Neuropathology
Questions

Level of difficulty 1.

1. The lesions in this 7-month-old baby girl shown below are most likely caused by:

   A. Coagulopathy
   B. Resuscitation
   C. Chest trauma
   D. Traumatic brain injury
   E. All of the above

Level of difficulty 1.

2. A 4–year-old boy with a history of headaches and on-and-off vomiting for 2 weeks had the MRI findings shown below. The most likely diagnosis is:

   A. Medulloblastoma
   B. Glioblastoma of the cerebellum
   C. Ependymoma of the 4th ventricle
   D. Aqueductal stenosis
Level of difficulty 2.

3. Which of the following statements about the lesion shown below is not true?

![Histological image]

A. There are over ten histological subtypes
B. The tumor is attached to the dura
C. Deletion of chromosome 22 is frequent
D. Brain invasion is frequent
E. It is more common in women

Level of difficulty 3.

4. Which of the following statements about the lesion shown below is not true?

![Histological image]

A. It may be an intra-spinal tumor
B. Malignant degeneration is more frequent after irradiation
C. The optic nerve is a common intracranial location
D. It may occur in an autosomal dominant pattern
5. A 43-year-old patient has had headaches and declining mental function for 5 weeks. MRI shows mild hydrocephalus with periventricular enhancing lesions. A stereotactic biopsy is obtained (shown below). The most likely diagnosis is:

A. HIV encephalitis  
B. Oligodendroglioma  
C. Cerebral lymphoma  
D. HSV encephalitis  
E. Cereral abscess

6. A 57-year old patient had fever, seizures and obtundation for 4 days. MRI shows a necrotic hemorrhagic lesion of the right temporal lobe with surrounding edema. A stereotactic biopsy is shown below. The most likely diagnosis is:

A. Cerebral abscess  
B. Hemorrhagic infarct  
C. Cerebral lymphoma  
D. HSV encephalitis

7. A 27-year-old woman with headaches and vomiting had a cystic cerebellar mass with a protruding nodule. Stereotactic biopsy is shown below. The most likely diagnosis is:
A. Metastatic clear cell carcinoma  
B. Hemangioblastoma  
C. Oligodendroglioma  
D. Old infarct with macrophage reaction  
E. Glioblastoma

Level of difficulty 3.

8. A 60-year-old previously healthy patient developed hemiparesis and aphasia. MRI showed an enhancing left hemispheric lesion. A brain biopsy was done (shown below). The most likely diagnosis is:

A. Changes around the wall of an abscess  
B. A gemistocytic astrocytoma  
C. A two month old ischemic infarct  
D. An old MS plaque
Level of difficulty 5.

9. This electron micrograph is obtained from the cross section of a peripheral nerve biopsy.

The arrow is pointing to a:
A. Reich granule  
B. Regenerating cluster  
C. Mitochondrion  
D. Tomaculum  
E. Bands of Büngner

Level of difficulty 4.

10. This tumor is obtained from the parietal lobe with a subventricular location.

The best diagnosis of this case is:
A. Choroid plexus papilloma  
B. Papillary ependymoma  
C. Subependymal giant cell astrocytoma  
D. Clear cell ependymoma  
E. Central neurocytoma
11. The neoplastic cells of this primary pineal tumor is most likely to be immunoreactive for:
   1. Neurofilament proteins
   2. CD-117 (c-kit)
   3. Synaptophysin
   4. Placental alkaline phosphatase (PLAP)

   A. I, 2, and 3 are true
   B. Only 1 and 3 are true
   C. Only 2 and 4 are true
   D. Only 4 is true
   E. None of the above

12. This primary cerebellar tumor is most likely to be immunoreactive for:
   1. Epithelial membrane antigen (EMA)
   2. Cytokeratin AE1/AE3
   3. CD 10
   4. Inhibin

   A. I, 2, and 3 are true
   B. Only 1 and 3 are true
   C. Only 2 and 4 are true
   D. Only 4 is true
   E. None of the above
13. This tumor is obtained from the filum terminale. The most appropriate diagnosis is:

A. Meningioma  
B. Schwannoma  
C. Disseminated medulloblastoma  
D. Myxopapillary ependymoma  
E. Paraganglioma

14. This type of astrocytoma is most commonly associated with:

A. Cowden Syndrome  
B. Von Hippel-Lindau syndrome  
C. Basal cell nevus syndrome  
D. Neurofibromatosis 1  
E. Neurofibromatosis 2

15. A 54-year-old man with an enhancing right parietal mass associated with substantial edema. This photo is obtained from the intraoperative cytologic preparation. The most likely diagnosis is:

A. Metastatic small cell carcinoma  
B. Primitive neuroectodermal tumor  
C. Glioblastoma  
D. All of the above are possible  
E. None of the above are possible
16. The two stellate cells being shown in this intraoperative cytologic preparation from a 56-year-old man are most likely:

- A. Oligodendrocytes
- B. Ependymal cells
- C. Reactive astrocytes
- D. Neurons
- E. Microglial cells

17. A 35-year-old woman with an exophytic ventricular mass around the foramen of Monro and hydrocephalus. This photo is obtained from the intraoperative cytologic preparation.

These cells are most compatible with:

- A. Meningioma
- B. Central neurocytoma
- C. Subependymal giant cell astrocytoma
- D. All of the above
- E. None of the above
18. The specimen is taken from a 45-year-old woman with a sacral mass. The photos are obtained from the intraoperative cytologic preparation.

The most likely diagnosis is:
A. Myxopapillary ependymoma
B. Schwannoma
C. Mucin producing metastatic adenocarcinoma
D. Chordoma
E. Ewing's sarcoma

19. A 54-year-old woman with a ring enhancing right frontal mass associated with substantial edema and midline shift. The surgeon described a cystic lesion. The intraoperative specimen has a fluid like consistency. This photo is obtained from the intraoperative cytologic preparation.

