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NEUROSURGERY OF THE PINEAL REGION TUMOURS: ROLE OF MICROSURGERY

Kemal Dizdarević

Aseer Central, University Hospital, Abha, Saudi Arabia and Medical Faculty, University of Sarajevo,
Bosnia and Herzegovina

Corresponding author:
Kemal Dizdarević
kemal.dizdarevic@icloud.com

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Abstract

Neoplasms situated at the pineal region are rare intracranial lesions and generally very diverse in nature. These tumours are more prevalent in males and children. Neurosurgery plays a crucial role in the management of the most pineal region tumours. Operative microsurgical resection is still considered as a gold standard for their treatment. The two usually suggested microsurgical approaches for resection of these lesions are infratentorial supracerebellar and occipital transtentorial. However, paramedial unilateral supracerebellar infratentorial approach and more invasive Shekar's transsinus approach can be very useful surgical options. The specifically trained neurosurgeon has a crucial role in successful resection of these tumours because only a thorough understanding of the relevant anatomy and pathology as well as the high technical skills can ensure favourable operative outcome.

Key Words: Microsurgery, Pineal tumours, Neurosurgical approaches

INTRODUCTION

Pineal gland is neuroendocrine organ that releases the hormone melatonin. It is embryologically derived from unpaired light-sensitive structure in roof of diencephalon. The pineal gland begins to develop as dorsal outpocketing of the diencephalon shortly after neural tube closure (1). It develops during the second month of gestation (2). As the pineal organ grows, it elongates

into a thin stalk that carries a pinecone-shaped body at its distal end, similar to the stalk-like attachment of the pituitary gland on the opposite side of the third ventricle. In mammals, the pineal organ modulates sleep, mood, food intake, breeding and sexual maturation in the context of diurnal and seasonal rhythms. It receives afferent sympathetic and parasympathetic innervation from the superior cervical, sphenopalatine and otic ganglia. Furthermore, the retina sends sympathetic noradrenergic input indirectly to the pineal gland via the hypothalamus, thereby relaying information about ambient light. In some non-mammalian vertebrates, the pineal gland is a photosensor whose pinealocytes share a resemblance with retinal photoreceptors (3).

Probably, the pineal gland as a part of epithalamus is the vestige of a third eye, that is found in the fossils of certain fish and reptiles and that still exists in one living reptile (the Tuatara from New Zealand). In humans, the pineal secretes a melatonin during dark hours and maintains daily rhythms. The pineal is stimulated to secrete melatonin through neuronal networks. Interestingly, level of melatonin is higher in the younger age, young brain has more melatonin and because of that is prone to sleep more (4). The principal cell of the gland is the pineal parenchymal cell. Obviously, Rene Descartes' hypothesis that pineal gland is "seat of the soul" is not true, but this idea of the great philosopher and mathematician shows us that this deeply seated anatomical structure intrigued prominent minds even centuries ago (5).

Pineal region is located in the midline and consists of crucial structures including pineal gland, deep venous system with vein of Galen, basal vein of Rosenthal and internal cerebral veins, venous sinuses, posterior choroidal arteries, superior cerebellar and posterior cerebral arteries, quadrigeminal plate, posterior segment of the third ventricle, upper part of vermis, falcotentorial junction, posterior and habenular commissures etc. Important parts of broadened pineal region are the surrounding cisterns of the quadrigeminal plate and velum interpositum but also the brainstem, the thalamus, and the over-lying splenium of the corpus callosum (6-12).

Tumours arising in pineal region are ten times more common in children than in adults and can be classified as pineal gland tumours (transformation of pineal parenchymal cells), germ cell tumours (from displaced embryonic tissue), glial tumours (transformation of surrounding glial tissue), and miscellaneous tumours (falcotentorial meningioma, trilateral retinoblastoma, tumours associated with neurofibromatosis, Li Fraumeni, etc.) (13-15).

According to the latest WHO classification of central nervous system tumours from 2016, the following pineal gland tumours can be distinguished as

the recognized entities: pineocytoma (9361/1), pineal parenchymal tumour of intermediate differentiation (9362/3), pineoblastoma (9362/3) and papillary tumour of the pineal region (9395/3) (16).

Germ cell tumours can be classified as germinoma, non-germinoma (embryonal carcinomas, choriocarcinomas and yolk sac tumours) and teratoma (mature, immature, malignant) (13, 16). These tumours make half of all pineal tumours (15).

The treatment options for pineal region tumours vary mainly according to their histological nature and tumour morphology. However, microsurgery still plays a central role in the management of most pineal region tumours, with the exception of germinomas (13, 14, 17-19).

