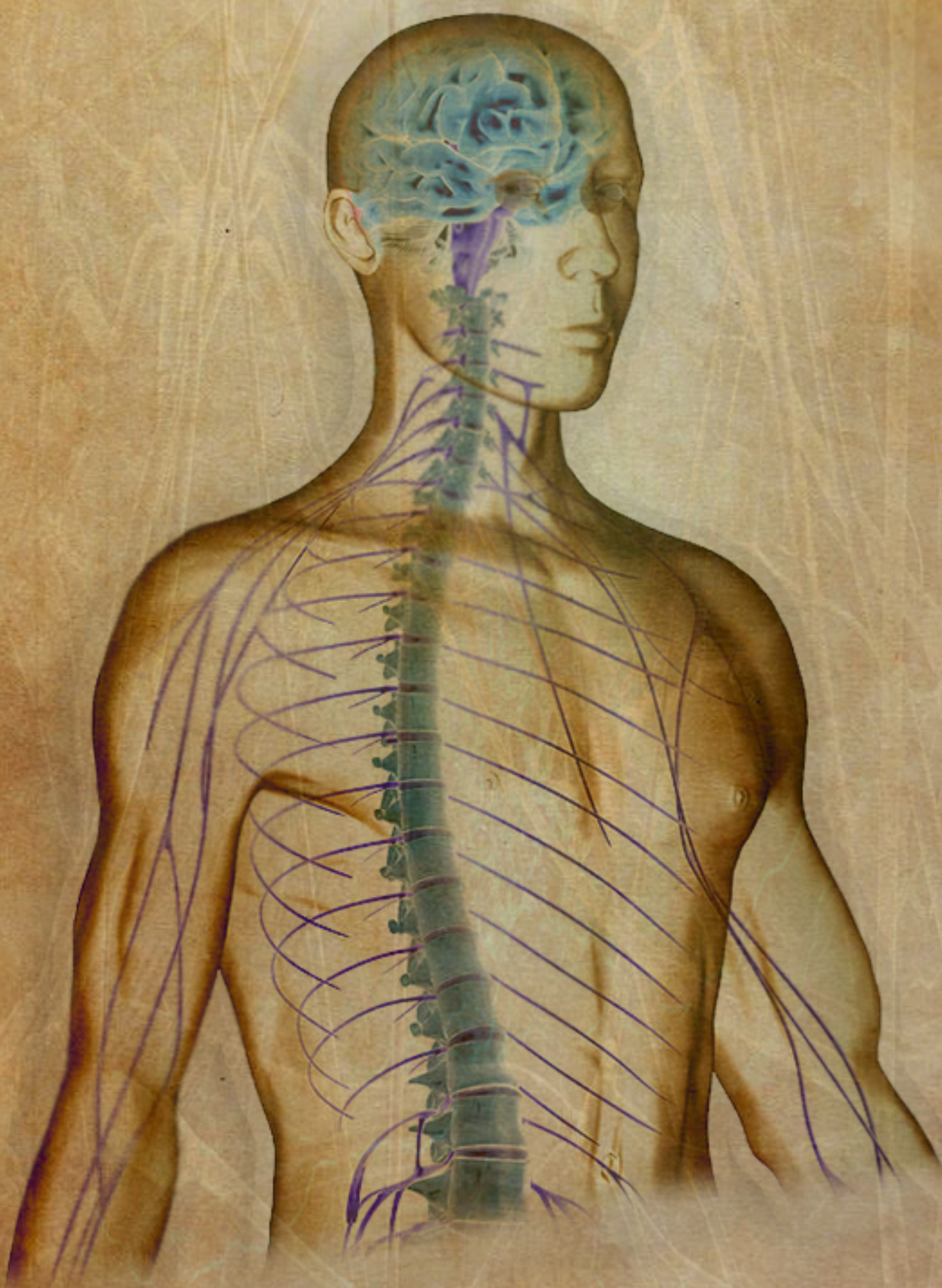
Prephiral Nervous System Pathology



Abdelrahman Ashour

TUMORS OF THE CNS

Epidemiology of the CNS tumors:-

1-Intracranial Tumors(T) has annual incidence of CNS T ranges from 100-170/per Million persons

2-Intraspinal T has annual incidence of the CNS ranges from 10 to 20/per Million persons

3-50% of CNS tumors are primary T

4-50% of CNS tumors are metastatic T

all childhood cancers are CNS T & those differ from 20% those in adults both in histologic subtype & location: T in childhood are likely to arise in the posterior fossa, while in adults they are mostly supratentorial

Characteristics of CNS tumor:-

T of the CNS have unique characteristics that set them apart from T elsewhere in the body, CNS tumors are:-

1-Histologically, the distinction between benign & malignant T may be less important in the CNS than in other organs! But Why ???!!!!

#Because of 3 reasons:-

A)the infiltration of most T (even the low-grade CNS T, which show low mitotic rate, cellular uniformity & slow growth) are infiltrative of adjacent brain tissues, leading to serious clinical deficits & poor prognosis

بحكيلك بالنسبة للCNS tumor مش مهم اميز اذا كان حميد ولا خبيث لأنه على الجهتين بعملinfiltration للخلايا المجاورة وطبعا هون الinfiltration شيء خطير جدا جدا

B) The anatomic site of the T can have ☠ lethal consequences, irrespective of histologic classification!For example, a benign meningioma, by compressing the medulla, can cause fatal cardiorespiratory arrest.

زي ما حكينا سابقا الدماغ او الCNSبشكل عام مناطق حساسة جدا واي tumor بصير فيها مهما كان صغير ممكن يعمل مشاكل كبيرة جدا بس يضغط على مناطق حساسة وحيوية بالدماغ زي الmedullaالتي تحتوي على مناطق مهمة زي الRS center&CVS center فلو صار عناtumor بهاي المنطقة وضغط على وحدة من هاي المناطق ممكن يقتل بايقاف التنفس او ايقاف القلب

2-The pattern of spread of primary CNS T differs from that of other body T which are:-

A)the tumor location may limits the ability to resect it!

كونه جراحة الدماغ صعبة وحساسة نظرا لصغر حجم الجمجمة فبالتالي ازالة اي ورم من الدماغ سوف تكون صعبة جدا

B)Before done craniotomy operation, even the most highly malignant gliomas rarely metastasize outside the CNS

C)The subarachnoid space does provide a pathway for T spread, so that seeding along the brain & spinal cord can occur

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Gliomas

Gliomas are T of the glial brain cells, and the 3 major types are:-

1-Astrocytomas

2-Oligodendrogliomas

3-ependymomas

(1)Astrocytoma

The most common two types of Astrocytoma are:-

(A)diffuse or fibrillary astrocytoma

(B)pilocytic astrocytomas

(A)Diffuse or Fibrillary Astrocytoma

Epidemiology of this tumor:-

1-Account for 80% of adult primary brain T

2-most frequent in the 4th to 6th decades

3-usually found in the cerebral hemispheres

Clinical manifestation of this tumor:-

(1) seizures (epilepsy)

(2) headaches

(3) focal neurologic deficits related to the anatomical site

طبعا احنا حكينا بالCNSعن خلايا الASTROCYTE وقلنا انها عبارة عن خلايا موجودة بين الneurons of the CNSوهي تساعد في تكوين الblood brain barrier وايصال الnutritionللخلايا العصبية داخل الCNS فلو هاي الخلايا صارت تتكاثر اكثر من اللازم وعملتbenign tumor بنسميهastrocytomaوهاي الخلايا كونها بين خلايا الCNS العصبية فلما تكبر راح تعملmass effect on CNS وتضغط عليها وتؤدي الى عدة اعراض منها الصرع ووجع الرأس وبعض المشاكل العصبية حسب المنطقة اللي بنمو فيها الورم فلو مثلا ضغط على الoccipital lobeراح يؤثر على الvision ولو ضغط على على الfrontal lobe ممكن يؤثر على الحركة وهكذا

classified histologically into 3 groups:
(I)well-differentiated astrocytoma
(II)anaplastic astrocytoma
(III)glioblastoma multiforme(GBM)
راح نحكي عن كل صنف من الdiffuse fibrillay astrocytoma والفروقات بين الانواع

(I) Well-differentiated astrocytomas

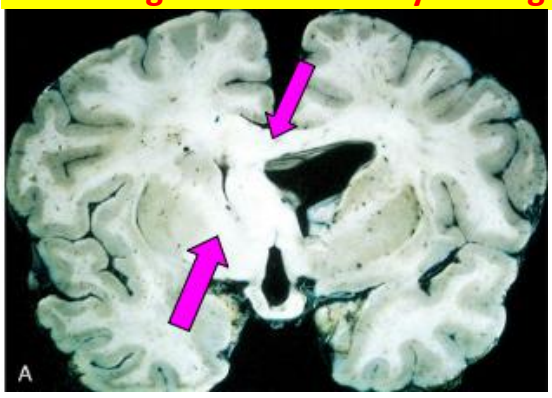
Progression of this tumor:-

This tumor is progress slowly, with a mean survival of more than 5 years. Eventually, however, patients usually enter a period of rapid clinical deterioration that is generally correlated with the appearance of anaplastic features & more rapid T growth

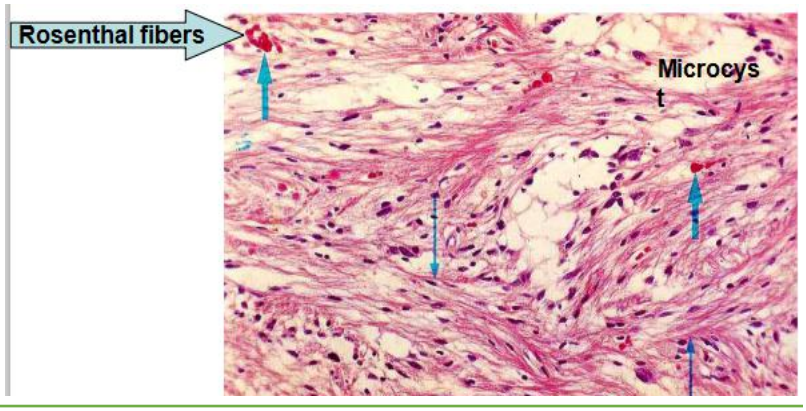
هذا النوع من الdiffuse astrocytoma بنقدر نقول انه اخف اشي لأنه ينمو ببطئ وبحتاج وقت لتبلش اعراضه تظهر فبالتالي معدل النجاة بعد 5 سنوات من التشخيص بكون اكبر ولكن قد يصل هذا الورم اثناء نموه لمرحلة يبدأ فيها التطور بشكل اسرع بكثير وبتبلش اعراضه تبين على طول وقد يتحول سلوكه بالنمو ليصبح شبيه بصنف الanaplastic astrocytoma واكثر سرعة بالنمو