The most likely diagnosis is:
A. Abscess
B. Lymphoma
C. Metastatic melanoma
D. Glioblastoma
E. Infarct
20. The pathologic changes in the brain illustrated here is resulted from:

A. Neoplastic changes  
B. Viral encephalitis  
C. Hypoxic/ischemic changes  
D. A leukodystrophy  
E. There are no pathologic changes here

21. In comparison to the classic type of medulloblastoma, the type of medulloblastoma being shown here has:

A. Better prognosis  
B. Worse prognosis  
C. The same prognosis as the classic type  
D. Prognosis is not related to histology  
E. This is not a medulloblastoma

22. The pathologic changes being illustrated here are diagnostic for:

A. Amnion rupture sequence  
B. Anton syndrome  
C. Caudal regression syndrome  
D. Down syndrome  
E. Fetal alcohol syndrome
23. Characteristics of the type of tumor being illustrated here include:
   1. Associated with neurofibromatosis 2
   2. Associated with neurofibromatosis 1
   3. Usually enhance on MRI
   4. Usually do not enhance on MRI

   A. 1, 2, and 3 are true
   B. 1 and 3 are true
   C. 2 and 4 are true
   D. Only 4 is true

24. The pathologic process being illustrated here is:

   A. Tonsillar herniation due to a posterior fossa tumor
   B. Dandy-Walker syndrome
   C. Chiari type I malformation
   D. Chiari type II malformation
   E. Chiari type III malformation
25. The diagnosis of the tumor being illustrated here is most likely:

A. Subependymal giant cell astrocytoma
B. Dysembryoplastic neuroepithelial tumor
C. Large cell medulloblastoma
D. Pleomorphic xanthoastrocytoma
E. None of the above.

26. In this preparation stained with Luxol fast blue-Cresyl violet, the most obvious loss of myelin is in:

A. The spinal nerve roots
B. The crossed portion of cortical spinal tract
C. The uncrossed portion of cortical spinal tract
D. The dorsal column
E. The lateral lemiscus
27. In this specimen stained with Bielschowsky stain, the round structures can be seen in:

A. Hallervorden-Spatz disease
B. Infantile neuroaxonal disease (Seitelberger disease)
C. Diffuse axonal injury
D. All of the above
E. None of the above

28. The macroscopic pathologic illustrated in this photograph is most likely associated with:

A. Shaken baby syndrome
B. Optic nerve glioma
C. Methanol intoxication
D. Osteogenesis imperfecta
E. None of the above
29. This electron micrograph is taken from an intradural extramedullary spinal tumor. The most likely diagnosis is:

A. Schwannoma
B. Meningioma
C. Metastatic carcinoma
D. Disseminated medulloblastoma
E. Ependymoma

30. This intraventricular-periventricular tumor removed from the lateral ventricle of a 2-year-old boy is most likely:

A. Choroid plexus carcinoma
B. Choroid plexus papilloma
C. Central neurocytoma
D. Hemangioblastoma
E. Dysembryoplastic neuroepithelial tumor

31. The condition illustrated here is:

A. Chiari type I malformation
B. Chiari type II malformation
C. Chiari type III malformation
D. Dandy-Walker syndrome
E. Caudal regression syndrome
Level of difficulty 3.

32. The pathologic changes illustrated by this specimen is:
   1. Most commonly occur in premature fetus with 25 to 30 weeks of gestation.
   2. Most commonly occur in premature fetus with 32 to 38 weeks of gestation.
   3. The source of hemorrhage is most often from the germinal matrix.
   4. The most common source of hemorrhage is the choroid plexus.

   A. 1, 2, and 3 are true
   B. 1 and 3 are true
   C. 2 and 4 are true
   D. 4 is true

Level of difficulty 3.

33. A 23-year-old woman with a large, eccentrically located cerebellar mass and obstructive hydrocephalus. This photo is obtained from the intraoperative cytologic preparation.

   The most likely diagnosis is:
   A. Medulloepithelioma
   B. Ependymoma
   C. Medulloblastoma
   D. Pilocytic astrocytoma
   E. Choroid plexus papilloma
34. A 54-year-old woman with an enhancing right frontal mass associated with substantial edema. This photo is obtained from the intraoperative cytologic preparation.

The most likely diagnosis is:
A. Metastatic adenocarcinoma
B. Secretary meningioma
C. Metastatic melanoma
D. Glioblastoma
E. Oligodendroglioma
Neuropathology

Answers


The picture shows hemorrhage around the optic nerve. The most common cause of optic nerve and retinal hemorrhage in a 7 month-old infant is traumatic brain injury, specifically the shaken baby syndrome. However, coagulopathy, resuscitation, and chest trauma have been implicated in rare cases.

2. A. Medulloblastoma.

The T2 MRI shows enlargement of the ventricles and transependymal edema. The findings indicate acute hydrocephalus which, in this case, is caused by a posterior fossa tumor. The recent onset of symptoms of increased intracranial pressure is most consistent with a medulloblastoma. Although ependymoma of the 4th ventricle can block CSF flow, it causes hydrocephalus less frequently than medulloblastoma does, and the course is more protracted. Glioblastoma of the cerebellum is uncommon. Aqueductal stenosis would be of much longer duration.

3. D. Brain invasion is frequent.

The picture shows whorls of tumor cells and a psammoma body (meningioma). Most meningiomas are benign and do not invade the brain.

4. C. The optic nerve is a common intracranial location

The image above shows an irregularly enlarged and tortuous nerve which is consistent with a plexiform neurofibroma. The image below is a microscopic view of the tumor and shows nerve fascicles that are expanded because of a proliferation of neoplastic cells. This lesion arises in peripheral nerves and spinal roots. It does not arise in the optic nerve. Optic nerve glioma is also seen in neurofibromatosis 1.

5. C. Cerebral lymphoma.

The biopsy shows perivascular lymphoid cells with anaplasia, consistent with cerebral lymphoma.