At the beginning of twentieth century, early attempts of pineal surgery included those of Horsley, Brunner, and Schoffler but without real results. The first successful removal of a pineal tumour was reported in 1913 by Oppenheim and Krause (20). More than a decade later, Krause was the first to describe successful usage of the infratentorial supracerebellar approach (1926) (21). During the 1970's, after introduction of microneurosurgery, Stein further developed this approach (22). Additionally, the occipital transtentorial approach was described by Poppen (23, 24) and modified by Jamieson in 1971 (25).

In 1966, Mahmut Gazi Yasargil developed the intracisternal dissection and widely opened the door of modern microneurosurgery which nowadays implies the safe and standard removal of the broad range of brain morphological lesions including pineal tumours (26, 27).

GENERAL MANAGEMENT OPTIONS FOR PINEAL REGION TUMOURS

Patient with pineal region mass should be only followed up if the MRI, clinical, and laboratory examination is compatible with an asymptomatic benign pineal cyst. Laboratory measurement of serum and CSF tumour markers is crucial procedure in establishing the proper diagnosis. These tumour markers are beta-human chorionic gonadotropin /beta-hCG/, alfa-fetoprotein/AFP/, and placental alkaline phosphatase /PLAP/ which can be found in germinoma and their confirmation prevent unnecessary craniotomy (18).

In the case that pineal tumour could be easily reached by biopsy (stereotactic needle or endoscopic transventricular) and other tumour characteristics are compatible with a germinoma, a biopsy without craniotomy should be

primary goal. The problem can persist with the needle biopsy due to a higher risk of haemorrhage in this region compared with other brain regions (abundant vascular structures, more than one pial plane for needle crossing, no tamponade from adjacent tissues).

Tumour histology can be obtained through mentioned types of biopsy or through direct biopsy during open surgery after craniotomy (frozen section procedure/cryosection). Biopsy is a good initial procedure for large pineal masses. Tumours extending into the posterior part of the third ventricle require an endoscopic biopsy, especially if the third ventriculostomy is necessary for treatment of hydrocephalus (28-31).

Pure germinomas can be cured without microsurgery only with chemo and radiotherapy.

Other germ cell tumours (embryonal carcinomas, choriocarcinomas, yolk sac tumours, teratoma) and malignant pineal parenchymal tumours require multimodality approach including chemotherapy, radiotherapy and microsurgery (13-15, 32).

The treatment of other pineal region tumours mainly requires microsurgery. Radicality of their resection will depend on the pathohistological diagnosis obtained by precraniotomy biopsy or by the intraoperative frozen section (18, 30-32).

Pineal region tumours can displace the venous system in different directions but most of them do it rostrally and dorsally. In some rare circumstances (meningioma velum interpositum, epidermoid tumours, tectal gliomas) the veins are displaced caudally and ventrally. This untypical displacement must be recognized preoperatively due to appropriate surgical strategy and adequate approach selection (9, 15).

General surgical management is different in benign and malignant tumours. Benign pineal region tumours (pineocytoma, meningioma, neurocytomas, mature teratomas, hemangioblastomas, cavernous hemangiomas, gangliogliomas, and symptomatic pineal cysts) require the radical resection whenever possible because it can be curative strategy. Microsurgery of malignant tumours is only a part of the treatment and radical resection is not a goal. Malignant tumours (immature teratomas, pineoblastomas (Figure 1), embryonal carcinomas, choriocarcinomas and yolk sac tumours) require a combination of surgery, radiation therapy and chemotherapy (14, 18, 31, 32). Importantly, the main objective of microsurgery should be avoiding the surgical morbidity even if it is connected with less radical resection (17, 32).

