
Central Nerve System Malignant Tumors

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Abstract: Tumors are classifying in two different types- non-cancerous (benign) or cancerous (malignant), which the malignant tumors are generally classified into meningiomas and gliomas tumors that varies in types. Some tumor occurrence are depend on the area that cells arise such as oligodendrogliomas, ependymomas and astrocytomas occur mostly from the meninges, which is outer part of brain and spinal cord. Even though they arise outside of the brain meningiomas do not be considered as brain tumor, because 85% of meningiomas are benign and can cure by surgery. Beside the three mentioned tumors meningiomas astrocytomas and glioblastomas mostly seen in adults, number of uncommon brain tumors containing medulloblastoma that arise from the cerebellum of primitive stem cells and most seen in children.

Keywords: Benign, Gliomas, Glioblastoma multiform, Meningiomas, Astrocytomas,

I. Introduction

Brain is center of nervous system in vertebrates. Brain located in skull which on animal's head and close to primary neurological body parts and organs which have senses like taste, vision, smell, hearing and balance. Among the vertebrate body, brain is the most complicated and complex organ. In normal human, the largest part of brain (Cerebral Cortex) is likely surrounds 15-33 billion neurons [1]. These neurons interlinked to other neurons over synapses.

Brain is the central control of body and organs. Brain can control different parts of body by hormones (secretion of chemicals) and generating patterns activity of muscles. This central control allows fast and synchronized reactions to changes in the environment. Some primary kinds of receptiveness such as reactions can be mediated by peripheral ganglia and spinal cord. But innovative fills with meaning control of actions based on complicated neurological feedback requires the information-integrating abilities of a central brain. Human brain has different three parts which called hindbrain, midbrain and set of common structure of vertebrate brain contain pons, optic rectum, medulla oblongata, thalamus, cerebellum, olfactory bulb, hypothalamus and basal ganglia.

The weight of brain in adult human is about 1.5 kg [2] and the volume of brain in adults are around 1130 cubic centimeters and 1260 cubic centimeters correspondingly, with a considerable variation among individuals [3]. Relatively, man's brain is heavier on average of 100 grams [4] compare to a woman's brain at same physical conditions but difference in brain weight does not associate in any way with actions of intellectual performance or IQ [5]. In largest part of the brain, cerebral hemispheres which located on top of other brain structure are covered with an elaborate topography with cortical layer [6]. Brainstem lies below the cerebrum. Cerebellum with horizontally structure and wrinkled surface can be easily identified as other brain areas is located behind the brainstem, at the back area of the brain and lower than cerebrum. A live brain have steadiness like soft tofu or gelatin and it is very soft. The color of live cortex also is pinkish beige and interior slightly white.

Group of diseases that relate to tolerant of cell growth are considered as cancer. Cancer cells grow and divide nonstop and invade different parts of body. They also can spread through bloodstream and lymphatic system. All tumors do not consider as cancerous, benign tumors do not attach tissues in neighboring and do not spread to the different parts of body. Nowadays there are more than 200 different known types of cancer which can cause serious problem on humans [7].

There are multiple reasons for cancer, such as exposure to UV radiation, diet, smoking including tobacco, certain infections, environmental factors like pollutants and [8]. There are factors that can damage the genes or cause mutation by combining to the genetic faults within cells that contributes to the occurrence of cancers as well [9]. Cancer can be identified in a several ways, like screening tests, and medical imaging. The usual treatments for cancers are surgery, chemotherapy, and radiation therapy. The chance of recovery depends to the type of cancer, the location of tumor, and how early is the disease being diagnosed. Whereas cancer can affect human in different ages like kids, teenagers and adult people but some types of cancers are common in children, while a few others are common in adults [10].

In the United States and Canada, One of the most common cancers in childhood is brain cancer [11,12]

. In United State of America, one of the most common tumor in children is solid tumor rose from 2.3 cases per

100k of population in 1975 to 3.0 cases per 100k in 1998 [11]. In Canada the rates were similar to United State [12]. There is different concern about factors that increase the risk of cancer. One of them is environmental factors which were increased by years. Another idea is improvements in detecting tumors and classifying brain tumors (MRI) have linked to increase in time, even though this it is contentious [13] The causes of brain cancer in children are basically unknown, But there are several fundamental causes which can due to brain cancer in children that linked to genetic and chromosomal conditions like Li-Fraumeni syndrome, Down syndrome and tuberous sclerosis that are small percentages of all cases [14]. Another factor that also connected to children's brain cancer is exposure of therapeutic irradiation [15]