The biopsy shows perivascular lymphocytes, macrophages and reactive changes. The histology, location of the lesion, and brief duration of symptoms is consistent with HSV encephalitis.
7. B. Hemangioblastoma.

The two images show aspects of a hemangioblastoma. The image on the right shows the vascularity of the tumor. The image on the left shows clear cells which are a component of the tumor.

8. C. A two month old ischemic infarct.

The picture shows loss of normal tissue and reactive (gemistocytic) astrocytes without anaplasia, consistent with an infarct. Lesions like this may be mistaken for tumor, especially at frozen section. Similar changes may be seen in old MS plaques.

9. A. Reich granule.

Reich granules: Also known as π granules, are lipid granules that can be found in normal Schwann cells associated with myelinated fibers. They are also seen in the cytoplasm of demyelinated fibers and in bands of Büngner but they are not found in Remak fibers. Reich granules can be found as single or in cluster. These cluster may be mistaken as abnormal lipid inclusions or evidence of lipid storage diseases. They are about 1 μm in length and with two components: one with a regular periodicity and the other being amorphous. As acid phosphatase has been identified in these granules, they can be regarded as a form of lysosome.

Mitochondria: The laminated structure may suggest a mitochondrion but mitochondria are subcellular organelles. The structure under discussion has the diameter of a myelinated fiber and could be far too big for a mitochondrion. Although dramatic expansion of mitochondria with "watery" content ("blown up mitochondria")s is a common feature of delayed fixation, the structure under discussion is still far too big for a mitochondria.

A regenerating cluster appears as a group of small fiber that, in consortium, gives the shape of a large fiber. It is a result of regeneration of a necrotic axon in axonal regeneration.

A tomuculum is an abnormally thickened region of the internode which would appear as a spindle or sausage-shaped expansion on teased fiber preparation. It is a characteristic finding in hereditary neuropathy with liability to pressure palsies (HNPP) but they can be seen in other neuropathies including hereditary motor sensory neuropathy (HMSN Ib), IgM paraproteinemic neuropathy, and occasionally in other neuropathies.

Bands of Büngner are rather disorganized and closely packed processes of Schwann cells that share a common basal lamina and is resulted from loss of myelinated fibers.
10. B. Papillary ependymoma.

In essence, this is a papillary tumor. The tumor cells are polarized and has a smooth luminal surface. The cytoplasm is fine and fibrillary and point towards a blood vessel. In between the blood vessel and the nuclei is a hyponuclear mantle. There is no basement membrane.

These features are diagnostic of a papillary ependymoma.

Differential diagnosis:

General: Ependymoma is a notorious imposter. First, they can occur in the brain and spinal cord with significant frequency. When they are cellular, they may suggest small blue cell tumors such as medulloblastoma; when they are relatively less cellular, they may closely mimic an astrocytoma or pilocytic astrocytoma. The papillary variant can mimic choroid plexus papilloma, metastatic papillary carcinoma, and other papillary tumors, particularly on frozen sections. Clear cell ependymoma can mimic oligodendroglioma, central neurocytoma, and metastatic clear cell carcinomas. Myxopapillary ependymoma occur predominantly in the spinal cord particularly at the cauda equina. They have a myxoid core. Recognition of ependymoma in intraoperative consultation is very important because gross total resection remains a very important favorable parameter in the treatment of ependymal tumors.

Choroid plexus papilloma: First, choroid plexus papilloma typically occur as a mass that protrude into the ventricles and do not exist as a subventricular tumor or demonstrate brain invasion. Second, a well defined basement membrane is present.

Subependymoma giant cell astrocytoma: They occur as subventricular tumors but do not have papillary structures.

Clear cell ependymoma: Clear cell ependymoma can occur in this location but there is no clear cells in this case to even suggest this diagnosis vaguely.

Central neurocytoma: Central neurocytoma can occur in this location. They often protrude into the ventricles with the forman of Monro as the most commonly affected site. The tumor cells have features very similar to that of oligodendroglioma and are small polygonal cells with clear perinuclear halo and small, round nuclei. These features are lacking in this case.

11. C. Positive for CD117 (c-kit) and PLAP.

The salient feature of this tumor is composed of a large population of cells admixed with cells with small round cells that appear morphologically to be lymphocytes. The large cells are in fact the neoplastic cells. This type of architecture is classic for germinoma.
Germinoma are immunoreactive for placental alkaline phosphatase (PLAP) and CD117 (c-kit). They are negative for neuroendocrine markers such as synaptophysin, neuronal markers such as neurofilament, and glial markers such as glial fibrillary acidic protein (GFAP).

12. D. Positive only for inhibin

Histologically, this tumor has large, polygonal cells with pale, and almost clear cytoplasm. The nuclei display a mild degree of pleomorphism. Within the tumor is also a rich vascular background.

From the histopathologic point of view, the differential diagnoses are metastatic renal cell carcinoma versus hemangioblastoma. Sometimes, it is difficult to separate these two entities on pure morphologic basis. One of the important information in the question is that the tumor under discussion is "primary cerebellar" tumor. With this clinical information in mind, this tumor is a hemangioblastoma.

Immunohistochemistry, hemangioblastomas are positive for inhibin. They are negative for CD10, cytokeratin, and epithelial membrane antigen (EMA). Renal cell carcinoma, in contrast, are reactive for CD10, EMA and cytokeratin.

13. E. Paraganglioma.

The characteristic organoid or “Zellballen” nest of cells is characteristic for a diagnosis of paraganglioglioma. These tumors can be seen in the filum terminale and other nerve roots. They are also common in the head and neck area.