Morphology(grossly&histology):-

Grossly--->fibrillary astrocytoma is a gray, poorly defined,infiltrative T which always infiltrate beyond the grossly evident margins, expands & distorts the brain, without forming a discrete mass . T C/S is either firm or soft & gelatinous with cystic degeneration



Histologically---->characterized by a mild to moderate ↑ in the number of glial cell nuclei, mild nuclear pleomorphism, & an intervening feltwork of fine, GFAP-positive astrocytic cell processes that give the background a fibrillary appearance(Rosenthal fibers)



Rosenthal fibers:-is the dens red bodies which contain acidic glial fibrillary filiment

(II) Anaplastic astrocytomas

Progression of this tumor:-T is growth rapidly

Morphology(histology):-

Histologically---->show more dense cellularity,greater nuclear pleomorphism, & ↑ mitoses

(III)glioblastoma multiforme(GBM)

Progression of this tumor:-

☠ GBM prognosis is very poor & current state-of-the-art treatment, comprising resection (when feasible) together with radiotherapy & chemotherapy, yields a mean survival of only 6 months (2007)which increased to 15 months in 2013

هذا الصنف للأسف هو اسوء نوع من انواع الdiffuse astrocytoma لأنه بتتدهور فيه صحة المريض بوقت كثير قصير فقد لا يتجاوز الmean survival rate فيه ال6 اشهر مما دعى الى وضع هذا المرض من ضمن خطط اوليات ايجاد انسب علاج له وفعلا بالفترة اللي ما بين 2007 وال2013 ارتفعت الmean survival rate من 6 اشهر ل15 عن طريق دمج خطة علاجية تشمل الازالة الجراحية للورم واعطاء الكيماوي

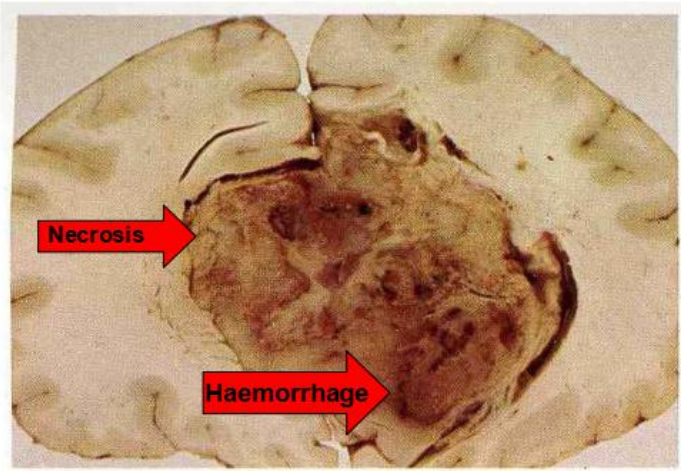
وتطلق منظمة الصحة العالمية على مفهوم التطور السريع بالعلاج خلال فترة قصير مصطلح الcurrent state-of-the-art treatment

Note:-"Many patients present with highest grade GBM, from the start rather than having their T evolve from a lower grade T"

يعني للأسف معظم الاشخاص اللي معهم GBM ما ببدأ المرض عندهم تدريجي انه يكون lower grade T وبتحول تدريجي الى high grade T لأ هذا بختصر على حاله الطريق من اوله وببلش high grade

Morphology(grossly&histology):-

Grossly--->In GBM, heterogeneity (variation in the appearance of the T from region to region, is characteristic).Some areas are firm & white, others are soft & yellow (due to necrosis), & others show cystic degeneration &hemorrhage



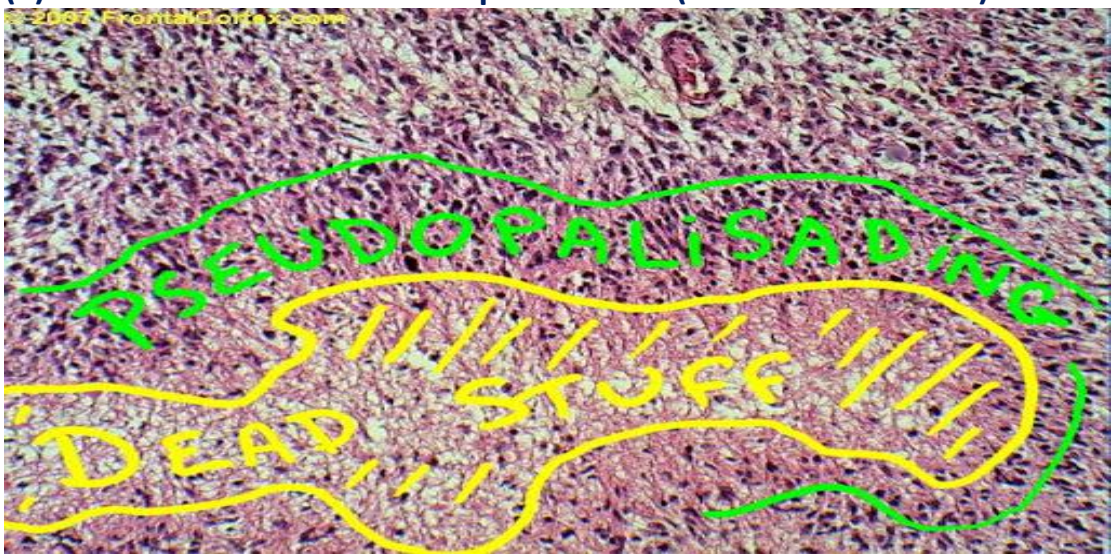
هذا النوع بتميز انه بعرفش سلوكه ومظهره الخارجي بالزبط فكل مرة بشوفه شكل مرة بشوفه اصفر ومليان necrosisومرة بشوفه بني او احمر ومليان heamorrhage

Histologically--->The highest grade GBM tumor has a histologic appearance similar to anaplastic astrocytoma with the additional features of:

(1)palisading necrosis

(2)pseudo-palisading nuclei

(3) vascular or endothelial cell proliferation(neovascluarization)



مكن اكثر اشي مميز مش لازم ننساه عن هذا النوع من الورم هو الpalisading necrosis وهو عبارة عن خط يتكون متكون من rapidly proliferating tumor cells تحيط بمنطقة من الpale necrotic area

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(B)Pilocytic Astrocytoma

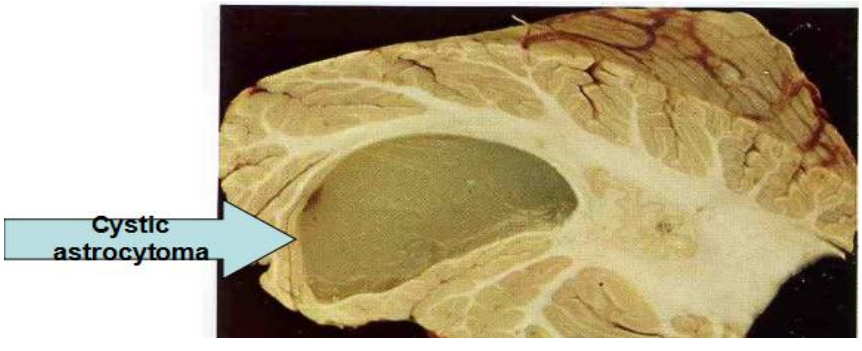
Pilocytic astrocytomas are relatively benign T,&often Cystic.

People at risk:-typically occurs in children & young adults

Most common site of the pilocytic astrocytoma:-usually located in the cerebellum,but may also appear in the floor & walls of the third ventricle, the optic nerves,&occasionally the cerebral hemispheres.

Morphology(grossly&histologically):-

Grossly---->pilocytic astrocytoma is often cystic, with a mural nodule in the wall of the cyst,&if it solid, it is usually well circumscribed.



كلمة CYSTتعني شيء منفوخ زي البلون اما بتكون فارغة او مليانة nodule&fluid

Histology--->it composed of areas with bipolar cells with long, thin "hairlike" processes that are GFAP positive; Rosenthal fibers, eosinophilic granular bodies, & microcysts are often present. Necrosis & mitoses are absent.

Note:-"Symptomatic recurrence from incompletely resected lesions is often associated with cyst enlargement rather than growth of the solid component"

بالعادة علاج هذا النوع من الtumorيتم عن طريق الresection of tumor فلو جراح ما قدر يشيل الورم بشكل كامل ممكن بعد فترة يرجع ينمو هالورم ويرجع يعمل اعراض مرة ثانية

Oligodendroglioma

Epidemiology of the disease:-

1-Constitute 5 % to 15% of all gliomas.
2-Most common in the 4th & 5th decades.
3-Found mostly in the cerebral hemispheres(mostly frontal lobe)

Pathogenesis:-

The most common genetic findings are loss of heterozygosity for chromosomes 1p 19 7q.And Patients may have had neurologic complaints, including seizures.

احنا بنعرف انه الoligodendrocyteمسؤولة عن صناعة الmyelin sheath فبالتالي نسمي الورم اللي بصير بهاي الخلايا باسم oligodendroglioma واذا بنطلع لصورة السكتش هاي بنستنتج كونه الدنيا ليل فيها والقمر مبين يعني بصير هذا المرض
بlate age باعمار بين ال40 وال 50 ويقال انه سبب حدوث هذا الورم هو فقدان بجينات موجودة على الكروموسوم 7q 19 1p بعدين لما يكبر هذا المرض راح يبلش يضغط على الfrontal lobeخصوصا ويعمل مشاكل عصبية منها الseizures

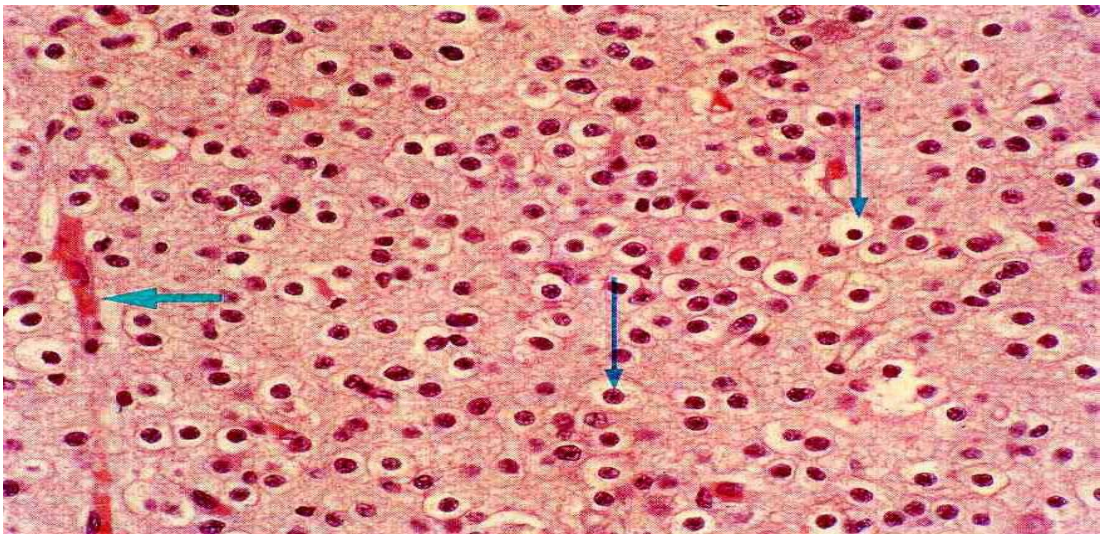
بتلاقوا الفيديو على اليوتيوب اذا بتحبوا تشوفوه بس اذا كتبتوا اسم الورم اول فيديو بطلع لكم

Morphology(grossly&histology):-

Grossly---->infiltrative gelatinous, gray T& may show cysts, focal hemorrhage, while calcification is present in 90% of T.