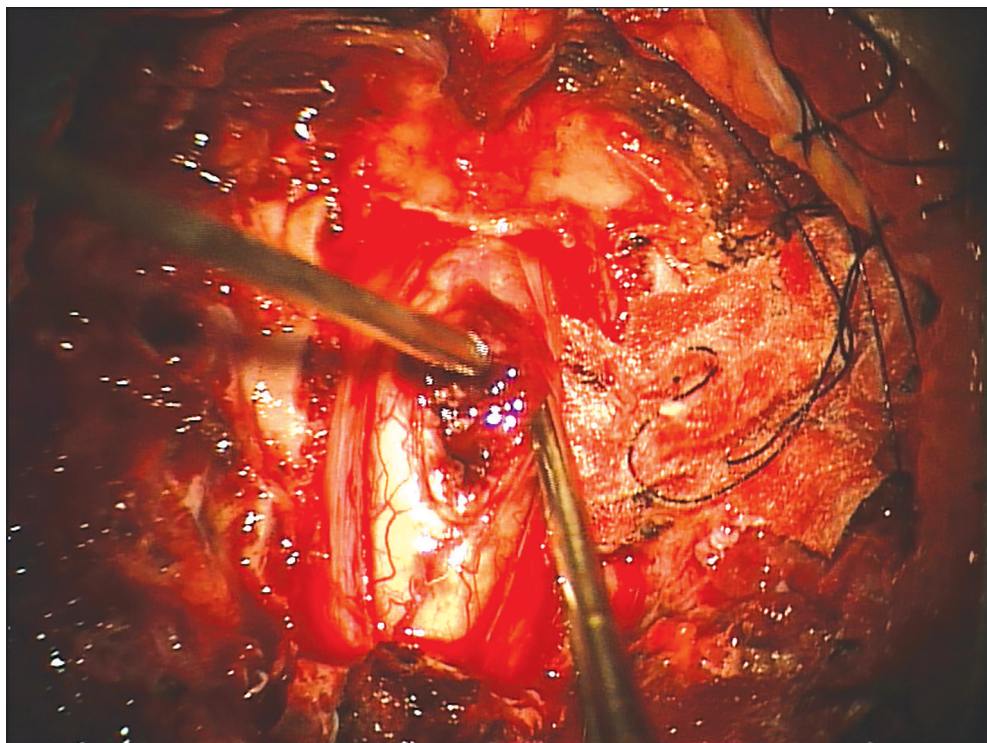


Figure 1. intramedullary cervical metastasis of pineoblastoma

Ventricular dilatation and Parinaud's syndrome (upgaze palsy, eyelid retraction, convergence nystagmus, light-near dissociation) are generally early manifestation of pineal region tumours. Hydrocephalus is obstructive and triventricular and caused by compression of the aqueduct. It can be acute or chronic. In slow growing tumours, chronic hydrocephalus may cause dementia. Shunt operations or third ventriculostomy could be options for hydrocephalus treatment (15, 18, 28, 29). In the case of radical tumour resections and CSF pathways restoring, the hydrocephalus shows frequent and spontaneous withdrawal and good outcome even without CSF diversion. Acute hydrocephalus with loss of consciousness requires emergent treatment with either external ventricular drain or shunt implantation. Additionally, the external ventricular drainage or endoscopic third ventriculostomy can provide an opportunity to test CSF for tumours markers (14, 18, 33).

MICROSURGICAL ANATOMY OF PINEAL REGION

Pineal region is the midline intracranial compartment whose complex content must be preserved during surgery at all cost. The pineal gland as the centre

of this region forms an appendix of the diencephalon embracing the pineal recess of third ventricle. The pineal body projects posteriorly in the quadrigeminal cistern and lies on the tectum between superior colliculi. The pineal gland is mainly vascularized by the medial and lateral posterior choroidal arteries which are usually displaced by pineal tumours in the lateral and rostral directions. The internal cerebral veins are mainly displaced together with arteries in the same directions. Other important arterial landmark is the superior cerebellar arteries that can be displaced inferiorly by pineal tumours. Deeply situated Galenic venous system is the major obstacle during microsurgery (12, 18, 34). The internal cerebral veins join the basal veins of Rosenthal to form the vein of Galen which lies in the quadrigeminal cistern. It drains into straight venous sinus (sinus rectus). The vein of Galen (also known as the great cerebral vein) is short midline unpaired vein which has several tributaries including the superior vermian vein, the precentral cerebral vein, the internal cerebral veins and the pineal veins. On the lateral aspect of this great vein, it can be seen the medial occipital veins, the third segment of the basal veins of Rosenthal, and the posterior mesencephalic veins to be joined (7, 8, 10, 11). The pineal veins are the draining veins of pineal tumours and drain into the internal cerebral veins or the vein of Galen. The pineal tumours are usually adherent to the internal cerebral vein and the vein of Galen. An injury to the basal veins or the internal cerebral veins produces serious complications. Also, homonymous hemianopsia or visual seizures can be induced by medial occipital vein cutting.

FIVE APPROACHES TO PINEAL REGION

The five most common surgical approaches to the pineal gland have been described (35-39).

