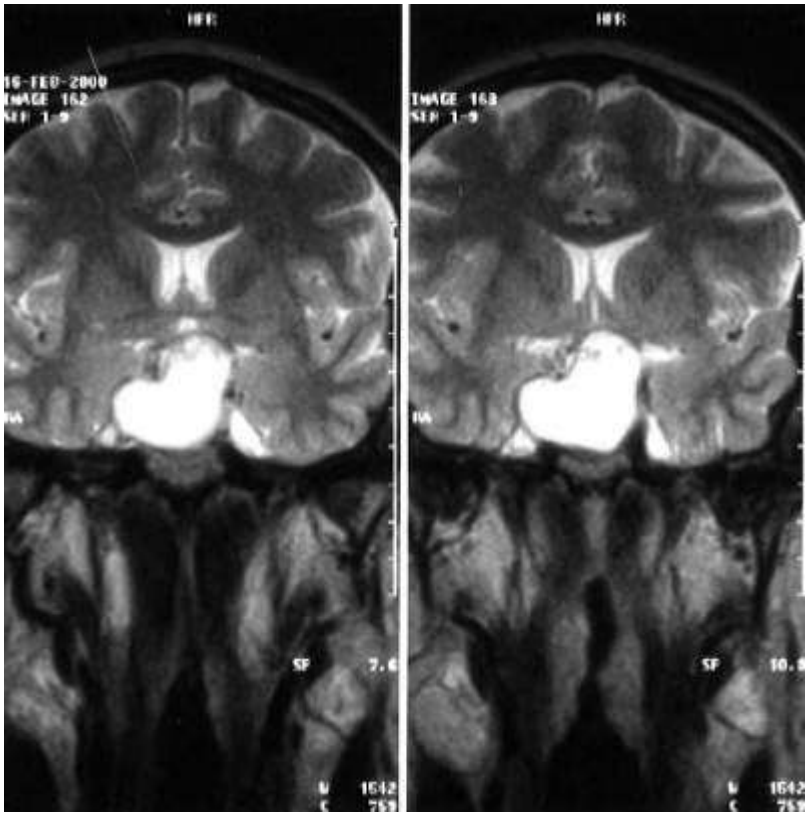




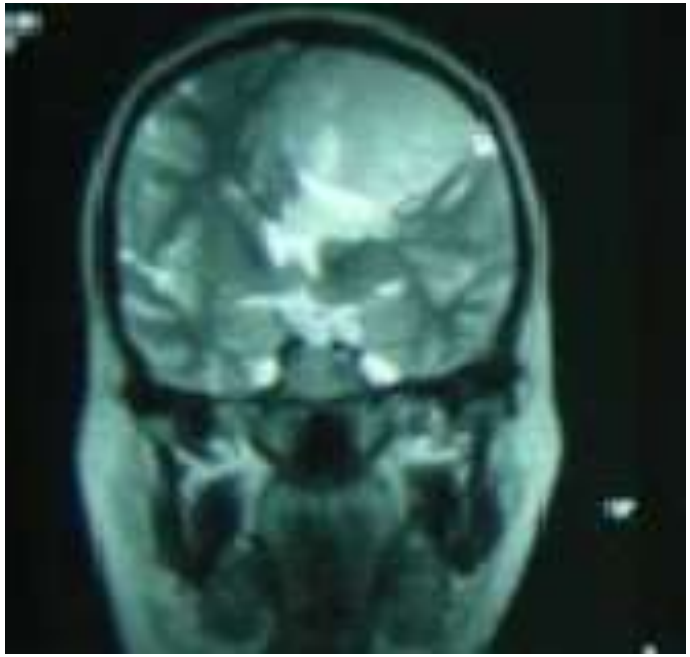


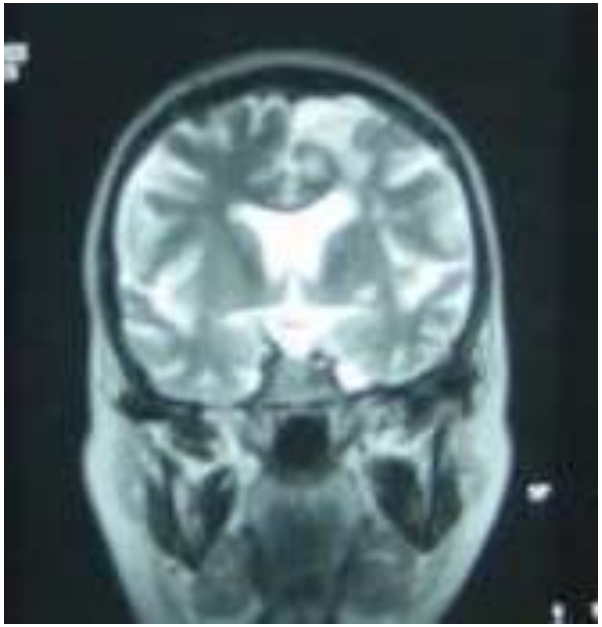
MRI



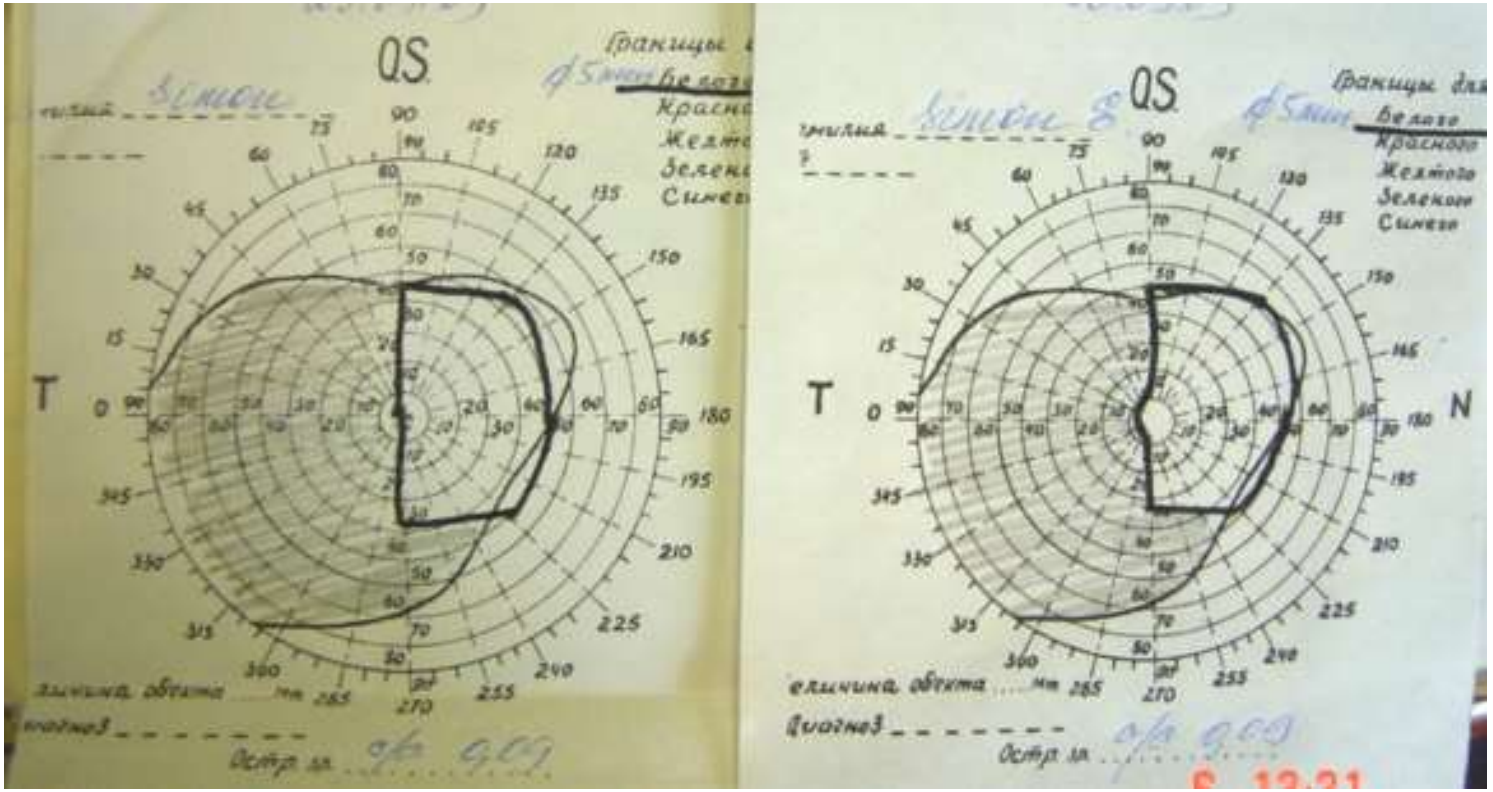


MRI





Ophtalmoscopy



Treatment

- Watchful waiting
- **Surgery**
- **Radiation**
- **Chemotherapy**
- Hormonal therapy
- Immunotherapy
- Hematologic Transplant & Endocrine procedures
- Combined therapy

Surgical Procedure

- Biopsy of tumor
- Partial resection
- Subtotal resection
- Gross total resection

Positioning

Once the plan for a surgical approach has been made, proper positioning of the patient is required.

Principals include the following:

(1) The position must permit the surgeon and assistants access for a planned approach.

(2) Access to special instrumentation such as the microscope, ultrasonic aspirator, laser, and so forth must be provided.

(3) The surgical team must be able to operate in comfort over the period of the procedure.

(4) The head must be stabilized and secured but capable of being repositioned.