These tumors are more common in male and present most often in between the 4th to 6th decades. Most of them have the classic Zellballen architecture that is illustrated here. Gangliocytic paraganglioma contains mature ganglion cells and cells that have transitional histology between chief cells and ganglion cells. Gangliocytic paraganglioma are also found in the duodenum and other regions. Other uncommon pattern include tumors that have morphologic features suggestive of ependymoma and also tumor cells arranging in cords and surrounded by fibrous tissue. Immunohistochemistry, paraganglioma cells are positive for chromogranin and synaptophysin. The sustentacular cells in periphery of the nest are positive for S100 and glial fibrillary acidic protein (GFAP). Cytokeratin are often demonstrated in paragangliomas of the cauda equina and filum terminale. At ultrastructural level, they have dense core (neurosecretory) granules.

The anatomic structure is optic nerve in cross section. The optic nerve ( ישראל) is separated from the dura ( רועי) by a layer of abnormal tissue. These features are highly suggestive of an optic nerve glioma with extension into the subdural space. The diameter of the optic nerve is dilated. The general architecture of the optic nerve is preserved although the diameter is greatly increased. Without comparison with a normal optic nerve or indication of scale on the photograph, sometimes it is difficult to be sure about the expansion on this magnification.

Both neurofibromatosis 1 (NF1) and neurofibromatosis 2 (NF2) are pleiotropic congenital multiple dysplasia syndromes. The cardinal features of NF1 and NF2 are multifocal focal hyperplasia and neoplasia in the supportive tissue throughout the entire nervous system. These include the nerve sheath elements of the cranial, spinal and peripheral nerve as well as glial and meningeal elements of the central nervous system. Neoplastic transformation of ganglionic elements resulting in pheochromocytomas, peripheral neuroblastomas and ganglioneuromas may also occur. Patients also have a 10-fold increased risk of learning problems.

15. D. Metastatic small cell carcinoma, primitive neuroectodermal tumor, and glioblastoma are all possible.

The background is necrotic and many pyknotic nuclei are present (_staff). The nuclei appear to have a dirty "salt and pepper" chromatin and there is some variation in nuclear size. The amount of cytoplasm is minimal to small. These features are highly suggestive of a metastatic small cell carcinoma. In fact, this specimen was obtained from a metastatic small cell carcinoma. It should be noted that the nuclei of small cell carcinoma may not look "small" in cytologic preparation.

Primitive neuroectodermal tumor (PNET): This is the less likely diagnosis although possible. PNET usually are not as necrotic as illustrated here. The age is also not uncommon.
Glioblastoma: This diagnosis is more likely than PNET in this case. The old name of glioblastoma multiforme reflects the possible diversification of this tumor. Although the cytologic features being shown here is uncommon for a glioblastoma, it is far from rare in my opinion.


These stellate cells have round nuclei without nucleoli. In contrast to non-reactive glial cells, the cytoplasmic processes are long and very well preserved. These cells are reactive astrocytes.

Neurons: They are usually associated with a large nuclei with prominent nucleoli. They cytoplasm is bluish on cytologic preparation. In my personal opinion, the cytoplasm of neurons are very delicate and not easy to be well preserved in cytologic preparation. In the end, the nuclei are often naked.

Ependymal cells: Ependymal cells are not stellate in shape. In reality, cytologic identification of normal ependymal cells is very difficult because of their rareness.

Oligodendroglial cells: The cytoplasmic processes of oligodendroglial cells are usually not well preserved and they often exist as nake nuclei. Some of the smaller nuclei in the picture are suggestive of oligodendroglial cells.

Microglial cells: they typically appear as cells with elongated, cigar shaped nuclei in cytologic preparations.

17. B. Central neurocytoma.

This is an interesting cytologic preparation. The nuclei are hyperchromatic and lack pleomorphism. In fact, they look monotonous. These features are suggestive of a glial neoplasm. The interesting point is that the cells seems to arrange in a rosette with an imaginary center. When this features is considered with the clinical features (35 year-old patient with an exophytic, ventricular mass) are highly suggestive of a central neurocytoma. The major differential diagnosis is ependymoma and, less likely, other glial tumors such as low-grade astrocytomas and oligodendrogliomas. In reality, it is quite difficult or impossible to distinguish neurocytoma from other low grade neoplasms on
Squash preparations. Neurocytomas often occur as monotonous tumor with clear cytoplasm.

Meningioma: Intraventricular meningiomas may arise in the tela choroidea or in the stroma of the choroid plexus with a distinct preference to the left ventricle as an exophytic mass. The cytologic features, however, is not typical for a meningioma. Nuclei of meningiomas are usually more open, round to oval, and often contain inclusion. Tumor cells arranged in whorls are also commonly seen in meningiomas.

Subependymoma giant cell astrocytoma: They are characterized by large, bizarre looking giant cells which are totally lacking here. However, they typically occur as intraventricular exophytic tumors in patients with tuberous sclerosis.

18. D. Chordoma.

In this particular case, it will be helpful to know Chordoma is a relatively uncommon, locally aggressive tumor that has features of the notochord tissue. They are seen predominantly in adults. Chordomas arises in areas where residual notochord tissue can be found, namely, cranial base and in the spine, particularly the lumbosacral area. The histologic features recapitulate the morphology of the notochord tissue. Macroscopically, they appear as a soft tumor with translucent cut surface. Histologically, the tumor cells have bubbly cytoplasm within a matrix of bluish chondroid background. The chondroid background bubbly cytoplasm is seen in this cytologic preparation. These bubbly cells are known as physaliphorous cells. The ultrastructurally and immunohistochemistry, they have some features of epithelial cells such as intercellular adhesion and cytokeratin filaments.

Mucin producing adenocarcinoma: There is more nuclear pleomorphism in metastatic carcinoma. The cytoplasmic vacuoles is usually more well defined and much larger. Carcinoma cells also form much tighter clusters. Necrosis is often seen in metastatic carcinoma but not in chordoma.

Schwannoma: They occur as tightly packed spindle clusters on cytologic preparation and lack the chondroid substance.