II. Brain cancer

Tumors can be two different types non-cancerous (benign) or cancerous (malignant) but cancers are surely malignant. General classification of primary brain malignant cancers include two main types: malignant meningiomas and gliomas tumors that varies in types. Tumors name depends to the area that cells arise such as oligodendrogliomas, ependymomas and astrocytomas occur from the meninges, which is outer part of brain and spinal cord. Even though they arise outside of the brain but cannot consider meningiomas as brain tumor, the 85% of meningiomas are benign and can be diagnose or cured by surgery. Beside the three mentioned types, number of uncommon brain tumors containing medulloblastoma that arise from the cerebellum of primitive stem cells and most seen in children. As well primary and secondary malignant tumors can arise in the brain. Actually the secondary tumors arise from different parts of body then extended to the brain (metastasis) [16]. Over 20% of all cancers diagnosed among 0-14 years old [17]. 75% of children's brain tumors is astrocytomas and the rest is medulloblastoma[16]. Generally after 10 years of age the chance of brain cancer increases with age (25-75). In adult people the common brain cancers are astrocytes tumor which is a multiform. Men have a higher chance compared to women to get this type of brain cancer, in broad brain and nervous system cancers can occur in white people which has higher incidence compare to black men and women. But meningiomas is common in black men and women compare to whites [18].

III. Types of brain cancers and grades classification

The tumors in human can be in two types malignant and benign that can be primary or secondary, which can grow different parts of body and spread in body. The tumor which started to grow in brain as divergent to a metastasis tumor (which spreads to the brain from different parts of body) is called primary tumor [19]. The chance of cancer cells spreading from other parts to brain compare to primary tumors 4 is to 1[20]. Some tumors have symptom but some doesn't have, but there are some methods which can prove the existence of tumors in body for instance imaging scan and autopsy. The tumors which are very common between people are gliomas(50.4%), meningiomas(20.8%), Pituitary adenomas(15%) and nerve sheath tumors(8%)[21]. There are numerous types of brain cancer (tumors), each with specific classification by grade. The tumor's grades help to find the best treatment method because different tumors with different grades have different structure and aggressive level. The most benign tumors are classified as grade I that appear under microscope. Grade II tumors are cells that can become to malignant more easily which can destroy and invade the healthy neighboring tissue and cells. The malignant tumors that are graded as III and IV, does not define prognosis because the location of tumor can influence the treatment and removing [22].

IV. Gliomas

Gliomas is a cancer that starts to grow in spine or brain, brain is the common site of gliomas. Its arise from glial cells that's why it's called gliomas.[23]. 30% of central nervous system and brain tumors are built up by gliomas and most of the malignant tumors in brain [24], gliomas also consider as tumors that demonstrate immunohistochemical, ultra structural and histological of indicate glial variation. The gliomas is classified by their cellular features by the world organization classifies. The gliomas types are Ependymal or oligodendrocytes and Astrocytes, gliomas malignancy grades are from I to IV [25]. The most common class of aggressive forms of cancers and one of the malignant primary brain tumors are GBM (Glioblastoma multiform) or Astrocytoma (IV) which the survival after diagnosis is usually 12 months for astrocytomas (IV) and 6 months for glioblastoma multiform [25][26]. Furthermore the GBM is highly resistance to chemotherapy and radiotherapy. These malignant features of tumors maybe related to the different types of mutation that occurs frequently in these tumors [26][27]. The current treatment strategies for GBM are only surgeries resection and pivotal radiotherapy. As GBM is resistance to chemotherapy, different chemotherapeutic agents are tested such as alkylating agents (temozolomide) and nitrosoureas (carmustine) but no improvement in patients has been succeed [28].

4.1. Types of high grade Glioma

There are three types of high-grade tumors which is consider as glioma according to their cells types that is closely look like. ependymomas arise and develop from cells called ependymal which can be high grade and low grade and they line the cavities of brain. The ependymomas classified in 2007 by world health organization to three grades. Grade I contains myxopapillary ependymomas and subependymoma. Grade II consistent to ependymoma and grade III including anaplastic ependymoma and normally clear cell and tancytic ependymomas, cellular and papillary belongs to one or more grades usually grade I and grade II [29].

Generally the ependymomas are well-defined, which can grow and arise to the meningeal carcinomatosis. Low grade ependymomas consist of monomorphic cells to elliptical the nuclei which contains discrete chromatin. In high grade neoplasms the cells are polymorphic, hyper chromatic and erratically shaped [30]. Appreciation of ependymomas contains perivascular rosettes, an anuclear perivascular zone contains of ependymal cell procedures outward of blood vessels. They characterized with GFAP and vimentine antibodies. When the density of tumor cell is low these structures are challenging to classify. Irregular distribution of nuclei which has fibrillary background recommend histological verdict of ependymoma. Perivascular are hard to evaluate in highly cellular regions. Another one is ependymal rosettes which is extremely representative of ependymoma. It is rarely observe, within rosettes. Generally this types of tumor cells essence around the lumen. These structures need to differentiated from the normal one to ependymal coating of ventricles when they are forming a canal and larger. In other side when they are small central contains of accumulation of microvilli which responds with antibodies against EMA, There is limited for ependymal tumors to intense Intracytoplasmic eosinophilia dense. Ependymal tumors in perivascular area are marked with GFAP, if GFAP was absence the strategy for diagnosis should change and take another treatment. Furthermore the ependymal tumors are very constructive for NCAM [31].