Walter Dandy was one of the most prominent neurosurgical pioneers and innovators (aetiology and pathogenesis of trigeminal neuralgia, first clipping of a cerebral aneurysm, description of the circulation of CSF and brain endoscopy, hydrocephalus surgery, the establishment of the first intensive care unit). He tackled the pineal tumour in 1921, a few years later first successful pineal tumour removal occurred. Dandy introduced the posterior interhemispheric transcallosal (parietal parasagittal transcallosal) approach with interhemispheric fissure as an entry point (40). Today, this approach is performed using microsurgical technique and it is mainly used for resection of posterior third ventricle tumours proper and those involving tectum. Tumour

of splenium can be easily reached by this trajectory as well. In fact, for this approach the bulk of the tumour should be within the ventricle, rather than in the inner pineal region. These posterior third ventricle tumours are among the most unreachable lesions because diencephalic veins are serious obstacle through this posterior route. Typically, patient with this tumour localization develops hydrocephalus because of obstruction of third ventricle and aqueduct. During operations the patient may be positioned supine or lateral. Craniotomy is centred one-third anterior and two-third posterior to coronal suture. All parasagittal veins in posterior part of craniotomy and most of the splenium must be preserved. Significant injury of splenium is cause of disconnection syndrome. Once the right ventricle is entered work should be done between the leaflets of the septum pellucidum. This is the way how to reach entry point between or around the internal cerebral veins. Working between the veins (intervenous) or around them (paravenous) gives an additional designation to this approach (posterior interhemispheric transcallosal intervenous or paravenous approach). Just below the raphe of fornix there is tenia choroidea which should be opened and gentle lateral separation of the internal cerebral veins encased in tenia choroidea is needed to be done. After doing this manoeuvre, disclosure of the tumour capsule is achieved. Microsurgical debulking of tumour is followed by tumour separation from tectal plate and cerebellum respecting the strict anatomical boundary of the pial-arachnoid plane. This plane is also crucial for separation of Galen's vein from tumour capsule. Even in the case that surgeon is confident that tumour is completely removed, the operative blind spots typical for this approach should be inspected. They lie below the splenium or edges of the corpus callosum and could be seen by angled mirrors or endoscopes.

Ten years later (1931) Van Wagenen describes lateral transventricular approach (41). He used the access on the nondominant side (mainly right hemisphere) through the cerebral cortex of posterior part of superior temporal gyrus. This approach is mainly abandoned for pineal pathology but its modification in the form of posterior transcortical approach is still useful for masses of the non-dominant trigone.