هسا ننسى اسمنا يا طلبة ولا ننسى انه هذا الورم اكثر اشي بميزه هو انه بصير له بعد فترة calcificationواذا بنتطلع للسكتش بنلاقي الزلمة ماسك كباية ice cream اسمها calci لنتذكر الcalcification

Histology--->T cells are regular (similar to normal oligodendrocytes), with spherical nuclei, containing finely granular chromatin surrounded by a clear halo of cytoplasm-boxing' of the nucleus-,with delicate network of anastomosing capillaries & very rare mitotic figures,but Anaplastic oligodendroglioma shows ↑ cell density & mitotic activity, nuclear anaplasia, &necrosis



هسا اهم اشي لازم نعرفه بالهستولوجي تبع هذا الورم انه الخلايا بالزبط بتكون شبه البيضة بس تفقسها بالقلاي الصفار بالنص والبياض الدائري حواليه فهون الخلايا بالزبط بتكون بيضوية الشكل بالنص النواة غامقة والسايتوبلازم بكون فاتح وابيض حواليها ومش بس كده ايضا هذا الورم بتشوف تحت المجهر انه مليان anastomosing capillaries

Progenosis:-

-Prognosis is better than that of astrocytomas.

-Anaplastic oligodendroglioma have worse prognosis

Treatment:-

Combine surgery, chemotherapy, & radiotherapy yields an average survival of 5 to 10 years.

Ependymoma

Mostly arise next to the ependyma-lined ventricular system, &the central canal of the spinal cord.

اخذنا بالCNSانه الventricular systemمبطن من الداخل بطبقة من الependyma cell
المسؤولة عن افراز الCSFداخل الventricular system فممكن يصير بهاي الخلايا ورم بنسميه ependymoma وهذا الورم اكثر اشي بصيب الاطفال

The most common location of ependymoma:-

1-In the first two decades of life(children)---->they typically occur near the 4th ventricle&they constitute 5% to 10% of the primary brain T

2-In adults---->the spinal cord(because the central canal of spinal cord has ependymal cells also)is their most common location;& in which they are particularly frequent in neurofibromatosis type

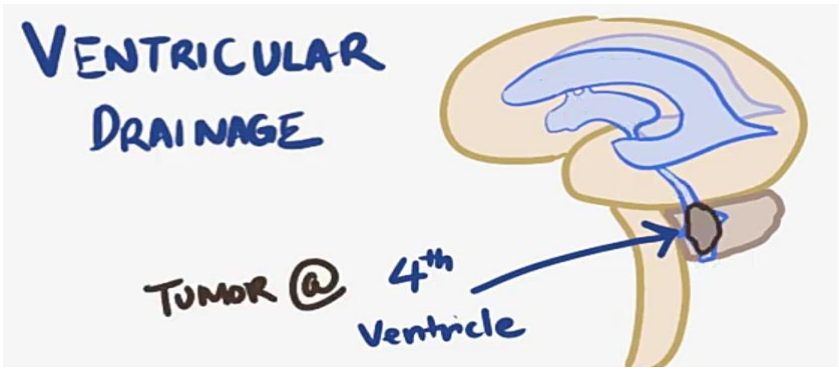
Neurofibromatosis:-is the genetic disorder or mutation which happend in nervous system and it will lead to develop of tumor in the nervous system

Note:-"Because ependymomas usually grow within the ventricles, CSF dissemination is a common occurrence"

للاسف كونه هذا الورم بصير داخل الventricular systemفهو يكون ملامس للCSF
وبالتالي يمكن ان ينتقل عن طريق الCSF الى مناطق اخرى بالدماغ ويعمل فيها مشاكل

Morphology(grossly&histology):-

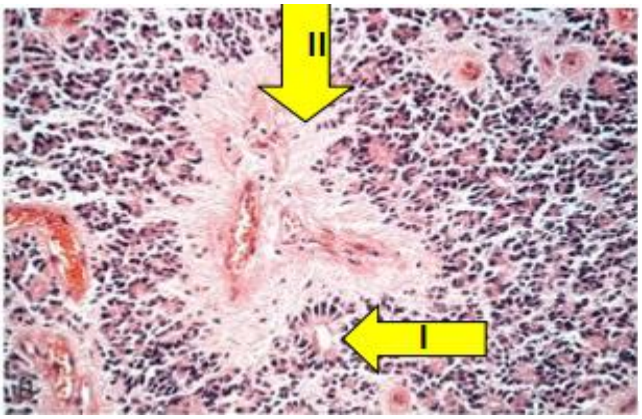
Grossly----->in the 4th ventricle, T are typically solid or papillary masses extending from the floor of the ventricle

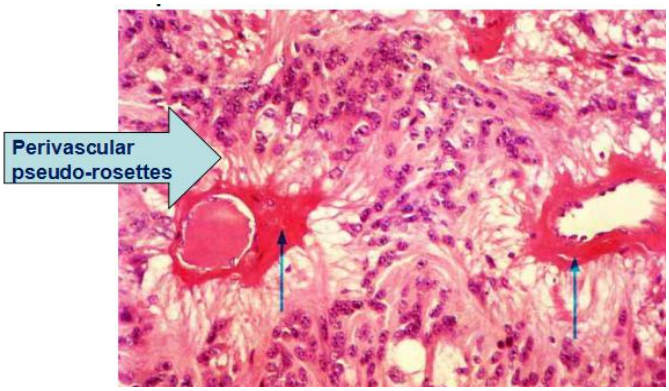


للاسف ممكن يكبر حجم الورم اكبر من اللازم ويسكر مجرى التصريف بال4th ventricle
ويمنع تصريف الCSFمما قد يؤدي الى hydrocephalus

Histology----->T cells, with regular round to oval nuclei & abundant granular chromatin. Between the nuclei there is a variably dense fibrillary background. T cells may form:
(I) rosettes or canals (round or elongated structures that resemble the embryologic ependymal canal, with long, delicate processes extending into a lumen.

(II)perivascular pseudo-rosettes are more frequently seen, in which T cells are arranged around vessels, with an intervening zone consisting of thin ependymal processes directed toward the wall of the vessel.





اكثر اشي بميز هذا الورم تحت المجهر هو رؤية الrosetes وهي عبارة عن شكل يشبه القناة او الانبوب وحوالين فتحة الانبوب بكون فيه processes extending into a lumen
وايضا بكون في عنا تحت المجهر ايضا بنشوف خلايا الورم بتتجمع حوالي الاوعية الدموية وبتترتب على شكل خيوط تلتصق بالسطح الخارجي للأوعية الدموية نسمي هذا الشكل perivascular pseudo-rosettes

-Anaplastic ependymomas show ↑ cell density & mitotic rates, necrosis, & less evident ependymal differentiation.

Neuronal Tumors

1-Central neurocytoma:- is a low-grade neuronal T found within & adjacent to the ventricular system (most commonly the lateral or 3rd ventricles), characterized by evenly spaced,round uniform nuclei & often islands of neuropil

هذا الورم نادر جدا جدا بصير بالعادة داخل او قريب من الventricular systemوهو طبعا يعتبر ورم حميد مش خبيث واذا بشوفه تحت المجهر بلاقي الخلايا فيه تحتوي على round uniform nucleiوالاهم انه يكون يحتوي على جزء من الneuropil

Neuropil:-is any area of nervous system composed mostly unmyelinated axons,dendrites&glial cells

2-Ganglio-gliomas:-are T with a mixture of glial elements(looking like a low-grade astrocytoma) & mature-appearing neurons (ganglion like). Most of these T are slow growing, but the glial component occasionally becomes frankly anaplastic, &the disease then progresses rapidly and these lesions often present with seizures.

يعني هو عبارة عن ورم مخلوط بين نوعين من الخلايا النوع الاول هو الglial cells والنوع الثاني هو الganglion cells ومن هنا جاءت تسميته ويعتبر هذا الورم حميد وبطيء النمو لحد معين فقط بحيث اذا صار frankly anaplastic بصير الورم ينمو اسرع واعراضه تظهر بشكل اسرع

Dysembryoplastic neuroepithelial tumor

Is a distinctive, low-grade T of childhood, showing slow growth & a relatively good prognosis after resection; it often present with seizures.

Most common location of this tumor:-

These lesions are typically located in the superficial temporal lobe.

Morphology(histology):-

1-consist of small round cells with features of neurons arranged in columns & around central cores of processes.

2-These typically form multiple discrete intracortical nodules that have a myxoid background.so there are well-differentiated "floating neurons" that sit in the pools of mucopolysaccharide-rich fluid of the myxoid background.