Subependymomas are tumor cells that grow slow, through a slender peduncle and broad base and devotee to the wall of the ventricles. Most common location for subependymomas (low-grade lesions) is fourth ventricles. The spinal cord and third ventricles are not very common grow locations for subependymomas. Generally subependymomas is in adult patients when they are symptomatic with clinical exhibitions. This tumor's background is cystic changes and very fibrillar, nuclear sometimes scant and change to form group, this hangs in vessels may be due to intravascular thrombosis resulting in necrosis and another tumor which called secondary intratumoural haemorrhage [32].

Myxopapillary ependymomas are slow growing tumors. The usually grow in filum or conus terminal and its common in all group of ages but most in young adults. They normally are shown by back pain. They can grow and rise to CSF distribution which very common in children than in adults like other ependymomas [32]. The histological feature of myxopapillary ependymomas is ring of mucin lined by cubical ependymal cells that surrounded pseudo papillary structures that containing of a centrally located vessel, which is the juxtaposition. The myxopapillary ependymomas is contains balloons when they have more solid feature that resemble to eosinophilic structures.

Two other types of ependymomas are cellular and papillary ependymomas that as consequence the cellular one is highly cellular scratches and presenting a monotonous feature and Lacking of anaplastic feature. The papillary one represented by papillary structure in central vascular and surrounded by cylindrical cells. One variant observed tumors in the supra tentorial compartment which less common in posterior fossa and spinal cord is called clear cell ependymomas. Teenagers have higher chance to affect to this tumor compare to other group ages. They cells arrangement is back to back with cytoplasm this similarity to oligodendrogliomas that shows chicken-wire structures spreads to blood vessels and GFAP needed to mark them. They grade III when the endothelial cell area explosion and mitosis happens in this tumor nonstop. They will be grade II in absence of lesions [33].

Another type of ependymomas tumor that occurs in spinal cord rather than brain is called tancytic ependymomas. Generally tumor cells arranged and elongated is important in treatment and diagnosis strategies, For instance in absence of a rich reticulin network and presence of perivascular rosettes the nuclei will labeled with antibody which against oligo2 make easy curing of ependymoma. Normally the monomorphous Angiocentric Glioma attacks the cortical abrasion, also its possible to rich to the white matter. This type, first described as epilepsy in patients usually with the long term. monomorphous angiocentric glioma reveal EVA positive intra cytoplasmic dots, it is differ from ependymomas because of the accumulating of tumor cells in the subpial area, and also they are highly infiltrative aspect [34].

One type of infrequent well circumscribed ependymomas tumors is astroblastoma which grows and arise in the cerebral hemisphere. It's presenting bubbly aspect in the cystic and solid areas. It doesn't contain perivascular fibrosis and ependymal rosettes that make easy to differentiate them from ependymal. In astroblastoma can see EMA positive staining which is another feature of astroblastoma [35]. Papillary glioneuronal tumor is completely supra tentorial distinction ornamental lesion that possibly is cystic. It contains

a pseudo-papillary GFAP positive network surround the centered on hyalinized vessels and core like structures and intermediate zones filled by synaptophysin positive neurocytic cells [36]. Oligodendroglioma is different kinds of ependymomas tumors which may have arisen from clear cell ependymoma, for example like GFAP positive and EMA staining with latter diagnosis. It is not grow in children because the deletion of 1p/19q normally doesn't happen in children [36].

Central neurocytoma another type of malignant tumors that referred to ependymoma of the foreman induce different diagnosis with clear cell ependymoma. This type of tumor occur and present in the third ventricular system and it's possible to evoke the intracranial hypertension. The nuclei area will change with fibrillary that are not positively stained for GFAP but stained for synaptophysin [37].

The last type of ependymomas tumors us pilocytic astrocytoma which is hard to cure and has challenging diagnosis, this diagnosis problem arise when this tumor located in the spinal cord. Nuclear immunopositive staining for olig2 favors an astrocytic neoplasm when areas of Rosenthal fibers, granular bodies and loose micro cystic textures be absent. Furthermore two types of tumors are recognize in adult people which should differentiate from ependymomas. An ependymoma like tumor in the pineal region and more lack of GFAP marking and stain for cytokeratins is called papillary tumor that has a very difficult diagnosis in adult people. The paraganglioma needs different diagnosis as ependymoma when it is located in the down area of spinal cord, the PS100 antibody will help to highlight the lobules of chief cells that are synaptophysin and chromogranin positive [38].

Astrocytomas tumors are arisen from glial cells, glial cells are structured in spinal cord and brain and another function as feeding nerve cells and important role in memory and playing in people. This tumor doesn't have any specific place to grow in other hand they can occur at any part of the brain, they can grow slowly and rapidly in invade surrounding brain tissue. The astrocytomas tumors classified as malignant tumors with grade I to IV. The fourth grade means doesn't look like brain tissue and grow fast. The I grade can happens in children and teenagers they are less invasive compare to grade III and IV. The grade III called anaplastic astrocytomas and last one which has hard diagnosis process and high mortality rate called glioblastoma multiforme (GBM), in other word astrocytomas grade IV [39].