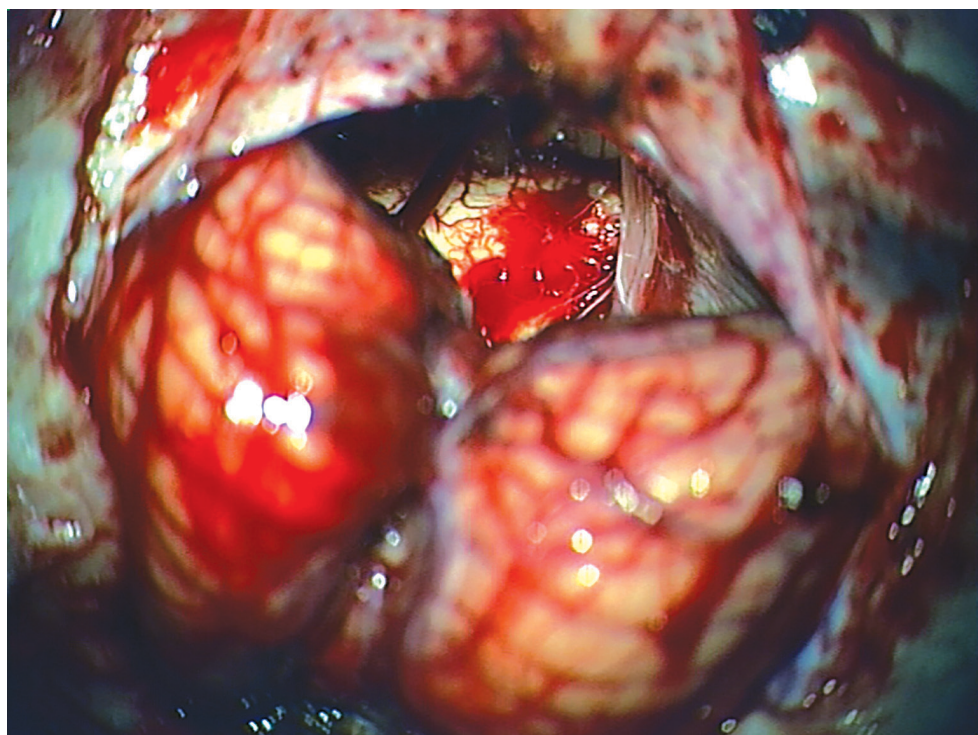


Figure 2. Supracerebellar infratentorial approach

F. Krause (1926) successfully used the midline supracerebellar infratentorial approach (Figure 2). He was also the first one who described extremely useful approach to pontocerebellar tumours (the lateral suboccipital approach, 1903). Krause published the report of three patients without mortality who harboured the pineal tumours and were operated through supracerebellar infratentorial approach (21). This surgical route was popularized by B.M. Stein (1971) who introduced microsurgical variant and resected six pineal tumours with minimal morbidity and no mortality (22). This is common pineal approach because it offers the most direct route to the pineal lesions (42). Importantly, most pineal tumours are ventral to the deep diencephalic veins so these venous structures can be almost undisturbed by this corridor. On the contrary, the numerous midline bridging veins are often sacrificed. Sometimes cutting these bridging veins leads to cerebellar congestions and limitation of exposure. In author's opinion, the prerequisite for this approach is the sitting (semi-sitting) position with gravity retraction and widening the operative route but some neurosurgeons utilize park bench position as well. The possible complication of sitting position is air embolism which puts

patients at nonsurgical risk. It can be said that only reasonable indications for sitting position are pineal lesions and some dorsal tumours located in the craniospinal junction or high dorsal intraspinal cervical region. Important disadvantage of this approach is the fact that inferior pole of tumour is covered by cerebellar culmen.

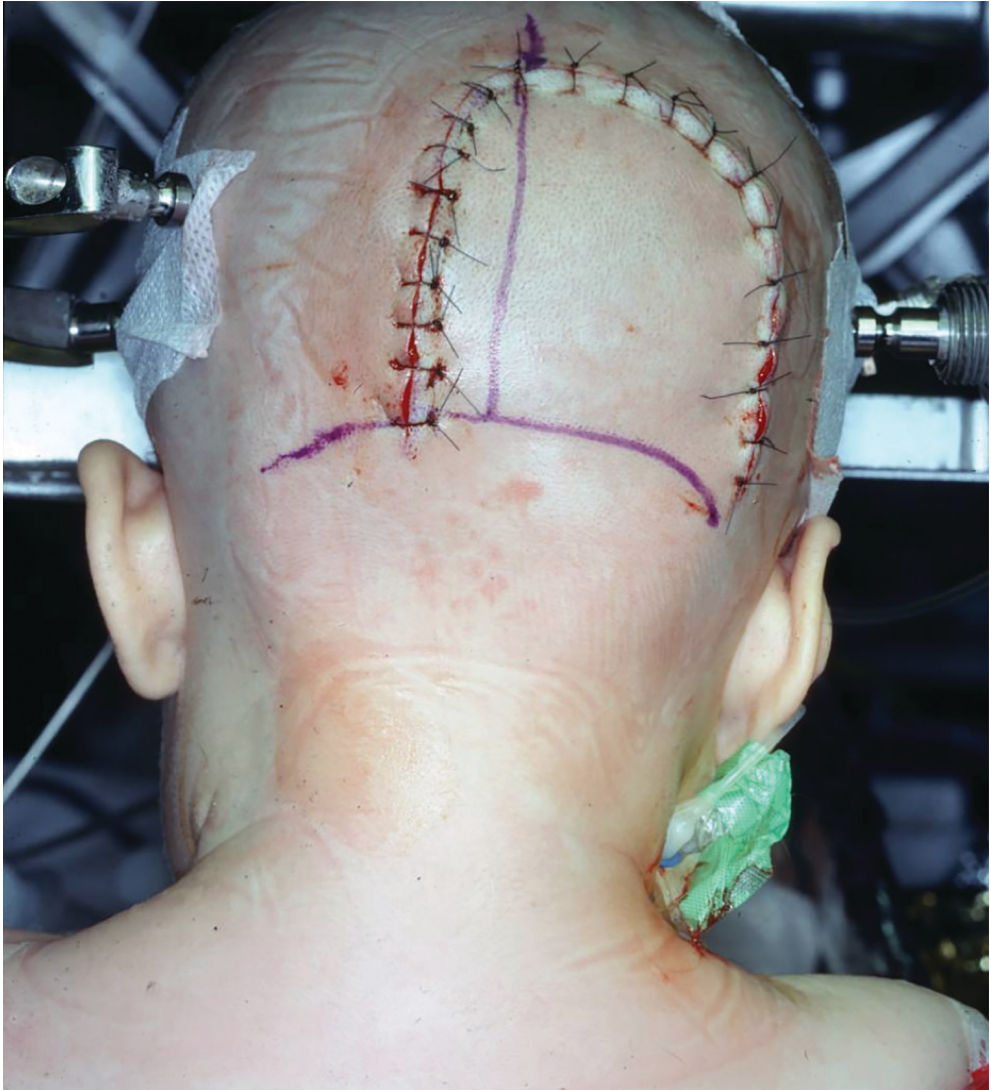


Figure 3. Occipital transtentorial approach

The occipital transtentorial approach (Figure 3) was pioneered by Foerster (1928) (43) but it is designated according to one other neurosurgeon - J. L.