هذا الورم يعتبر ورم حميد ومن الاورام التي تنمو ببطئ ومش شائع كثير واذا بدنا نحكي عن اهم اشي بهذا الورم انه تحت المجهر بشوف الخلايا العصبية زي القوارب التي تطفو داخل بحيرة من الmucopolysaccharide materials

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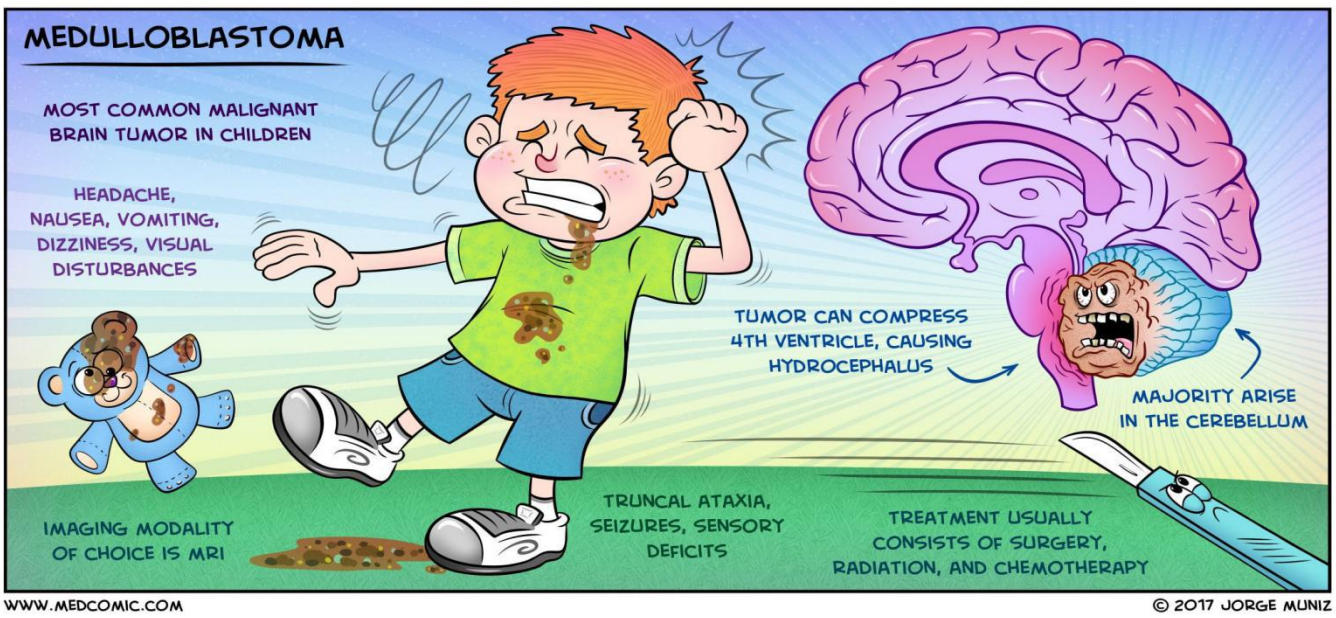
Medulloblastoma



Medulloblastoma:-It is highly malignant largely undifferentiated T, although it is of neuroectodermal origin& may express neuronal & glial markers.

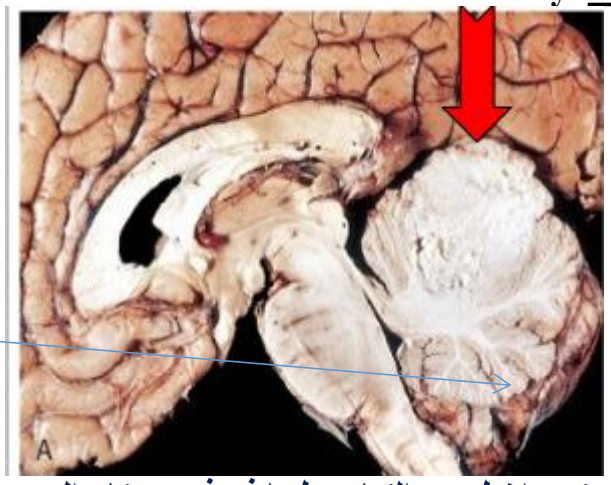
Epidemiology of this tumor:-

This tumors occurs mainly in children (which accounting for 20% of pediatric brain T) & exclusively (ONLY) in the cerebellum.

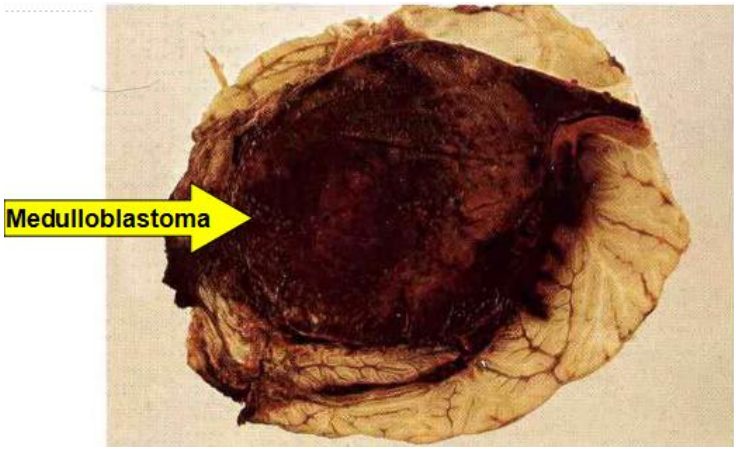
طيب بالنسبة لهذا الورم فهو ورم بصيب اكثر اشي الاطفال حيث يشكل 20% من كل الاورام التي تصيب الاطفال وهذا الورم يعتبرhighly undifferentiated malingnant والسبب انه undifferentiatedلأنه بطلع من neuroectoderm وهي خلايا اولية بمرحلة الامبريولوجي ما بكون صاير لها differentiation لسا وطبعا من الاسم ممكن يتهأي لنا انه الورم هذا بطلع بالmedulla oblongataبس ولكن بالغالب هو ما بطلع من الmedulla انما مكان حدوثه الاساسي والاكثر شيوعا هو الcerebellum(مش اسم على مسمى)

Morphology(grossly&histology):-

Grossly----->in children, medulloblastomas are located in the midline of the cerebellum; lateral T occur more often in adults. T is well circumscribed, gray, & friable, & may be seen extending to the surface of the cerebellar folia&may involving the leptomeninges.

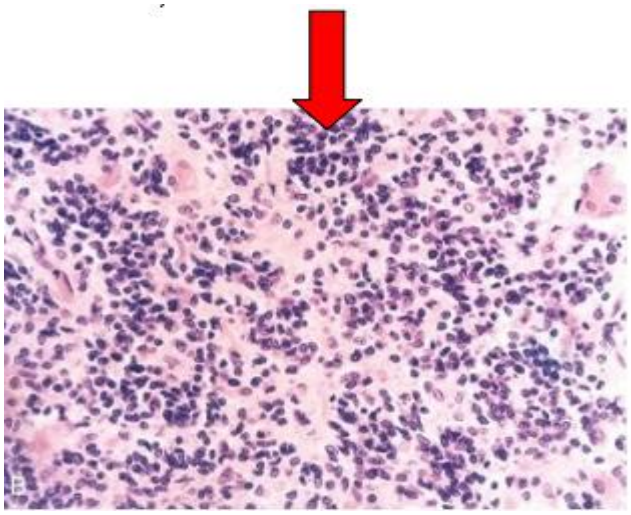


cerebellar folia



اهم حاجة لازم نعرفها انه الورم ده بالاطفال بكون اخطر من الكبار وطبعا في فرق بمكان الورم بين الاطفال والكبار فمثلا بالاطفال بكون الورم بالغالب بالmidline يعني اقرب للوسط واقرب للventricle 4th يعني ممكن يضغط على قناة تصريف الCSF ويعمل مشاكل منها الhydrocephallusاما بالكبار بالعمر بكون الورم laterally وابعد عن مكان تصريف الCSFوابعد عن الventricle 4th ولكن ممكن يكبر الورم اكثر عند الكبار ويخبط بال leptomeningesوايضا الخطر الاكبر انه هذا الورم كونه قريب من الCSF فهناك خطر من انتشاره بكل الCNS

Histology---->T are extremely cellular, with sheets of anaplastic ("small blue cells") . The Individual T cells are small, with little cytoplasm & hyperchromatic nuclei; mitoses are abundant
T cells spread by the CSF



يمكن ننسى اي حاجة ولا ننسى انه بالهستولوجي بتاع الورم ده بكون عندي خلايا زرقاء صغيرة"small blue cells" نتيجة سرعة انقسام النواة

-T of similar histology & poor degree of differentiation can be found elsewhere in the CNS T which called CNS primitive neuroectodermal tumor or CNS PNET.

طيب زمان هذا الورم كانوا يصنفوا من ضمن مجموعة خاصة من الاورام التي تصيب الCNS بنسميها PNET وهي مجموعة من الاورام الoriginبتاعها كلها منneuroectoderm ولكن بالوقت الحالي فصلوا الmedulloblastoma عن هاي المجموعة لأنه احنا بنعرف من الCNSانه اللي بيفصل الcerebrum from cerebellumحاجة اسمها tentorium فوجدوا انه معظم اورام مجموعة الPNETبتصير بالcerebrum ما عدا ورم medulloblastoma بصير بالcerebellum ففصلوه عن مجموعة الPNET

Treatment:-

It is highly malignant with poor prognosis for untreated patients, however, it is very radiosensitive.So with total excision & radiation, the 5-year survival rate may be 75%.

هذا المرض بدون علاج عنده very poor prognosis ولكن الاشي المطمئن انه هذا الورم very radiosensitive يعني يستجيب كويس للradiotherapy

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Parenchymal Tumors

(1)Primary Central Nervous System Lymphoma(PCNSL)

Epidemiology:-

1-It is the most common CNS neoplasm in immunosuppressed individuals (including transplant recipients & AIDS patients); in which lymphomas are nearly all driven by Epstein-Barr virus.

2-PCNSL is accounts for 2% of extranodal lymphomas & 1% of intracranial tumors.

احنا بنعرف انه الlymphomaهي عبارة عنtumors of lymphocyte cellsوخصوصا بتصير بالβ-lymphocyte.ودلوقتي نتكلم عن الPCNSL وهو عبارة عن نوع من الlymphomaاللي بيحصل بالCNSوسميناه primary لأنه ما بجي من مكان اخر من الجسم كmetastasisبل يحدث بالlymph tissue in CNS or spinal cord خصوصا لما تنزل المناعة بمرضى الايدز تحديدا فاحنا بنعرف انه جهاز المناعة هو المسؤول عن القضاء على الcancer cells فلو نزلت المناعة الخلايا السرطانية راح تتهيج او مش بس كده ممكن تزيد احتمالية الاصابة بالفيروسات التي تسبب cancer زي الEPV اللي بعمل lymphomaبمرضى الايدز منها الPCNSL

3-In non-immunosuppressed populations the incidence ↑ after 60 years of age; most of these T are diffuse large B-cell lymphomas.

احنا حكينا انه الPCNSLمعظمها يحدث بال-immunosuppressed patient-AIDS ولكن برضه وجدوا انها ممكن تصيب ناس ما عندهم امراض تنزل المناعة ولكن احتمالية الاصابة بتزيد بس بالاعمار الكبيرة فوق ال60 وخصوصا نوع ال diffuse large B-cell lymphomas

Morphology(grossly&histology):-

Grossly---->T often infiltrate all of the white, gray matter &cortex Periventricular spread is common.And the T are relatively well defined as compared with glial neoplasms but are not as discrete as metastases.