Myxopapillary ependymoma: The chondroid-mucoid appearing background is suggestive of myxopapillary ependymoma. However, cells of myxopapillary ependymoma have long cytoplasmic processes on cytologic prepartion, a share features among different types of glial neoplasm. In contrast, their cytoplasm is not bubbly.
Ewing's sarcoma: Primary Ewing's sarcoma in the vertebral column is uncommon. They occur as monotonous small blue cells with only a thin rim of cytoplasm in cytologic preparation.

19. A. Abscess.

The cells are exclusively composed of neutrophils and the background is dirty looking because of necrosis. Many of the neutrophils are degenerative. This is pus and is consistent with an abscess.

Lymphoma: They appear as monotonous cells with atypical nuclei. The amount of cytoplasm is at most medium. Hodgkin's lymphoma can contain a mixed inflammatory background. Hodgkin's lymphoma is very rare in the central nervous system and usually do not associate exclusively with degenerative neutrophils as illustrated here. The total lack of atypical cells also argue against a malignant process.

Metastatic melanoma: Metastatic melanoma may have a moderate to, sometimes, large amount of cytoplasm. The cytoplasm may carry a greyish hue under the microscope. Bubbly cytoplasm is unusual. The nuclei are usually large, pleomorphic, with prominent nucleoli and often with pseudonuclear inclusion.

Glioblastoma: Glioblastoma may have some inflammatory cells but never to this extent. In addition, there is no atypical cells here to suggest glioblastoma.

Infarct: Some inflammatory cells may be seen at the early stage of an acute infarct but not to this extent. Foamy macrophages are usually present.

20. C. Hypoxic/ischemic change.

In this coronal section, several symmetrical changes are present. Part of the parietal cortex are reduced to a chalky line; this finding is known as laminar necrosis. This feature could be easily recognized when it is compared to the temporal cortex that is of normal thickness. There are also symmetrical necroses involving the basal ganglia. Focal discoloration is present in the thalamus. The pathologic changes are therefore symmetrical, widespread and associated with necrosis. The most possible scenario would be a generalized
hypoxic/ischemic insults such as those produced by hypotension. In addition, the patients must have survived after the episode for some time in order for the lesions evolve to the morphology being illustrated here.

Neoplastic changes: First, there is no identifiable mass lesion here. Assuming that there is a diffusely infiltrating process is present, there is no distortion of the structure. This made this diagnosis highly improbable if not impossible.

Viral encephalitis are associated with inflammation. In most cases they have widespread congestion and petechial hemorrhage. Some viruses, such as herpes simplex virus, also produce localized necrosis. All these features, however, are not present in this picture.

Leukodystrophies are associated with greyish discoloration and degeneration of the white matter, a feature which is absent in this case. The arguable exception is metachromatic leukodystrophy which is characterized by chalky-white white matter with enhancement of the gray-white junction. Honestly, it is not fair to ask you to judge if there is any chalk-white discoloration based on this picture. However, there is no enhancement of gray-white junction. In addition, the laminar necrosis is typical for a hypoxic/ischemic injury.


This is a desmoplastic medulloblastoma and carries better prognosis than the classic type of medulloblastoma. They also tend to occur in older patients such as young adults. In contrast to the classic type, they also tend to occur in the cerebellar hemispheres rather than midline. A reticulin stain will demonstrate the desmoplastic changes.

22. A. Amnion rupture sequence.

Amnion rupture sequence: This is an umbrella term that covers three very similar but overlapping conditions namely amniotic band syndrome, amniotic adhesion sequence, and limb-body wall complex. They are probably disruptive sequences secondary to vascular disruption or tissue necrosis and adhesion. The spectrum of pathology includes encephalocoele and defects of cranium, cleft palates and other facial abnormalities, autoamputation of digits and limbs, and body wall defects with anomalies of internal organs. The brain is usually normal but cases with developmental abnormalities have also been reported. Karyotypes of affected individuals are normal. In this particular case, it is probably an amniotic adhesion sequence which is characterized by part of the fetus, usually the head, adhering to the placenta.
Anton syndrome is produced by bilateral infarction of the visual cortex. It is often resulted from bilateral obstruction of the posterior cerebral artery. Typically, the patient does not realize that they could not see.

Caudal Regression Syndrome (sacral agenesis): The caudal regression syndrome is a variable defect of lumbar vertebrae, sacrum, and coccyx. This is a severe developmental field defect of the posterior axis caudal blastema. The severest form is sirenomelia (mermaid syndrome). It is frequently associated with abnormalities of the anorectal and urogenital systems and lower limbs. The entire urinary tract can be absent. The pathogenesis is probably related to the failure of growth of the caudal eminence. The strongest association of caudal regression is with maternal diabetes, it has also been related to deletion of chromosome 7q, autosomal dominant and, probably, autosomal recessive transmission.

Both Down syndrome and fetal alcohol syndrome are associated with characteristic facial characteristic but not adhesion of the fetus to the placenta.

Fetal alcohol syndrome is resulted from the teratogenic effects of alcohol on human fetuses secondary to in utero exposure. The classic cases have the clinical triad of growth retardation, characteristic facial dysmorphology and dysfunction of the central nervous system (CNS). The degree of involvement is highly variable. Dysfunctions of the CNS include mental retardation in 85% of patients, irritability and poor suck in the newborn period, hypotonia, hypertonia, seizures and hyperactivity. In Fetal alcohol syndrome (FAS), patients must have all three characteristics, namely, prenatal and postnatal growth retardation (<2 SD for length and weight), characteristic facial features, and CNS dysfunction. When the features of the syndrome are not fully expressed, the term fetal alcohol effects (FAE) can be used. Characteristic morphological abnormalities of FAS include the followings:

Growth retardation: Patients remained more than 2 standard deviations below the norm. Some patients may have postnatal catch-up growth.