Poppen. He published detailed description of this very popular approach (1966) and stressed that this kind of surgery requires lifting of the occipital lobe after CSF drainage via a ventricular catheter which implies surgical proceeding below the brain and over the tentorium with significant brain retraction (23, 24). Poppen's famous atlas on neurosurgical techniques (1960) (44), his description of a tacking suture (Poppen's stitch) and prefrontal lobotomy are integral parts of collective neurosurgical experience. The occipital transtentorial approach was modified by Jamieson (1971) (25) who preferred to mobilize the occipital lobe laterally rather than lifting it, meaning that necessary brain retraction is lesser. Generally, this approach places a number of important anatomical structures at risk including the straight sinus with its anastomosing veins and splenium of corpus callosum. This approach is based on unilateral occipital craniotomy and offers wide exposure of quadrigeminal plate. It is useful for large pineal tumours and falcotentorial meningiomas which show tendency to extend laterally and inferiorly (including toward the roof of the fourth ventricle) and require expanded working angles. If the deep venous system is displaced inferiorly by tumours, the logical choice could be this approach. Arteriovenous malformations localized in splenium or parasplenial region often require this approach because of early control of feeders coming from posterior cerebral arteries (Figure 4). Patient is put in three-quarter prone (park bench) position exploiting gravity with used trajectory on nondominant side. Brain relaxation can be achieved by direct tap of occipital horn or lumbar CSF drainage. Two burr holes are placed in the midline over superior sagittal sinus and torcula. Dura is opened along the sinuses and everted cranially and laterally. Tentorium is divided 10 mm away from straight sinus and parallel with it. The division of tent is directed anteriorly up to trochlear nerve which is just at the tentorial edge. Typical and some persistent bleeding from tentorial venous lakes should be controlled by bipolar, surgical and gelfoam. In majority of cases inferior sagittal sinus and lower half of falx should be divided as well. The arachnoid bands are dissected and deep diencephalic veins must be identified. If these veins are displaced dorsally and anteriorly tumour dissection and removal is much easier and safer.

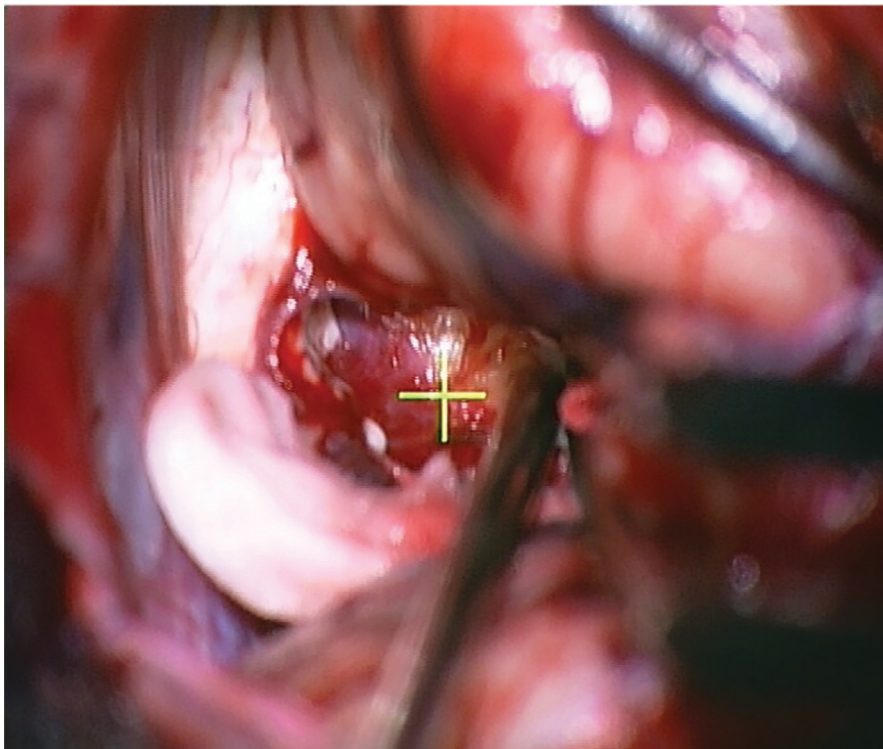


Figure 4. Parasplenic arteriovenous malformation through occipital transtentorial approach