Histology---->most commonly, they are large-cell lymphomas, showing extensive areas of central necrosis; infiltrating the parenchyma of the brain & accumulate around BV

Treatment&prognosis:-

All primary brain lymphomas are aggressive with relatively poor response to chemotherapy as compared with peripheral lymphomas

للاسف انواع الPrimary lymphomaبتكونvery aggressive وممكن يصير لها metastasisبسهولة والمؤسف اكثر ان نوع الPCNSL لا يستجيب بشكل كويس للChemotherapyعلى عكس النوع الperipheral lymphomas اللي بتكون استجابتها احسن للchemotherapyفبالتالي ورم الPCNSLبكون عنده bad prognosis

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(2)Germ-Cell Tumors

Is the primary brain germ-cell T occur along the midline,most commonly in the pineal & the suprasellar regions.

احنا اخذنا بالGUعن الgerm cell tumor وحكينا انه بصير بالgerm cell الموجودة بالtestis&ovaries ولكن ايضا ممكن نتيجة embryonic defect يصير هذا الورم في اماكن خارج الgonadمثل حدوثه بالCNSتحديدا بالpineal & the suprasellar قريب من الhypothalamus

Epidemiology:-

1-This tumor is account up to 1% of brain T in people of European descent but as many as 10% of brain tumors in Japanese.

2-occurs during the first two decades of life .&90%Germcell T in the pineal region show a strong male predominance(male will affected more than female)

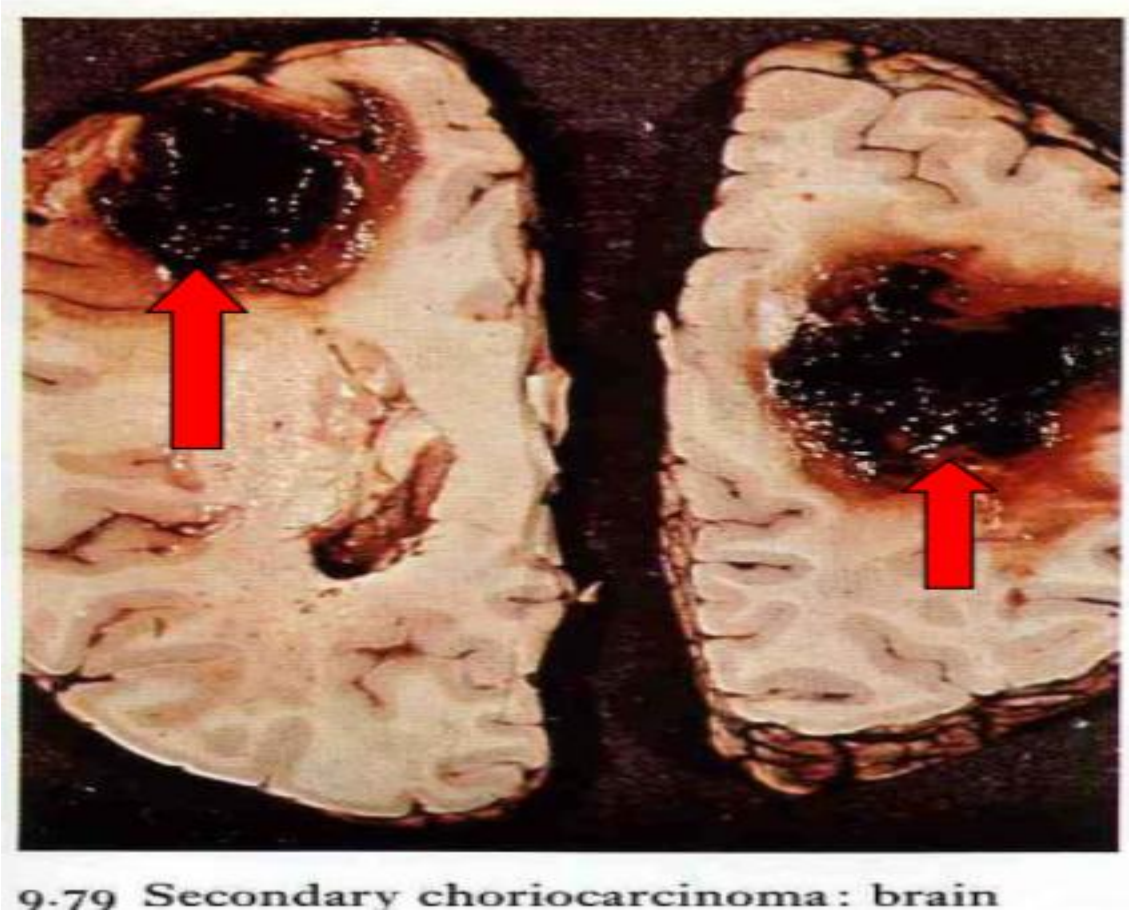
Notes:-

1-Germ-cell T in the brain share many of the features of their counterparts in the gonads.CNS T that is the counterpart to the testicular seminoma is called a germinoma

يعني الgerm cell tumorاللي بتصير بالCNS تشبه في خصائصها والهستولوجي بتاعها الgerm cell tumorاللي بتصير بالgonad بس الفرق بالاسم فمثلا كنت اسمي الgerm cell tumorاللي بتصير بالtestisهي testicular seminoma اما بسمي اللي بتصير بالCNSبgerminoma

2-CNS involvement by a gonadal germ-cell T secondareies is not uncommon

بحكيلك انه اغلب الgerm cell tumors in CNSبتكونprimary tumors ونادرا ما تكونsecondareiesوتجي من مكان اخر بالجسم زي الgonad



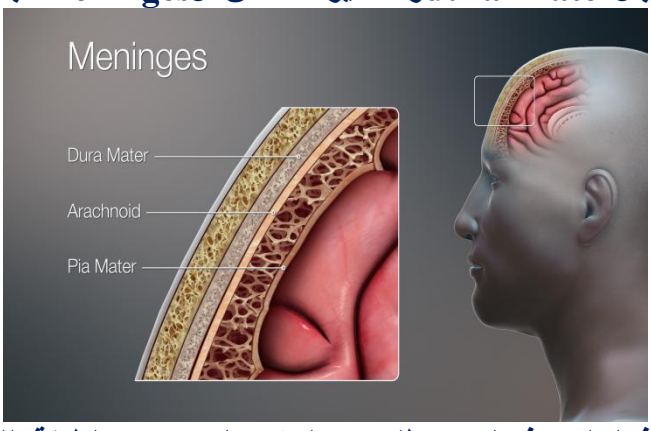
9.79 Secondary choriocarcinoma: brain

(3)Meningiomas

Meningioma:-it is a predominantly benign T of adults,which arising from dome-shaped meningeal arachnoid cells with base on meninges which attached to the dura

الورم ده من الاورام المهمة كلينيكالي وهو ورم حميد يصيب الكبار اكثر من الاطفال وخصوصا النساء وهذا الورم يحدث بالmeningeal arachnoid cells وبيفضل يكبر لحد ما يشبك بالdura mater وللتذكير فقط فان الmeningesعبارة عن 3 طبقات هي:-

1-pia mater
2-Arachnoid
3-Dura mater



فبالتالي هذا الورم بطلع من الخلايا الموجودة بالطبقة اللي بالنص"Arachnoid" وممكن يكبر هالورم ويشبك بالطبقة الخارجية اللي فوقه الdura mater

Site of tumors:-

This tumor may be found along any of the external surfaces of the brain(along the meningeal layers not in brain tissue)as well as within the ventricular system, where they arise from the stromal arachnoid cells of the choroid plexus.

Pathogenesis of this tumor:-

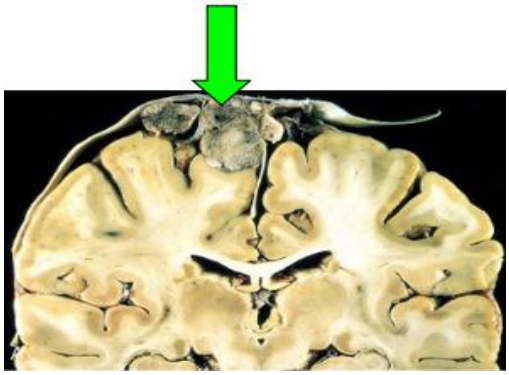
When multiple meningiomas are present, especially in association with 8th cranial nerve schwannomas or glial T, so the possible diagnosis is neurofibromatosis type 2,and %50 of cases of neurofibromatosis type 2 it has mutations in the NF2 gene on the long arm of chromosome 22.

وجد العلماء انه 50% من حالات الmultiple meningiomas لا يحدث فيها هذا الورم لوحده انما يكون معاه كوكتيل كده بقا من الاورام الثانية فبلاقي نفس المريض هذا معاه ورم اخر يسمىschwannomas وهو ورم يحدث بالschwann cells in myelin sheath وهي الخلايا المسؤولة عن صناعة الPNS myelin sheath in ويعود السبب بحدوث هذا الكوكتيل من الأورام الى حدوث mutations in NF2 gene المسؤول عن صناعة بروتين اسمه merlin حيث يكون هذا البروتين مسؤول عن تنظيم انقسام الخلايا الموجودة بالschwann cells&meninges وبالتالي اذا حدثت طفرة في هذا الجين المسؤول عن صناعة هذا البروتين فانه لن يتم صناعة هذا البروتين وبالتالي سوف يحدث انقسام غير منظم وسريع بخلايا الschwann cells&meninges مما يؤدي الى حدوث اورام فيها

ملاحظة:-المكتوب بالازرق هون من برة المادة للفهم فقط

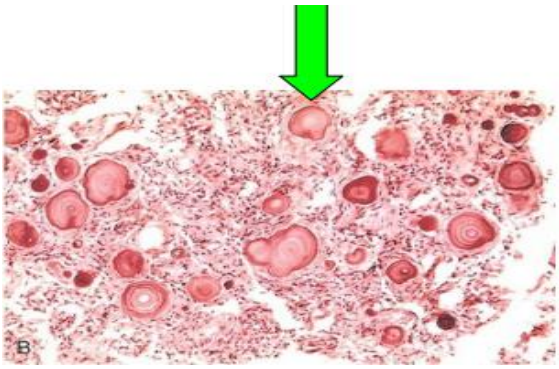
Morphology(grossly&histology):-

Grossly---->meningiomas grow as well-defined dural-based masses that compress underlying brain but are easily separated from it . Extension into the overlying bone may be present

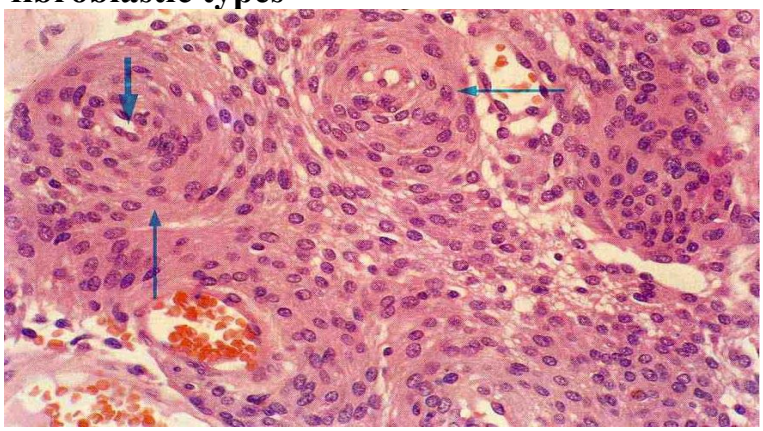


Histology---->(very imp)

1-Psammomatous(psammoma bodies),with Syncytial whorled clusters of cells that sit in tight groups without visible cell membranes



2-Fibroblastic,with elongated cells(spindle cells) &abundant collagen deposition between them
3-Transitional type,which shares features of the syncytial & fibroblastic types



4-Secretory type,with PAS-positive intracytoplasmic droplets
5-Microcystic type, with a loose,spongy appearance.