Characteristic facial features: The facial features are mainly hypoplastic in nature. These features include short palpebral fissures, maxillary hypoplasia with relative prognathism, epicanthal folds, thinning of vermilion border and hypoplastic upper lip, low nasal bridge and anteverted nostrils, hypoplastic upper helix, and apparent hypertelorism due to short palpebral fissure (blepharophimosis).

CNS malformations include microcephaly and malformations of the brain, particularly those of abnormal neuronal migration in nature.

23. B. Associated with neurofibromatosis 2 and enhances on MRI.
The tumor being illustrated here is a meningothelial meningioma.

Neurofibromatosis 2 (NF2):

NF2, also known as central neurofibromatosis, is transmitted in an autosomal dominant pattern. The gene involved is located on chromosome gene 22q12 and encode for the protein merlin.

The incidence of NF2 is only about one-tenth that of NF1.

The cardinal features of neurofibromatosis are multifocal focal hyperplasia and neoplasia in the supportive tissue throughout the entire nervous system. These include the nerve sheath elements of the cranial, spinal and peripheral nerve as well as glial and meningeal elements of the central nervous system. Schwannomas and meningiomas are most common, followed by ependymoma. Hamartomatous lesions in the central nervous system are also very frequent.

Neoplastic transformation of ganglionic elements resulting in pheochromocytomas, peripheral neuroblastomas and ganglioneuromas may also occur.

24. D. Chiari type II malformation.

This is a case of Chiari type II malformation. In addition to displacement of the vermis (black arrow), there is also malformation of the brain stem (white arrow).

Tonsillar herniation due to a posterior fossa tumor: In this situation, the tonsils tends to bulge out of foramen magnum which is a feature that is lacking here. In addition, the herniated tonsils is usually dusky in appearance and edematous because of the increase in intracranial pressure; this feature is also absent here.

Dandy-Walker syndrome: The three essential features of Dandy-Walker syndrome include complete or partial agenesis of the vermis, cystic dilatation of the fourth ventricle and enlargement of the posterior fossa. The vermis is present in this cases and is free of hydrocephalic changes. Hydrocephalus is a frequent but inconstant finding. Other CNS findings include elevation of the tentorium cerebelli and lateral, transverse sinuses and torcule (torcular Herophilli), and lack of patency of the foramina of Magendie and Luschka. Other cerebral and visceral anomalies are present. It is the presence or absence of other cerebral and visceral abnormalities that determines the prognosis.
Chiari type I: Conical elongations of the cerebellar tonsils and neighboring parts of the cerebellar hemispheres that extend into the vertebral canal (i.e., below the foramen of magnum). The protruded cerebellar tissue could be histologically normal, infarcted or sclerosed. The medulla is either unaffected or flattened by the cerebellar tongues. Often associated with syringomyelia, hydromyelia, syringomyelia, and less commonly hydrocephalus.

Chiari type II: Displacement of the cerebellar vermis combined with deformities of the medulla and tectal plate. Often associated with syringomyelia, hydromyelia, spinal bifida, meningocele, and hydrocephalus. It can also associate with other malformation of the brain, cranium and meninges, cardiovascular, gastrointestinal and genitourinary systems. Most, if not all, Chiari type II malformations are associated with with neural tube defects.

Chiari type III: Encephalocele formed by herniation of the structures of the posterior fossa, including the cerebellum, through an occipitocervical or high cervical bony defect. There may also be beaking of of the tectum, elongation and kinking of the brain astem and lumbar spina bifida.


The lesional tissue is composed of neoplastic cells with substantial pleomorphism. The salient diagnostic clue is the large cell with foamy cytoplasm located at the upper part of the field; a typical feature in pleomorphic xanthoastrocytoma (PXA).

Dyembryoplastic neuroepithelial tumor (DNET): The histology can be quite variable but the large cells and cytologic atypia being shown here is not a feature of DNET.

Large cell medulloblastoma: Large cell medulloblastoma essentially maintains the appearance of medulloblastoma but with large nuclei and increased pleomorphism. The large nucleus in large cell medulloblastoma often "hug" on a smaller nucleus. The tumor being illustrated here has no resemblance to medulloblastoma.

Pleomorphic xanthoastrocytoma (PXA): This is an uncommon tumor that accounts for less than 1% of all astrocytic tumors; most of them are seen in children and young adults. Although they have favorable prognosis, about one-fifth of the cases may have malignant transformation. They tend to occur in supratentorial locations as superficial tumors with leptomenigeal involvement. Histologically, there is a variegated appearance of the tumor with spindly elements intermingled with mono- or multinucleated giant cells, the nuclei of which display great variation in size and staining. Mitotic activity is not very conspicuous, if present. Necrosis is not seen. As being illustrated here, there is intracellular accumulation of lipid droplets that often occupy much of the cell.
body; the nuclei and the more basophilic cytoplasm are often pushed to the side. As a result, immunostaining often demonstrate crescents of cytoplasm that are immunoreactive for GFAP. Reticulin fibers can be well demonstrated in the tumor and in leptomeninges being invaded by tumor cells.


Staining: Luxol fast blue (SFB) is a stain that stains myelin blue. It can be combined with other stains such as LFB-cresyl violet as being used here, LFB-PAS, and LFB-HE.

This is a case of X-linked adrenal cortical leukodystrophy (X-ALD). There is substantial demyelination in the lateral (crossed) cortical spinal tracts (LCS).

Other structures: There is some reduced staining in the anterior cortical spinal tract (white arrow) but its degree is far less than that in the LCS. The staining in the dorsal column (DC), and spinal nerve roots (↗) are within normal limits. The lateral lemniscus is a major myelinated fiber tract in the brainstem and is not present in this photograph.

The lateral lemniscus is a brainstem auditory pathway and is not present in the spinal cord.