Shekar (1992) (38, 45, 46) described the occipital transtentorial supracerebellar transsinus approach which combines the advantages of the supracerebellar infratentorial and occipital transtentorial approaches. This complex approach is suitable for giant falcotentorial meningiomas (Figure 5) because it provides wide exposure, multiple working angles, significant decreasing of brain retraction, and better view of posterior third ventricle. The suboccipital-occipital craniotomy is performed in three pieces. After removing the bone, wide presentation of operative field is gained including torcula, ipsilateral venous sinuses, infratentorial and supratentorial dura. A 20-gauge needle attached to a manometer is put in nondominant transverse sinus and sinus is occluded for 5 minutes by clip, placed lateral to the needle. If the venous pressure does not rise more than 5 mm and there is no brain swelling, the transverse sinus can be divided. The next step is division of tentorium from posterior to anterior toward tentorial edge. The significant working space is gained and complete control of pineal region can be achieved. Leaving sinus permanently occluded is usually safe procedure. Reconstruction of sinus with

vein graft can be attempted in some situations in which there are signs of brain swelling at the end of operation.

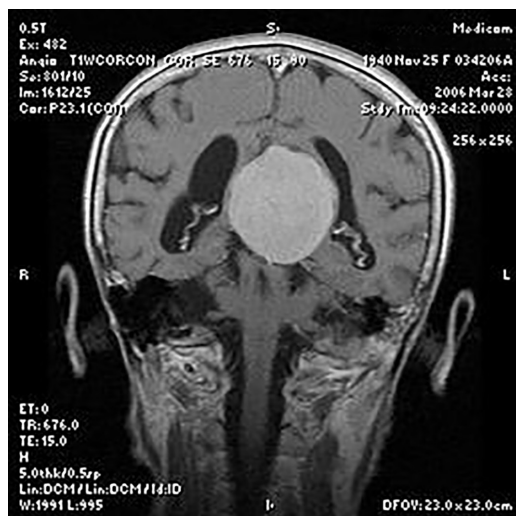


Figure 5. MRI of the giant falcotentorial meningioma

The infratentorial supracerebellar and the occipital transtentorial approaches are still the main accesses to the pineal region (47, 48). The left supracerebellar intratentorial paramedial approach as a modification of Stein's approach is author's preference whenever it is possible to be used concerning morphology, size, location and exact relationship to deep veins of pineal regions (49, 50).

The choice of approach is a matter of evaluating the anatomical relation of the tumour with the surrounding structures. A steep angle of the straight sinus makes the infratentorial supracerebellar approach difficult as an extensive retraction of the cerebellum is required to visualize and reach the pineal area. Moreover, in this case the lateral exposure of the surgical field is restricted and the resection of larger tumours is more complicated. The relationship of the tumour and the quadrigeminal plate is especially important. For smaller midline tumours located in the posterior part of the third ventricle and displacing the quadrigeminal plate and the tectum of the midbrain caudally, the infratentorial supracerebellar approach is favoured as it allows simple, direct and symmetrical exposure of the walls of the third ventricle and internal cerebral veins on both sides. But lesions in this location can be safely reached by posterior interhemispheric transcallosal approach as well. In the case where tumour lies more caudally and extends in the upper portion of the

aquaeductus Sylvii, lying therefore caudally to the tectum, the infratentorial approach is inappropriate as the quadrigeminal plate obstructs the surgical exposure. Finally, the occipital transtentorial approach is also preferred in large tumours with lateral extension in the pulvinar thalami as it gives a better lateral exposure of the walls of the third ventricle.

The giant tumours of the pineal region, especially huge falcotentorial meningioma, can be removed by the occipital transtentorial supracerebellar transsinus approach described by Sekhar (45) (Figure 3).

LEFT-SIDED PARAMEDIAL SUPRACEREBELLAR INFRATENTORIAL APPROACH AS THE FIRST CHOICE

The paramedial unilateral supracerebellar infratentorial approach (Figure 6) has advantages over traditional midline bilateral supracerebellar infratentorial approach.

This one-sided approach is performed on the left side utilizing unilateral small paramedial craniotomy which does not place dominant right transverse sinus and confluence of sinuses (torcula of Herophilus) at risk (48). The vermician bridging veins are protected and only upper part of left cerebellar hemisphere are surgically manipulated. It is important to emphasize that this approach provides a more inferior trajectory to the lower part of the tumour due to slight slope of the superolateral hemisphere and more direct and less steep route. Both sides of the midline are accessible, meaning giant masses can be safely removed as well. The main disadvantage is narrow and long corridor. If it is necessary, the tentorium can be divided to increase exposure but in vast majority of cases this manoeuvre is not required. Patient can be in the sitting or the lateral position.