-Atypical meningiomas:-
Are T recognized by a higher mitotic rate, showing more aggressive local growth,higher rate of recurrence.&Anaplastic (malignant) meningiomas are highly aggressive T, which resemble high-grade sarcoma

Prognosis of meningiomas:-
Prognosis of meningiomas is influenced by the size & location of the lesion, surgical accessibility, & histologic grade.but Most meningiomas are easily separable from underlying brain, but some infiltrate the brain. Brain invasion is associated with ↑ risk of meningioma recurrence.

Sympotoms of meningiomas:-
They usually present with vague nonlocalizing symptoms, or with focal findings due to compression of underlying brain
اعراض هذا الورم ممكن تكون مبهمة ومش متوقعة "vague" او انه ممكن يعمل اعراض حسب المنطقة اللي بضغط عليها بالدماغ

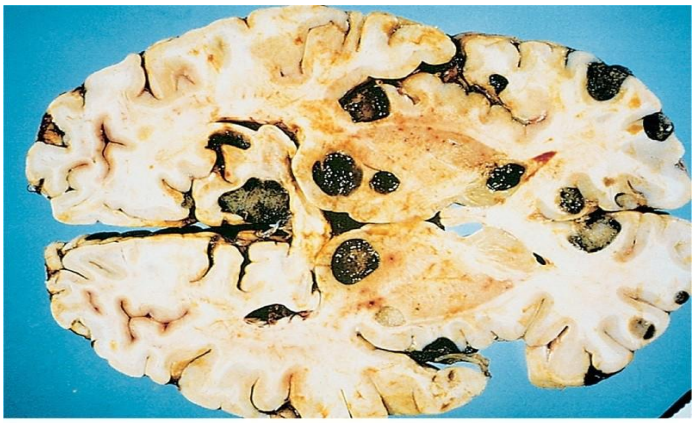
Metastatic Tumors in the CNS

Epidemiology:-
1-Tumors of intracranial (Brain & meninges) are 50% metastatic & mostly are carcinomas.

2-The commonest 5 primary cancer sites, which account for about 80% of all metastases are:
A-lung

B-breast
C-skin melanoma
D-kidney
E-GIT

Morphology(grossly&histology) of metastatic tumor in CNS:-
GROSSLY----->In the brain, metastases may be single but often are multiple,form sharply demarcated masses,usually surrounded by a zone of edema



يعني اذا بنتطلع على هذه الاورام اللي جاي على الدماغ من skin melanoma بنلاقيها well-demarcated margins يعني بقدر اميز بالزبط حدود الورم عن الخلايا اللي مش مصابة كانه الورم محاط بجدار عازل

Microscopically--->the boundary between T & brain parenchyma is well defined.
حتى على مستوى الهستولوجي بقدر اميز حدود الورم عن الخلايا الطبيعية

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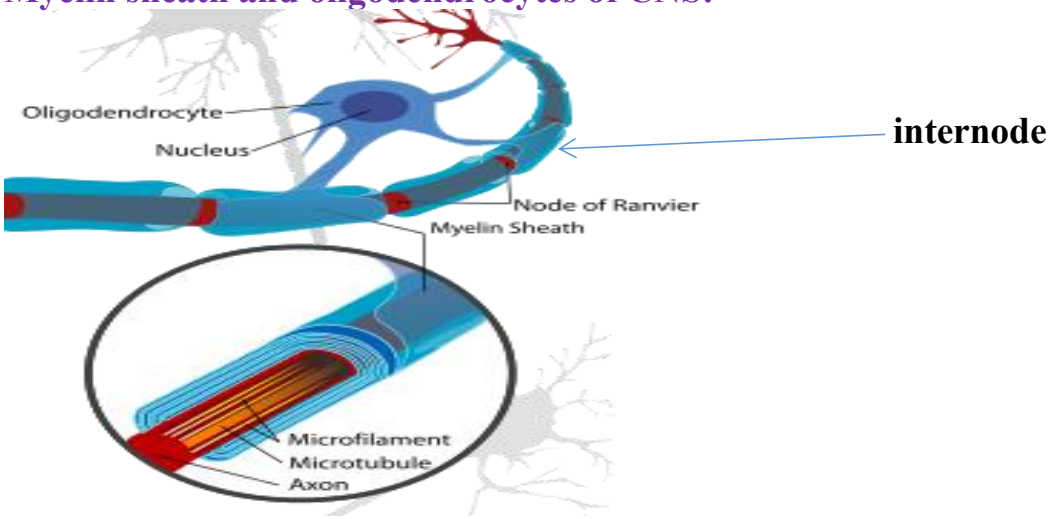
Paraneoplastic syndromes

Paraneoplastic syndromes:is a syndrome which may involve the peripheral organ(lung,breast…)& CNS due to over-activity of immune system against tumor&sometimes, even before the clinical recognition of the malignant T. These syndromes are most commonly associated with small-cell ca of the lung.
اللي بصير بهاي الsyndromeانه الجسم ببلش يكون Ab ويهاجم خلايا السرطان ومن اشهرها سرطان الlung small cell Ca of ولكن كونه جهاز المناعة تهيج زيادة عن اللزوم فبتبلش الAbوخلايا المناعة تهاجم الnormal tissueومنها الCNS مما يؤدي الى عدة امراض بالCNS منها:-

Characteristic paraneoplastic syndromes patterns of CNS include:-
1-Limbic encephalitis causing a subacute dementia
2-Subacute cerebellar degeneration resulting in ataxia, with destruction of Purkinje cells
3-Subacute sensory neuropathy leading to altered pain sensation with loss of sensory neurons from dorsal root ganglia.

PRIMARY DISEASES OF MYELIN

Myelin sheath and oligodendrocytes of CNS:-

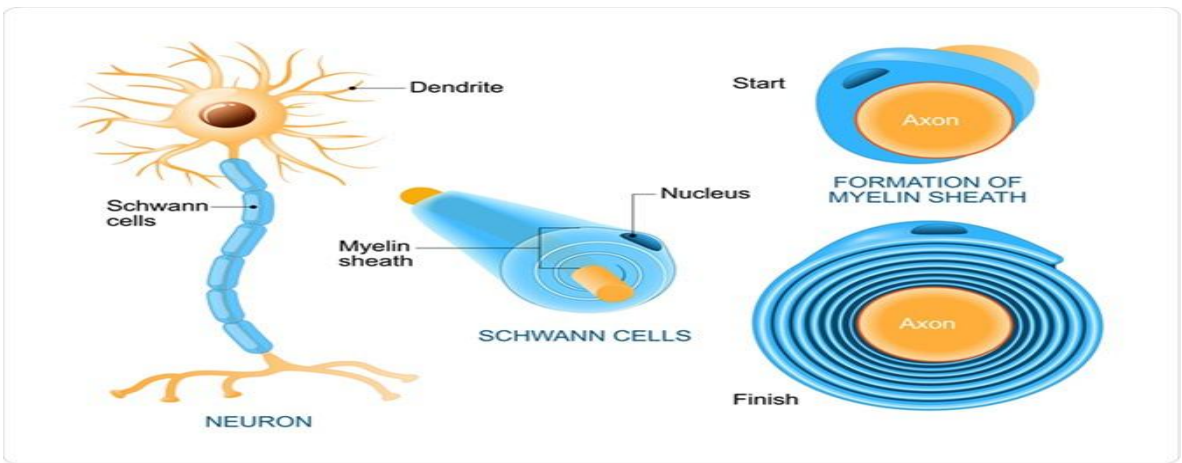


Normally,within the CNS,axons are tightly ensheathed by myelin, which serves as an electrical insulator to allow rapid propagation of impulses.
Myelin consists of multiple layers of the specialized plasma membrane of oligodendrocytes,with most of the cytoplasm excluded These portions of the oligodenrocyte membrane contain specialized proteins & lipids that contribute to the orderly packing of the layers&One oligodendrocyte cell extends processes toward many different axons & wraps a segment of roughly a few hundred microns of axon

احنا بنعرف من الCNSانه الoligodendrocytesهي المسؤولة عن صناعة ال Myelin sheath
ويمثل الmyelin sheathال electrical insulatorالذي يسرع الaction potential
وكما نرى بالصورة فان الcell membrane of oligodendrocytes بتتفرع وبتروح بتلف وبتغلف الaxonsويحتوي الmyelin sheath على بروتينات ونوع خاص من الليبيد

-Each of these segments is called an internode, & the gaps between internodes are known as nodes of Ranvier. Although myelinated axons are present in all areas of the brain, they are the dominant component in the white matter; therefore,most diseases of myelin are primarily white matter disorders

Myelin sheath and Schwann of PNS:-



Normally, the myelin in peripheral nerves is similar to the myelin in the CNS but, has several important differences:-

1-Peripheral myelin is made by Schwann cells, not by oligodendrocytes

2-Each Schwann cell in the peripheral nerve contributes to only one internode,while in the CNS, many internodes comes from a single oligodendrocyte.

3-The specialized proteins & lipids are also different, so because of that the most diseases of CNS myelin don't significantly involve the peripheral nerves,& vice versa(Thanks God)

-If the myelin along a set of axons is disrupted, there are changes in the ability of these axons to transmit signals, &the symptoms depends on the site(or sites, since most diseases of myelin are multiple, affecting many regions of the brain at the same time) where demyelination occurs

يعني زي ما حكينا سابقا فان الmyelin sheathمسؤول عن نقل الnerve impulse
بكفاءة فبالتالي اذا تكسر الmyelinراح تقل سرعة انتقال الaction potential

The natural history of demyelinating diseases is determined, in part, by:-

(1) the limited capacity of the CNS to regenerate normal myelin
(2) the degree of secondary damage to axons that occurs as the disease runs its course

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Myelin disease

Generally, diseases involving myelin are of 2 broad groups:-

(I)Demyelinating diseases of the CNS:are acquired conditions, characterized by damage to previously normal myelin.and there are many reasons which may cause demyelinating disease such as:-

1-immune-mediated injury,which is the commonest cause of the disease in this group such as multiple sclerosis (MS)&related disorders.