(5) The anesthesiologist must have adequate access to the patient.

(6) Pressure areas and structures, including the eyes, must be adequately protected.

Radiation Therapy

- Beam radiation (Conventional radiation therapy: from an external beam directed at the tumor)
  - Particle or proton beam
  - Stereotactic radiosurgery
  - Linac radiosurgery
  - Gamma knife
- Boron neutron capture therapy (BNCT)
- Intensity modulated radiation therapy (IMRT)
- Conformal radiation

Chemotherapy

- Type of chemotherapy
  - Chemotherapy
  - Single-agent chemotherapy
  - Multi-agent chemotherapy
  - Intrathecal chemotherapy (drugs directly injected into the cerebrospinal fluid by spinal injection or Ommaya reservoir)
  - Interstitial chemotherapy (administered directly to involved tissues)

Hormone Therapy

- Records systemic hormonal agents administered as 1st course treatment
  - Tamoxifen and RU-486 (Mifepristone) may be used to treat meningioma
  - Steroids given to treat swelling caused by CNS tumors are not coded as hormone therapy

Immunotherapy

- Angiogenesis inhibitors
  - Block the development of new blood vessels and starve the tumor
- Interleukins
  - Growth factors that manipulate the tumor's ability to grow
- Gene therapy
  - Replaces or repairs the gene responsible for tumor growth
- Vaccine therapy
  - Allows the immune system to detect the tumor antigens and attack the tumor cells

Combined therapy

- Surgery + radiotherapy
- Surgery + chemotherapy
- Surgery + radiotherapy + chemotherapy

Determining a Prognosis

The survival rates in people with brain tumors depend on many different variables:

- Whether the tumor is malignant or benign.
- Cancer cell type and location. (Location affects whether the tumor can be removed surgically or not.)
- Tumor grade. (This is the tendency to spread and the growth rate.)
- Patient's age. (The outlook is poorer in the very youngest and very oldest patients, although younger patients who survive two years after diagnosis have a much better outlook than older patients.)
- Patient's ability to function.
- Duration of symptoms.