27. D. All of the above.

Axonal spheroids are essentially contraction balls of axons. Although axonal spheroids are best demonstrated by silver stains or immunostaining for neurofilament proteins, it can often be seen with hematoxylin-eosin stain. Formation of axonal spheroids as being illustrated here is a salient features in some diseases that are mainly seen in children and young adults. The differential diagnoses in this category include Hallervorden-Spatz disease, neuroaxonal dystrophy (Seitelberger disease), late juvenile, juvenile, and adult onset neuroaxonal dystrophy, neuroaxonal leukodystrophy Nasu-Hakola disease (polycystic lipomembranous osteodysplasia with sclerosing leucoencephalopathy), neuroaxonal dystrophy associated with a deficit in alpha-N-acetyl- galactosaminidase. However, it can also be seen in other pathologic conditions such as diffuse axonal injury, vitamin E deficiency, mitochondrial encephalopathies, areas around stroke, and many other conditions.

Hallervorden-Spatz disease is a progressive early onset neurodegenerative disease affecting predominantly the motor system. Macroscopically, it is characterized by brown discoloration in the globus pallidus, substantia and red
nuclei. On imaging, the globus gives the “eye-of-tiger” sign. Histologically, it is characterized by neuroaxonal dystrophy, neuronal loss and gliosis, and iron deposition in the globus pallidus. Clinicopathologic consideration is necessary for diagnosis in particular for separation from neuroaxonal dystrophy (Seitelberger disease).

Neuroaxonal dystrophy (Seitelberger disease) is an autosomal recessive disease characterized by widespread axonal spheroids in the CNS and PNS. It has a infantile form and a juvenile form. These spheroids are essentially dystrophic changes involving mainly terminal axons and presynaptic terminals. The infantile form begins with pyramidal tract signs. Severe dementia develops later and accompanies by increasing spasticity that eventually evolves into decorticate rigidity. Seizures are unusual and late. Clinicopathologic consideration is necessary for diagnosis in particular for separation from Hallervorden-Spatz disease. The spheroids are more numerous in the small nerve endings but relative spare in larger branches of peripheral nerves such as sural nerve. Biopsy of skin, muscle, and conjunctiva will have a higher yield than peripheral nerve biopsy.

Diffuse axonal injury are often seen in head injuries produced by high speed acceleration and deceleration such as those in motor vehicle accidents.

28. A. Shaken baby syndrome.

This is a globe with the attached optic nerve. A Bluish discoloration is noted under the optic nerve (↑) and in the sclera (↑) and are most consistent with subdural and subsceral hemorrhage. These hemorrhages are virtually hallmarks of shaken baby syndrome, also known as shaken-impact baby syndrome. It should be noted that these hemorrhages are primary hemorrhages. Extension of subdural blood from intracranial hemorrhage into the subdura; space of the ptic nerve should be ruled out.

Shaken baby syndrome: Shaken baby syndrome (shaken-impact baby syndrome) are usually seen before 3 years of age, most frequently occurred within the first year of life. Extracranial injury suspicious of or consistent with child abuse are seen in many but not all of the cases. A good number of cases are completely free of external injury. The nature of the injury is that of a diffuse injury of the central nervous system resulted from sudden deceleration and rotation of the brain about its center of gravity. Such angular deceleration will increase 50 times in magnitude at the time of impact of the baby on a surface. It is important
to note that impact on a relatively soft surface can also cause shaken baby this type of injury. The cause of death is usually uncontrollable increase in intracranial pressure. Detection of hemorrhage in the retina and in the subdural space of optic nerves are highly suggestive of shaken baby syndrome. CT scan is a handy instrument to detect hemorrhage at the early stage. Extensive loss of gray white differentiation and hypodensity are addition features on CT scan that suggest shaken baby syndrome. Pathologically, the findings are similar to those seen in acceleration-deceleration injury in motor vehicle accidents. Macroscopically, there are gliding (parasagittal) contusions. Histologically, salient feature is diffuse axonal injury characterized by neuroaxon spheroids. Superficial contusions in the olfactory bulbs and gyrus recturs are also common. Bruising of the scalp, cranial fracture, several subdural hemorrhage can also be seen but uncommon. It is very important to note that the severity of injury to the central nervous system in shaken baby syndrome is often not well reflected by external injury to the scalp and cranial bone. Hemorrhage along the sheath of the optic nerve is typically most obvious at the junction of the neureve and the globe. A point of warning is that subarachnoid hemorrhage in the brain can extend along the subarachnoid space and mimic nerve sheath hemorrhage. Therefore, a large subarachnoid hemorrhage should be ruled out. Retinal hemorrhage is also a common feature. Cervical injury from C1 to C4 is also common. Dissection of the neck and vertebral accompanied by in situ examination of the cervical cord and brain with a posterior approach (i.e., from the back) is a good way to demonstrate injury in these regions.

- Optic nerve glioma characteristically lead to expansion of the optic nerve. Subdural hemorrhage along the optic nerve is not a characteristic feature.
- Methanol intoxication is associated with spongiotic changes of the optic nerve which is a microscopic feature. Subdural and subretinal hemorrhage is not a typical feature.
- Osteogenesis imperfecta: A blue hue is often seen in the sclera which is due to increased transparency of the sclera. Subdural hemorrhage is not a characteristic feature.

29. A. Schwannoma.

Schwannoma: Several features of schwannomas are recognized in this photograph. The thin, elongated cell processes covered by a layer of electron dense basal lamina (→). Another common finding for schwannoma is long spacing collagen (→) fibrils. These fibrils have cross bandings with a periodicity of 120 to 150 nm and are often admixed with excessive basement
membrane material. These fibers are not found only in schwannoma. Other features that are seen in schwannoma but are not shown in this photo include whorls and lamellae composed of closely apposed stacks of double membranes.

Meningioma: At the ultrastructural level, interdigitations of the cytoplasmic membrane, hemidesmosomes, and desmosomes are usually seen in meningothelial and transitional meningiomas. There is also an abundant amount of intermediate filaments, sometimes with prominent whorls that are immunoreactive for antibodies against vimentin. These filaments are firmly anchored to the desmosomes, a feature that is also seen in normal arachnoid cells. Calcium deposits can also be seen.