V. Meningiomas

Meningiomas is a type of brain cancers which can happen from all Dural constructions, spinal and cranial are outside of these structures and meningiomas arise from arachnoid cells[40]. The human skull is a place that has different neural system and structure as well as brain contributing nearby veins and arteries. Meningiomas, can grow on different places such as on or within the skull which can be very inspiring for neurosurgery. In surgeries usually is not possible to remove all tumor cells without any damage [41][42] and normally these surgeries in petroclival meningiomas area are very dangerous. But microsurgical technique allows control of recurrent tumors and residual as well as removing the meningiomas.

One of the brain cancer types that consider as most primary intracranial neoplasm is meningiomas, that expressive

14% -19% of all intracranial tumors. Also, estimated occurrence is around 0.001 with attuned sex and an age, incidence rate of 0.000036 and 8.4 in a year. Meningiomas tumors are classified by grades I , II and III. The aka benign meningioma (grade I) is a majority of meningiomas around 80% - 90%. About 4.7% up to 20% of meningiomas are consider as aka atypical (grade II) which has d to 2.8% of all meningiomas[43]

. Meningiomas tumors are arise in different ages even newborns can affect to this tumor. Occurrence peaks distinctly in the fourth and sixth decades [44]. Distribution of sex shows women pre-dominance in different ages with a significant peak of about 2 to 1 in the 30s and 40s[45].

In general one out of three of meningiomas are consider as skull-base meningioma, the tumors normally arise from three different parts of brain, for instance less than 10 percent of meningiomas tumors are arise arachnoids of the olfactory groove, 12.8 percent tuberculum sellae, 17 percent sphenoid ridge and less than 4 percent from foramen magnum. The least meningiomas tumors arise can arise different parts of brain such as medial 30.1%, alar or outer

6.9%, clinoidal, temporal or pterional 16% of the sphenoid ridge[46][47].

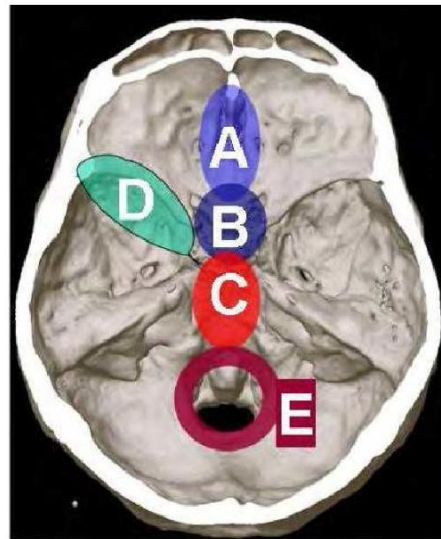


Fig. 1. Computed tomography of the skull base with marked areas of meningioma occurrence, A: olfactory groove, B: para- , suprasellar, C: petro-clival, D: sphenoid wing, E: foramen magnum.

In general brain cancers have nonspecific symptoms before diagnosis and treatment like headache for years. Seizures also have seen in skull base meningiomas and disobediently to tumors of the bulge. Seizures most happen in sphenoid wing cases among skull base meningiomas[48].

Meningiomas tumors also can grow in frontal skull base, most in the olfactory groove and before diagnosed the size can reach to grotesque (fig2), may occur very slowly and doesn't change the quality of patient's life immediately due to that hypo or anosmia. Other neurological symptoms will appear in patient when the tumor spread along midline and grow enough to get to the tuberculum sellae. The frontal base lobe can psychotic and induce incontinence after affecting to the cancer for instance can mention to some of them like psycho-motor disabilities, mental weakening and personality changes. Visual disorder can happen due to reduction of vision and blindness or bitemporal hemianopsia. Moreover there are some other reasons for inducing endocrinological disturbance such as compression of hypothalamus and pituitary stalk [54].



Fig. 2. T1-weighted triplanar magnetic resonance tomography after application of gadolinium, revealing a huge tuberculum sellae meningioma with homogenous contrast enhancement

Meningiomas tumors can arise and grow in sphenoid ridge which causes different neurological symptoms. When it spread to the middle skull groove and the optic nerves affected by cancer cells can persuade visual disorders. Due to compression of eye movement nerves and loss of ultimately and sensibility even principal to a keratitis, diplopia can happen in this patients. When meningiomas invades the Bone sphenoid wing it causes hyperostosis [49].

Cranial nerves may get affected due to extensions of tumors going through the cilvus. Mono or hemiparesis, paresthesia besides occlusive hydrocephalus can occur according to the location and the mass of tumor (fig3).