Figure 6a. Sitting position for unilateral paramedial supracerebellar approach



Figure 6b. Pineal tumor resected by unilateral paramedial supracerebellar approach

FALCOTENTORIAL MENINGIOMAS: SURGICAL CHALLENGE AND SPECIFIC PINEAL REGION PATHOLOGY

Falcotentorial meningiomas can be divided into four types according to their origin: superior, inferior, anterior, and posterior ones. They are rare lesions and present in only 1% of all intracranial meningiomas. From surgical point of view, these neoplasms are considered as pineal region tumours. Difficult radical removal, strong dural attachment with involvement of tentorium and falx, proximity and frequent occlusion of deep veins and dural sinuses are specificities of falcotentorial meningiomas.

In majority of cases, they produce only mild and nonspecific symptoms. Even large falcotentorial meningiomas have this clinical characteristic as a standard feature.

Aggressive surgery can endanger the venous return leading to permanent neurological deficit so an acceptable strategy in management of these lesions can be waiting for several months which are needed for the invaded venous structures to be occluded and collateral circulation to be developed. The occipital transtentorial approach is the approach of choice for majority of falcotentorial meningiomas. Exception of this is giant falcotentorial meningiomas which can be safely removed by occipital transtentorial supracerebellar trans-sinus approach (45) (Figure 7 and 8). Radiosurgery (Gamma knife or Linac) is suitable treatment option for tumour remnant or recurrence.

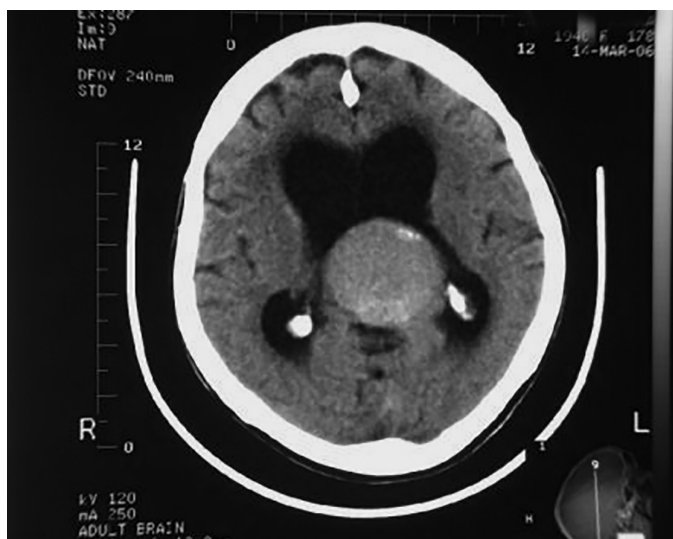


Figure 7. Giant falcotentorial meningioma attacked by Sekhar's approach



Figure 8. Radical removal of meningioma performed by author. See the figure 7.

CONCLUSION

Contemporary management of pineal region tumours requires a multidisciplinary cooperation where microsurgery represents very important aspect of the treatment strategy. The role of the neurosurgeons still remains prominent as resection of pineal region tumours requires microsurgery in majority of cases. The exception is germinoma management which requires only a biopsy from neurosurgical side and asymptomatic benign pineal cyst which needs follow up without any active treatment. The high technical skill and experience as well as precise clinical judgment is obligatory for neurosurgeons who deal with this complex intracranial pathology. The infratentorial supracerebellar approach and the occipital transtentorial approach when used appropriately allow access to nearly every type of pineal neoplasms. Nowadays, the paramedial unilateral supracerebellar infratentorial approach is suggested for majority of pineal region tumours. The giant falcotentorial meningioma can be radically removed through occipital transtentorial supracerebellar transsinus approach.

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NEUROHIRURŠKI TRETMAN NEOPLAZMI PINEALNE REGIJE: ULOGA MIKROHIRURGIJE

Apstrakt

Neoplazme lokalizirane u pinealnoj regiji su rijetke intrakranijalne lezije i generalno su vrlo različite prirode. Prevaliraju kod muškaraca i djece. Neurohirurgija ima ključnu ulogu u managementu većine tumora pinealne regije. Operativna mikrohirurška resekcija je još uvijek zlatni standard za tretman ovih lezija. Dva najčešće sugerirana mikrohirurška pristupa za njihovu resekciju su infratentorijski supracerebelarni i okcipitalni transtentorijski. Međutim, paramedijalni supracerebelarni infratentorijski pristup i invazivni Shekarov transsinusni pristup mogu biti vrlo korisne hirurške opcije. Uloga ciljano treniranog neurohirurga u uspješnom tretmanu pinealnih tumora je iznimno važna, jer jedino detaljno razumijevanje relevantne anatomije i patologije, te tehnička vještina mogu osigurati prihvatljiv operativni ishod.

Ključne riječi: mikrohirurgija, pinealni tumori, neurohirurški pristupi