يعتبر امراض الautoimmuneمن اشهر الامراض التي تسبب demyelination dz
حيث تتكون مثلا auto-Abتهاجم الmyelin sheath وتكسرها وراح نفصل بهذا النوع اكثر زي الmultiple sclerosis

2-viral infection of oligodendrocytes as in progressive multifocal leukoencephalopathy{PML}

كونه الoligodendrocytesهي اللي بتصنع الmyelin sheath فاذا صار فيها infection راح تتدمر وتبطل تصنع Myelin sheath

3-injury caused by drugs & other toxic agents

(II)Leukodystrophy or dysmyelinating diseases:-it is occur when the myelin is not formed properly or it has abnormal turnover kinetics; &are usually associated with mutations affecting the proteins required for formation of normal myelin, or mutations that affect the synthesis or degradation of myelin lipids.

هون عكس النوع الاول هاي الامراض تنتج نتيجة حدوث طفرة بالجين المسؤول عن صناعة البروتين او الليبيد اللي بكون myelin sheathفاما انه بوقف تصنيع الmyelin sheath او انه بتنصنع بس بتكونfunctionally inactive

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Multiple Sclerosis (MS)

قبل البدء انصح بمشاهدة فيديو اسموزيز لهذا الموضوع على اليوتيوب شامل الموضوع بشكل مرتب كثير وبسم الله نبدأ عافانا واياكم الله من هذه الامراض

MS is an autoimmune demyelinating disorder which characterized by

(1) distinct episodes of neurologic deficits,separated in time

(2) white matter plaques that are separated in space.

راح نحكي عن نقطة 1 الخاصة بالنوبات بهذا المرض بالتفصيل كمان شوي ان شاء الله

Pathogenesis of the disease:-

Immune mechanisms that may be the cause of myelin destruction have been investigated because of prominence of chronic inflammatory cells within & around MS plaques.

So Experimental allergic encephalomyelitis is an animal model of MS in which demyelination & inflammation occur after immunization with myelin, myelin proteins, or certain peptides from myelin proteins.

In this model, the lesions are caused by a T cell-mediated DHR (Type IV) to myelin proteins, & the same immune mechanism is thought to be central to the pathogenesis of MS

طيب اول اشي لازم نعرفه عن مرض التصلب اللوحيMSانه مرض autoimmune dz يعني يحدث فيه hypersensitivity reaction type IV(cell mediated) بحيث تهاجم خلايا الT-cellخلايا الoligodendrocytes وبتدمرها ومش بس كده دي كمان بتنادي خلايا الB-cellوبتخليها تصنع autoAbعشان تهاجم خلايا الoligodendrocytes الغلبانة وكونه تكسرت خلايا الoligodendrocytesالمسؤولة عن صناعة الmyelin sheath داخل الCNSتكسرت فانه لن يتم صناعة الmyelin sheath وراح تبدأ تتكسر الaxons of nerve fibers in CNS اللي بتعملك اعراض هذا المرض

طيب كيف العلماء فسروا الية حدوث هذا المرض؟

جابوا العلماء فأر وحقنوه بmyelin sheath&protein فلاحظوا انه تكونت خلايا T-cellهاجمت هاي البروتينات ومش بس كده برضه راحت خلايا الT-cell هاي على الدماغ وعملت تدمير للmyelin sheathعند الفأر وعملت عنده اعراض الMS

نقطة اخرى بهاي الفقرة ايضا كونه هذا المرض عمل hypersensitivity type IV فاحنا بنعرف انه هذا النوع من الimmune reactionبعمل plaque فاكيد راح يعمل برضه بهذا المرض white matter plaques

Reasons of the disease:-

MS, like other autoimmune diseases, is believed to be caused by a combination of genetic & environmental factors that result in a loss of tolerance to self proteins (the myelin antigens in the case of MS),so the disease it may be caused by:-

1-genetic cause,MS concordance rate for monozygotic twins is 25%, with a much lower rate for dizygotic twins indicates a strong, but not causative, role for genes. Genetic linkage of MS susceptibility to the HLA-DR2 extended haplotype is well established

2-environmental cause,as a transmissible agent(such as viral infection) has been proposed as a cause of MS, but never been conclusively identified

Epidemiology of the disease:-

1-MS is the commonest demyelinating disorders, having a prevalence of 1/ 1000 persons in US & Europe like Malignancy

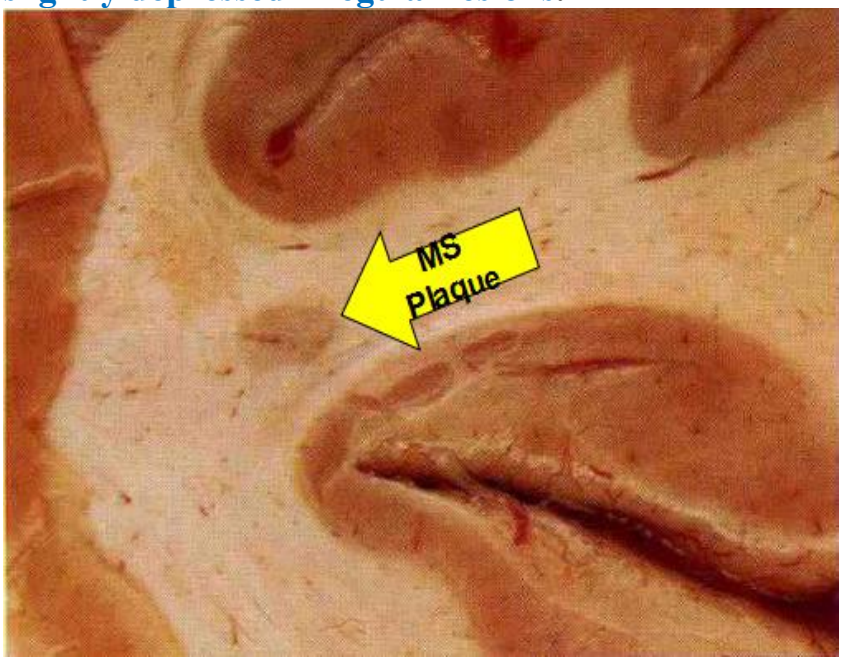
2-MS may affect any age, but onset in childhood or after age 50 years is relatively rare(most commenly affected 20-40y)

3-MS M/F ratio is 1:2(like other autoimmune dz which affected the female more than male)

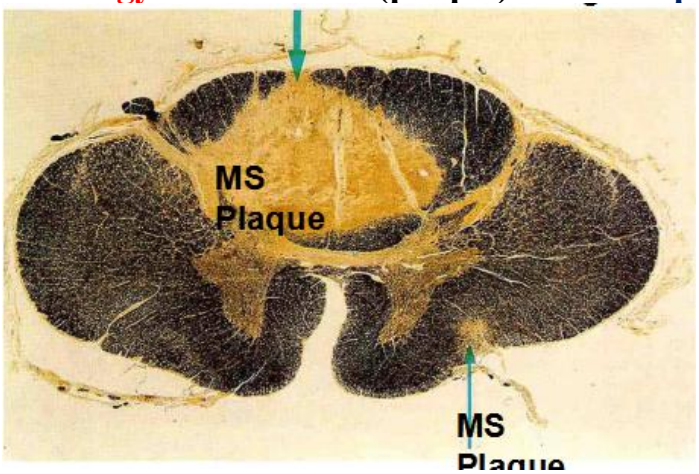
4-MS risk of development is X15-fold higher when the disease is present in a first-degree relative.

Morphology(grossly&histology):-

GROSSLY---->MS is a white matter disease, The affected areas show multiple well-circumscribed plaques, glassy, gray-tan, slightly depressed irregular lesions.



Histology--->the lesions(plaque) have sharply defined borders



Plaques

Plaques common location:-

Plaques are commonly occur beside the ventricles, & are frequent in the optic nerves & chiasm, brain stem, ascending &descending fiber tracts, cerebellum&spinal cord.

Active plaques VS inactive plaques:-

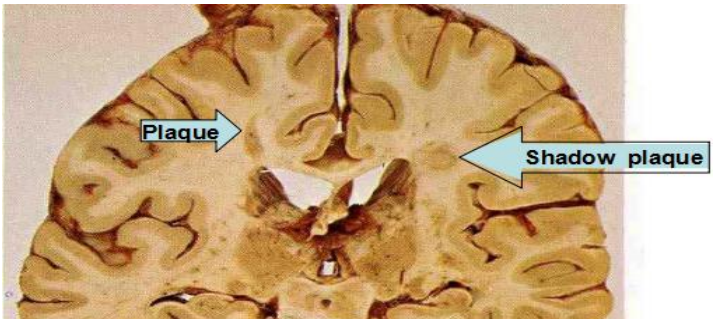
-In an active plaque there is evidence of ongoing of:-

1-Perivascular cuff of lymphocytes & monocytes.(inflammation is found)
2-Abundant macrophages containing myelin debris.
3-Myelin breakdown.
4-Small active plaques are often centered on small veins
5-Axons are relatively preserved, although they may be reduced in number.

Note:-While MS characterized by demyelination out of proportion to axonal loss, however some injury to axons does occur

-Inactive plaques MS (when plaques become quiescent) there is evidence of ongoing of:-

1-Disappearance of inflammation
2-We have little or No myelin.
3-Gliosis & prominent astrocytic proliferation
4-Shadow plaques may be seen , where the border between normal & affected white matter is not sharply circumscribed. Here, thinned-out myelin sheaths can be demonstrated, especially at the outer edges, suggesting that this border region represents either
(1) incomplete myelin loss
or (2) partial remyelination

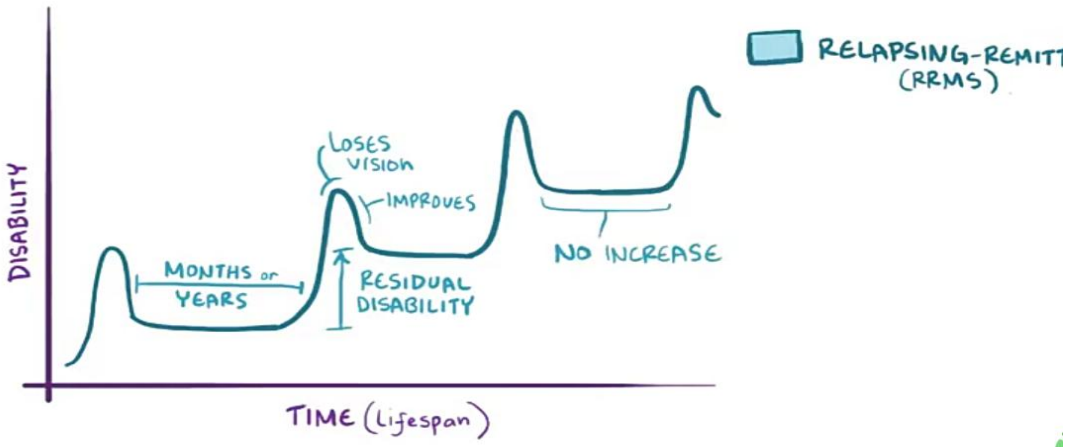


Clinical manifestation of MS:-

MS shows relapsing & remitting episodes of neurologic deficits in most individuals. The frequency of relapses tends to during the course of the illness, but there is a steady neurologic deterioration in a subset of patients.