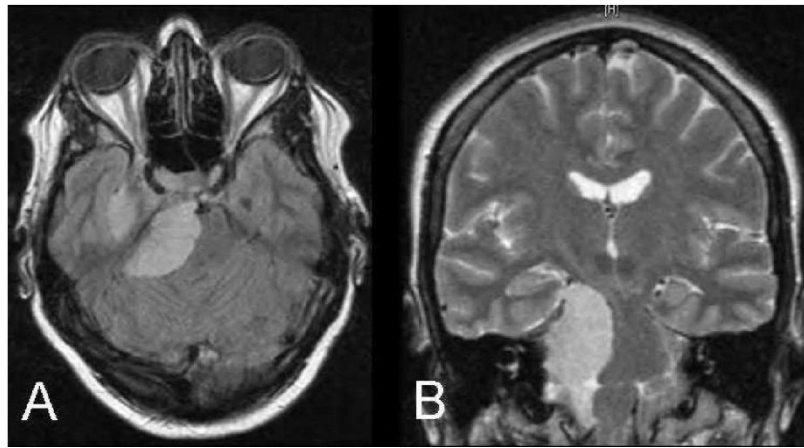


Fig. 3. Magnetic resonance tomography (A: T1 weighted, B: T2 weighted, both after application of gadolinium), showing a right sided petroclival meningioma.

Meningiomas tumors can expand and grow within the ventral, foramen magnum, dorsal or lateral it is possible to affect the lower eye movement nerves besides brain function. Furthermore the occlusive hydrocephalus may occur because of disorder of the aqueduct. In addition the tumors (meningioma within the posterior fossa) arise from the tentorium may wrap or attack the cerebral sinus and arteries. There is possibility that meningiomas tumors (within posterior fossa) infuriate dysmetria, cerebellar function, inducing ataxia, tremble and dizziness [48].

VI. Pituitary adenomas

The tumors that arise in sella region are vary and numerous. They include tumors such as craniopharyngiomas, pituitary adenomas, primary and secondary Carcinomas and meningiomas, etc. the pituitary adenomas generally is benign tumors but some types of pituitary adenomas can invade the neighboring cells and tissue and the growing rate also is fast, some benign types that are not able to invade the neighboring cells are slow-grow, restricted to the sella turcica, one of the characteristic feature of the pituitary adenomas are able to spread to others parts.

Like other brain cancers pituitary adenomas also has some symptoms which can say most of them are same as astrocytomas, gliomas and meningiomas tumors like headache, increased intracranial pressure, optical disturbances and damage of numerous cranial nerves. Many of them due to main changes in endocrine homeostasis and increase some hormones in blood.

The pituitary adenomas contains gigantism, the amenorrhea–galactorrhea syndrome, hyperthyroidism, Cushing’s disease and acromegaly. This tumor is very common in the sella region, Base on the surgical experiences approximately 10% to 15% and according to the sections examined they renowned in 3% to 24% of unselected autopsies of intracranial tumors are represent by pituitary adenoma in sella region. Pituitary adenomas frequency is not different between women and men if one includes every type.

Though the diagnosis of pituitary adenomas in prepubertal ages is very rare and it can appear and form in all age groups from children to adult. There are some parameters for classifying the pituitary adenomas such as biochemical methods measuring blood hormone’s concentrations using radioimmunoassay. In the other hand classifying different types of pituitary adenomas by analyzing separately, because they have significant differences for instance the corticotroph adenomas occur in women rather than men, gonadotroph and oncocytomas adenomas is more common in men with age over 40 than women, prolactin secreting adenomas is generally common in null cell adenomas and surgical material in young women.

There is other method in classifying the pituitary adenomas which is morphologic characteristic of the stress different markers of the disease but nowadays there is modern pathologic classification is based on cultured morphologic techniques like molecular methods and morphometric analysis (*in situ* hybridization), immunocytochemistry, immunoelectron microscopy and transmission electron microscopy. Some types of pituitary adenomas with their prevalence percentage are somatotroph adenoma (13%), lactotroph adenoma (29%), corticotroph adenoma (10%), thyrotroph adenoma (1%), gonadotroph adenoma including (47%) and null cell adenoma and o=Oncocytomas.

In conclusion pituitary adenomas is classified by size, giant adenomas (>40mm), macro adenomas (>10mm) and micro adenomas (<10mm) [50], staining affinities of the cell cytoplasm, hormone production and contents, endocrine activity, histologic characteristics, cytogenesis, cellular composition, growth pattern, granularity of the cell cytoplasm, ultrastructural features and by they function they divide to two types with different subtypes which is depends to the grow hormone and prolactin and etc, NSPA (non-secreting

pituitary Adenomas) and SPA (secreting pituitary adenomas).

The symptoms of pituitary adenomas is caused by different reason such as producing abnormal amount of hormones or abnormal secretion of hormones deficiency or hyper secretion like Cushing's disease and acromegaly Another reason of symptoms can be by the type of tumor, tumor dimension and structures [51]. For the last reason can mention to that some patients will have other pathology such as blindness and consciousness, intracranial hypertension which caused by changing of tumor volume that mean changing tumor from secondary to intratumoral hemorrhage and infarction [51][52]. Although there are so many diagnosis strategies but surgery still is main method for removing pituitary adenomas tumors and curing patients [53].

VII. Nerve sheath tumors

Other type of brain tumors which is a rare soft tissue of sarcoma of ectomesenchymal origin, called MPNST (Malignant peripheral nerve sheath tumor) [55,56]. WHO devised these malignant peripheral nerve sheath tumor confusing terminology and replacing previous heterogeneous, like malignant neurilemmoma, and neurofibrosarcoma and malignant schwannoma for neurogenic origin tumors [57, 58]. Diagnosis of this tumor is difficult because of the histopathological similarities between their cells and spindle cells such as leiomyosarcoma, fibro sarcoma and monophasic [59]. Minor and major peripheral nerve branches and sheath peripheral nerve fibers generally are the place this tumor arises [60]. MPNST tumors are arise in adults which 5% to 42% of them are multiple neurofibromatosis Type-I [61-64]. For diagnosis of this type of tumor different strategies and treatments is use such as histopathological, immunohistochemical and combination of gross. Another wondering feature about these tumors with same histology is growing and change to secondary tumors and being multifocality [59],even though these tumors are aggressive in nature but surgery still is main treatment [59,64,65].

Malignant peripheral nerve sheath tumor is not a very common tumor that's why the incidence is 1 per 100000 in population and its constituents is between 3 to 10% of all soft tissue sarcomas [55, 56]. In most examples the tumors demonstrate fascicles of spindle cells interlaced into herringbone shape with different degrees of necrosis and mitosis division. Nevertheless it is not possible always to display especially when it arise from a small peripheral branch from a nerve of origin. Most of them about 61% of this tumors don't demonstrate in cases of MPNST [64] and in

45%-56% of cases the nerve origin could be identified only [66]. MPNST Still has different features for instance proliferation of tumor in small vessels in the walls of large vessels and the sub endothelial area of nepotistic cells herniation into vessel lumen. MPNST tumor occurs in male and female with the same frequency [60]. But still it is difficult to say gender could cause and increment in chance of getting MPNST base on referral prejudice. MPNST sometimes arises from unusual sites like pelvic retro peritoneum. Normally the preoperative electrophysiological examination is done because will confirm that diagnosis will affect the treatment plan or not [56]. Imaging is a routine way to decide the diagnosis and surgery plan [65]. One of the investigation ways is doing MRI because it can expose the origin of nerve and its relationship to adjacent structures [67]. But MRI has limitation for example we are using CECT (contrast enhanced computed tomography) for valuation of pulmonary metastasis where MRI cannot show that.

VIII. Mortality and survival

The mortality and survival rates of brain cancers in Western Europe, Australia and North America are around 3 to 5 per 100000 per year in women and 4 to 7 per 100000 persons per year in men [68, 69]. Incidence rates are similar to mortality rates in all areas. Survival of glioma cases are still very poor except pilocytic astrocytomas [70, 71]. The survival cases with ages -20, -15, -10 and -5 are diagnosed with a supratentorial low grade glioma. According to national cancer institute in 1973-2001 the cured cases with low grade glioma reported to epidemiology, surveillance and end results were 60%, 42%, 42.6% and 26% [72]. The chance of 5 years old glioma survival is less than 3%

[70]. Older ages has significantly lesser and poorer rate of survival which can consider to the all ages group of glioma [70]. A research in wales and England with more than 30000 patients showed that some of them have longer survival that has socioeconomic status [73]. According to the same research in England and wales showed the diagnosis and survival of glioma increased from 1971-1990 [74]. Demonstrating of modern diagnosis and treatments still hasn't improved the outcome of cases with glioma tumors [75]. The rate of survival of children who were cured in Europe countries is different and vary but the probability of survival cases increased in 1982 compare to 1981. Chance of brain cancer can increase by some specific occupations such as diet, chemicals exposures, cell phones, smoking, therapeutic X-Irradiation, medical history (head injury, allergy and acute infections), electromagnetic fields and hereditary of tumor syndrome [76].

IX. Intracranial, Brain and other CNS tumors mortality statistics in the UK

The recent mortality rate and statistical data for intracranial brain and other CNS are for 2011 in the UK. The presented charts are about mortality statistics of brain cancer and CNS and intracranial tumors in the UK. Brain and other parts of CNS have ICD codes which different codes present different brain and CNS cancers the presented tumors in this data are ICD-10C70-C72, C75. 1-c75.3, D32-D33, D35.2-D35.4, D42-D43 and D44.3-D44.5 these codes represent for primary tumors of the brain, spinal cord and other parts of CNS, meninges, pituitary gland, pineal gland all of these cancers are included malignant, benign unknown behavior tumors.