So Clinically, commonly, there are multiple episodes of injury (relapses) followed by episodes of recovery (remissions);typically, the recovery is not complete, with gradual, often stepwise, accumulation of ↑ neurologic deficits

In any individual patient, it is hard to predict when the next relapse will occur!



دلوقتي اهم حاجة نعرفها عن المرض ده انه مزاجي وبتلاقيه شوي بتروح اعراضه عن المريض لفترة معينة بعدين بترجع تجيه الattack بعدين بتروح وبعدين ترجع وهكذا ولكن الاسوء من كده انه كل مرة بغيب فيها المرض عن المريض لما يرجع له برجع له باعراض اسوء من الاول بكثير وهاي الاعراض بتضلها تتطور مع مرور الوقت فبالتالي ممكن يعمل التالي كاعراض:-

1-Unilateral visual impairment,occurring over the course of a few days is a frequent initial symptom of MS due to optic nerve involvement (optic neuritis, retrobulbar neuritis).

2-Involvement of the brain stem produces cranial nerve signs & ataxia, & can disrupt conjugate eye movements.

3-Spinal cord lesions give rise to motor & sensory impairment of trunk & limbs, spasticity, & difficulties with the voluntary control of bladder function.

Diagnosis of the disease:-

1-CSF shows (1) in 3/1 of cases there is moderate pleiocytosis

2-A mildly elevated protein level with an ↑ proportion of γ-globulin, which when examined further, show oligoclonal bands, representing antibodies directed against a variety of antigenic targets Although these antibodies constitute a marker for disease activity, it is not clear if they are a critical part of the disease mechanism.

3-MRI can show the distribution of lesions across the CNS during active disease. From this, it has become clear that there are often more lesions in the brains of MS patients than might be expected by clinical examination & that lesions can come & go much more often than was previously

Acquired Demyelinating Diseases

Pathogenesis of acquired demyelinating disease:-

Immune-mediated demyelination can occur after a number of systemic infectious, including relatively mild viral diseases,which are not thought to be related to direct spread of the infectious agents to the nervous system, rather…

So it is believed that the immune response to pathogen-associated antigens cross-reacts with myelin antigens, &resulting in myelin damage(Cytotoxic reaction, Type II)

هاي الامراض مبدأ حدوثها بالزبط بصير زي حالة الrheumatic fever انه اللي بصير بدخل فايروس معين على الجسم فبهاجمه الجسم وبكون ضده Antibodies ولكن لسوء الحظ بكون الانتيجن الخاص بالفايروس بشبه الانتيجين الموجود على سطح الmyelin sheath فيحدثcross reactivityبينهم فبتصير الAb اللي تكونت ضد الفايروس بتصير تهاجم الmyelin sheath لانه الانتيجين للثنتين متشابهات

(1)Post-infectious demyelination disease

Two patterns of post-infectious, immune-mediated demyelination recognized, both, unlike MS, are monophasic illnesses with relatively abrupt onset

هسا اهم شغلة لازم نميزها بين الMSوامراض الpost-infectious demyelination انه الMSهوtype IV hypersensitivity اما الpost infectiousهوtype II وتشمل هذه المجموعة ما يلي من الامراض:-

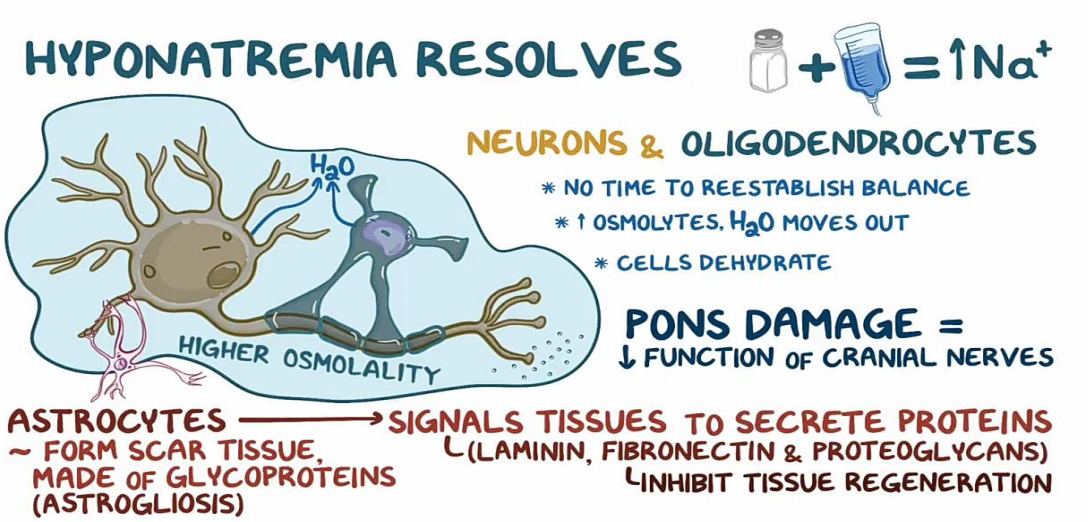
(I)Acute disseminated encephalomyelitis,symptoms typically develop a week or two after the antecedent infection &suggest diffuse brain involvement (rather than the focal findings typical of MS) with headache, lethargy, & coma, which progress rapidly, to a fatal outcome in about 20% of cases; in the remaining patients there is complete recovery.

اهم اشي لازم نعرفه بهاي الفقرة انه هذا المرض بكون فيهdiffuse inflammation اما بالنسبة للMSبكونfocal destruction or inflammation على شكلplaques

(II)Acute necrotizing hemorrhagic encephalomyelitis is a more devastating, typically affects young adults & children.

(2)Central pontine myelinolysis

Is nonimmune process characterized by loss of myelin involving the center of the pons, most often after rapid correction of hyponatremia &It may occurs in a variety of clinical settings which including severe electrolyte or osmolar imbalance & alcoholism.



هذا المرض لو بدنا نحلل اسمه بنفهمه فمثلا كلمة pontine بنعرف منها انه بصيب الpons وكلمةmyelinolysisتعني lysis of myelin sheath والميكانيزم تبعت هذا المرض هي انه لما يصير عند شخص حالةhyponatremiaبتقل نسبة ايونات الصوديومNa^+خارج الخلية بالextracellular spaceفلما يجي على المستشفى بنعطيه IV fluid يحتوي على ايونات الصوديوم فاذا اعطيناه اياه بسرعة ممكن يصير عندي بالextracellular space Hyperosmolar concentration of Na+ نتيجة الايونات اللي اعطيناه اياهم واحنا زي ما بنعرف بالفسيو فالماء تنتقل من الhypotonic to hypertonic فراح تنتقل هاي الماء من داخل الmyelin sheathالى خارج الخلية مما يؤدي الى تدمر الmyelin

Clinical manifestation:-

Most characteristic lesion occurs in the pons fibers,which carry signals to motor neurons in the spinal cord, resulting in rapid quadriplegia(paralysis of all four limb and torso)

(3)Progressive multifocal leukoencephalopathy(PML)

is a demyelinating disease that occurs following reactivation of JC virus in immunosuppressed patients

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Leukodystrophies

Leukodystrophies:-are inherited dysmyelinating diseases in which the clinical symptoms derive from either abnormal myelin synthesis or turnover. Some disorders involve lysosomal enzymes,while others involve peroxisomal enzymes; a few are associated with mutations in myelin proteins.

فيديو اسموزيز شارح المرض كويس للي بحب يشوفه هسا هذا المرض بسميه اسم اخر هو Dysmyelinating disease ويعني انه الmyelin sheath فيه خلل جيني انه ما بتكون

اصلا او انه بتكون بس فيه خلل يعني functionally inactive.
طيب الميكانيزم الاخر اللي بتفسر هذا المرض انه في عندي انزيمات بال lysosome or paroxisome بتكون بالوضع الطبيعي بتضلها تكسر ال lipid and fat of myelin عشان يتجدد يعني بتشيل القديم عشان تحط مكانه جديد بس اللي بصير بهذا المرض انه بصير فيه طفرة جينية بالجينات المسؤولة عن صناعة هاي الانزيمات فبصير عندي Overactivity of these enzymes فبتصير تأكل من ال lipid of myelin زيادة عن اللزوم فبتسبب هذا المرض

Epidemiology of the disease:-

Most are autosomal recessive, although it may be X-linked diseases

Morphology(grossly&histology):-

GROSSLY---->lesions of leukodystrophies are found in the white matter, in some diseases, there may be early patchy involvement; however, in the end, nearly all leukodystrophies show diffusely affected abnormal white matter:

(I) in color(gray & translucent)

(II) in volume (decreased)

With the loss of white matter, the brain becomes atrophic& the ventricles enlarge, & secondary changes can be found in the gray matter

Histology---->myelin loss is common, with macrophages stuffed with lipid.Some leukodystrophies also show specific inclusions, due to accumulation of particular lipids

مش احنا حكينا انه بهذا المرض بتكسر الانزيمات ال lipid or fat of myelin فاكيد راح يجي عامل النظافة بالجسم(macrophages) وينظف كل هالوسخ الناتج من عمليات التكسير فلو نظرت تحت المجهر بتلاقي macrophages with lipid debris inside it

Clinical manifestation:-

Clinically, Each disorder of the various leukodystrophiesh as a characteristic clinical presentation, &Affected children are normal at birth,but begin to miss developmental milestones during infancy & childhood

Diffuse involvement of white matter leads to deterioration in motor skills, spasticity, hypotonia, or ataxia.

يعني الطفل اللي بنولد مع هذا المرض ببين طبيعي بالبداية بس لما يبلش يكبر ويتطور جسديا وعقليا بصير الاحظ انه في اشي غلط بمشيته مثلا بعضلاته او ايديه الى اخره

Diagnosis of the disease:-most can be diagnosed by genetic or biochemical methods.