CNS, brain and other intracranial tumors are the 8th most common cause of death in the UK at 2011 compare to other types of cancers. In 2011 4,975 deaths were from CNS, brain and other intracranial tumors in the UK. Table 1: Brain, Other CNS and Intracranial Tumors (C70-C72, C75.1-C75.3, D32-D33, D35.2-D35.4, D42-D43, and D44.3-D44.5), Number of Deaths, Crude and European Age-Standardized (AS) Mortality Rates per 100,000 Population, UK, 2011. According to the (Table 1), the deaths numbers from brain and other CNS and intracranial tumors in 2011, in the UK were 4.975. Men has 2.688 and women 2.287 which mean men with 54% and women 46% with the ratio of 12:10 [76-79]. The European AS rates do not have significant difference between constituent countries of the UK (Table 1) [76-79].

		England	Wales	Scotland	Norther	UK
Male	Deaths	2,229	157	219		832,688
	Crude	8.5	10.4	8.6	9.3	8.6
	ASRate	7.1	7.9	7.1	8.6	7.2
	ASRate-	6.8	6.7	6.2	6.8	6.9
	ASRate-	7.4	9.2	8.1	10.5	7.5
Female	Deaths	1,910	126	200		512,287
	Crude	7.1	8.1	7.4	5.5	7.1
	ASRate	5.1	5.4	5.5	4.3	5.1
	ASRate-	4.8	4.5	4.8	3.1	4.9
	ASRate-	5.3	6.4	6.3	5.5	5.3
Persons	Deaths	4,139	283	419	134	4,975
	Crude	7.8	9.2	8.7	7.4	7.9
	ASRate	6	6.6	6.3	6.3	6.1
	ASRate-	5.9	5.9	5.7	5.3	5.9
	ASRate-	6.2	7.4	6.9	7.4	6.3

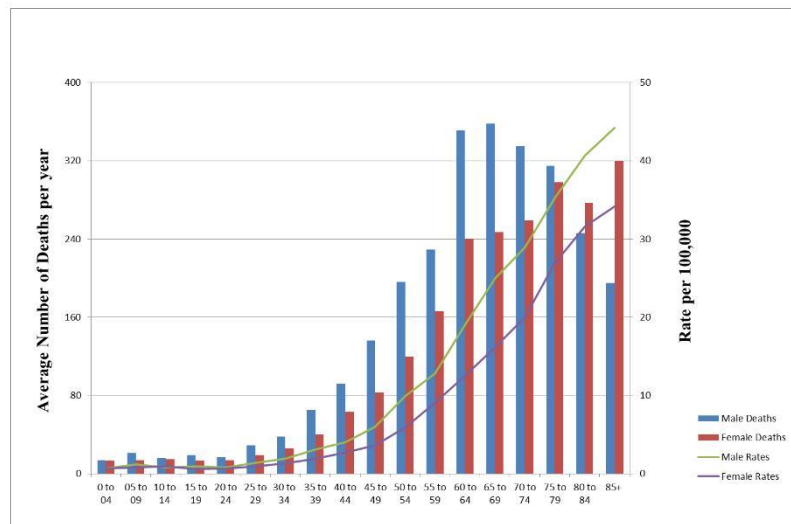
Table, 1: Brain, Other CNS and Intracranial Tumours (C70-C72, C75.1-C75.3, D32-D33, D35.2-D35.4, D42-D43,

and D44.3-D44.5), Number of Deaths, Crude and European Age-Standardised (AS) Mortality Rates per 100,000 Population, UK, 2011

9.1. By age

According to researchers in years and decades they show that the age is related to the CNS brain and other intracranial tumors mortality. The highest death rates is belongs to older women and men. But the brain, CNS and other intracranial tumors happen in all group of ages, however between 2009 and 2011 in the UK, men and women with the ages of 75 years and over have 34% of brain, other CNS and intracranial tumors death and 70% is belongs to the people with group age of 60 and over [76-79] (figure, 4.1).

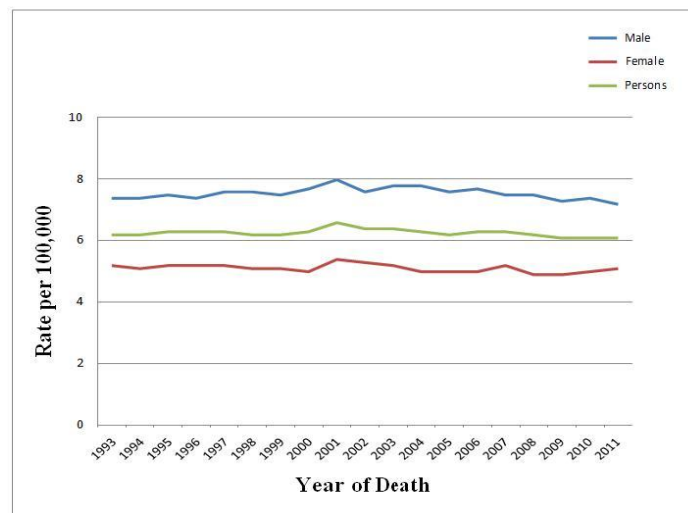
The mortality rates in specific age are relatively stable in ages 25 to 29 years old, then has a steady arise until the 45 to 59 years old, but the rates has sharper arise with the group age of 85 years old and over. Death rates between male and female is close and is not really significant difference in age of 45 to 49 and 50 to 54. Mortality ration between male and female in age specific mortality is almost 17:10 [76-79].



Figure, 4.1: Brain, other CNS and intracranial tumours (C70-C72, C75.1-C75.3, D32-D33, D35.2-D35.4, D42-D43, and D44.3-D44.5), Average Number of Deaths per Year and Age-Specific Mortality Rates, UK, 2009-2011

9.2. Trends over time

Since 1993 for the UK the Other CNS, brain and intracranial tumors mortality trends as shown in [76-79] (fig. 4.2). Between 2000-2002 and 2009-2011, European age standardized mortality rates have decrease in males by 6% and stable rate in females.

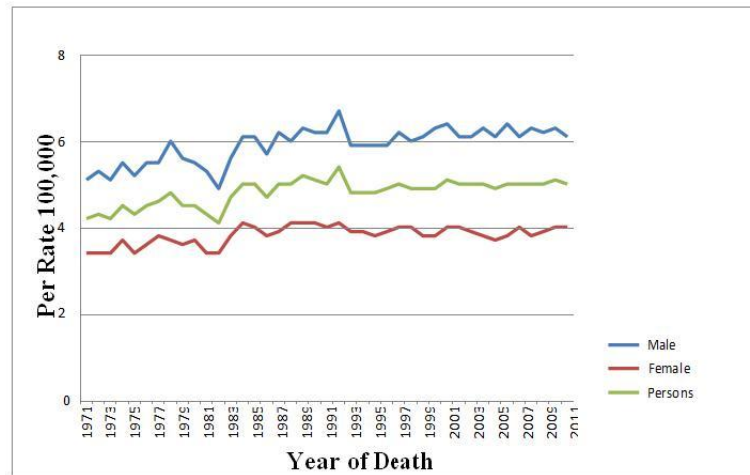


Figure, 4.2: Brain, Other CNS and Intracranial Tumours (C70-C72, C75.1-C75.3, D32-D33, D35.2-D35.4, D42-D43, and D44.3-D44.5), European Age-Standardised Mortality Rates, UK, 1993-2011

Improvements in registration and different, new and more effective diagnostics are likely effect the mortality rates and decreased them in last decades. The effect is more obvious for benign and unknown or uncertain tumors than malignant tumors because for malignant tumors the records should be for long time which more reliable for malignant tumors, but overall the malignant brain, other CNS and intracranial tumors decreased in the UK since

1970s, though it had increased the late 1980s and early 1990s, according to (fig. 4.3) [76-79]. In males the age standardized mortality rates mortality rates in European increased by 24% between years 1971 to 1973 and 1990 to

1992. The male’s pattern is same with women with the increasing rates of 21% between the years of 1971 to 1973 and 1998 to 1990.

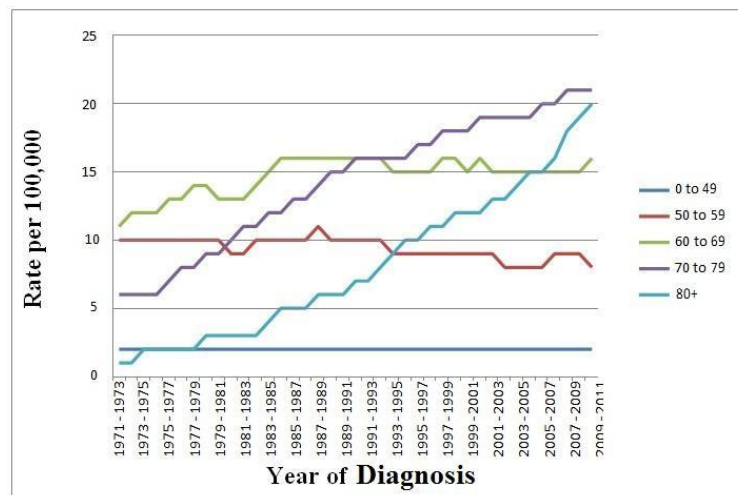


Figure, 4.3: Malignant Brain, Other CNS and Intracranial Tumours (C70-C72, C75.1-C75.3), European Age-Standardised Mortality Rates, UK, 1971-2011

Malignant other CNS, brain and intracranial tumors are decreased in rate overall in all group of ages under 60 in the

UK from early 1970s but increased in ages over 60 (fig, 4.4) [76-79]. The largest increase rate is in people with age of

80 and over and the largest decrease is belong to the people with age of 49 and under, with European age standardized mortality rates decreased between years of 1971 to 1973 and 2009 to 2011 by 36%.



Figure, 4.4: Malignant Brain, Other CNS and Intracranial Tumours (C70-C72, C75.1-C75.3), European Age Standardised Mortality Rates, By Age, Persons, UK, 1971-2011

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