Metastatic carcinoma: They basically retain their epithelial features at the ultrastructural level. Since the type of metastatic carcinoma in the brain is diversified, it is difficult to cover all of them here. However, the presence of desmosomes, hemidesmosomes and other membrane junctional complex are share features of many carcinomas.

Medulloblastoma: The ultrastructural features are quite constant. In essence, there is generally a lack of cytoplasmic organelle and no distinguishing feature. The nuclei are lobulated to round nuclei without prominent nucleoli. There may be closely packed neuritic cell processes with synaptic complexes. Dense core granules as well as clear-centered vesicles can be seen. There is also microtubules and intermediate filaments.

Ependymoma: The development of 9+2 cilia, with their basal blepharoplasts, should be regarded as the most important hallmark of ependymal cell. Ependymomas also have intracytoplasmic microrosettes and junctional complex.

30. A. Choroid plexus carcinoma.

Chorodi plexus carcinoma: The pathology of this case is that of a papillary neoplasm without associated brain tissue. Since it is removed from the lateral ventricle, the absence of accompanying brain parenchymal tissue suggest that the part of the tumor being shown here is probably an exophytic mass that
protrudes into the ventricle. In general, the papillary structure is only partially maintained. Areas composed with sheets of cells and with focal necrosis (↗). On higher magnification, the papillary structures has a basement membrane (↗) and fibrovascular core. There is significant nuclear pleomorphism and a mitotic figure (↗) is in the photograph. In general, the focal loss of papillary pattern, and necrosis are features suggestive of a papillary carcinoma and in this case, a choroid plexus carcinoma.

Clinical information: Choroid plexus tumors are common in children. Most often, they are choroid plexus papilloma and less frequently, choroid plexus carcinoma. The most common site is lateral ventricle and followed by the 4th ventricle. Tumors that are found in children under 2 years of age are mostly arising from the lateral ventricle. The third ventricle is an uncommon location. Although choroid plexus papilloma can be seen in adults, choroid plexus carcinoma are almost unknown to adults. Choroid plexus papilloma in adults tend to occur more frequently in the 4th ventricle. To make a diagnosis of choroid plexus carcinoma in adults, metastatic carcinoma must be ruled out. On the contrary, metastatic carcinoma is uncommon in childrens.

Choroid plexus papilloma: It should not have loss of papillary structure, necrosis, and substantial pleomorphism. Mitotic figures should not be seen in choroid plexus papilloma.

Central neurocytoma: Although central neurocytoma usually arise within the lateral ventricle, they are uncommon in young children. In addition, their morphology is almost indistinguishable from oligodendrogliomas and do not possess architecture.

Hemangioblastoma: These tumors have clear cells and rich vascular supply. They do not form papillary structures.

Dysembryoplastic neuroepithelial tumor: These tumors are essentially benign glial-neuronal tumors and do not have papillary structures. Similar to choroid plexus tumors, they are usually seen in children.

31. A. Chiari I malformation.

In this case, the tonsil (↗) is herniated into the upper cervical cord. There is no obvious deformation of the pons and brain stem. The cerebellar vermis (➔) does not appear to be malformed. These findings are that of a Chiari I malformation.
32. 1 and 3, i.e., B. The diagnosis is germinal matrix hemorrhage. It is most common in premature infants with 25 to 30 weeks of gestation and the source of hemorrhage is from the germinal matrix.

This is an immature fetal brain. The salient pathologic change is a large hematoma that occupies the right side of the lateral ventricles. Some small hemorrhages (—are also present in subependymal areas (corresponding to the germinal matrix microscopically).

Age: Periventricular hemorrhage in the germinal matrix is most common in premature babies (22-30 weeks). Lesions in the white matter (periventricular leukomalacia) are seen in premature babies after 28 weeks of gestations. Hemorrhage from the choroid plexus is more commonly seen in term babies.

Body weight: Intraventricular hemorrhages among infants weighing <1500 g and who come to necrospy ranges from 23 to 75%. The frequency drops dramatically to 8% in babies weighing >2000 g.

Etiology: By the 18th to 20th week of gestation, the neocortical ventricular wall is lined by a prominent hypercellular well-vascularized zone known as the germinal matrix. This germinal zone is composed of undifferentiated, differentiating and migrating cells, radial glial fibers, polymorphous astrocytes, and thin-walled blood vessels. The germinal cells have very little structural support and the vessels are very fragile. A lot of angiogenesis and vessel remodeling is going on during this period and this may be the reason why this area is so susceptible to hemorrhage in younger premature infants. The control of blood pressure in the brain is not well developed in these infants. The hemorrhage is usually resulted of damage of the vessel wall. The mechanism may be damage of the endothelial cells by acidosis secondary to hypoxia. Birth injury seems to play a role as one-third of cases have difficult deliveries due to forceps rotations and breech presentation.

Papile’s classification:

- Grade I: Subependymal hemorrhage
- Grade II: Intraventricular hemorrhage.
- Grade III: Intraventricular hemorrhage with ventricular dilation
- Grade IV: Intraventricular hemorrhage with ventricular dilation and parenchymal extension.
Locations: The most common site is the periventricular matrix zone located between the caudate nucleus and thalamus at the level of or slightly posterior to the foramina of Monro. The next common site is the occipital lobe. The least common site is the temporal horn of lateral ventricle. Hemorrhage may originate over the head of the caudate nucleus. Some of the smaller hemorrhage may be confined to the germinal matrix without rupture into the ventricle. In these cases, the hemorrhage may be clinically asymptomatic.

33. E. Choroid plexus papilloma.

The cells arrange in a papillary pattern. The nuclear pleomorphism is at most moderated. Scattered single cells do not have the elongated cytoplasmic process that are commonly seen in glial neoplasms. In fact, these cells are highly suggestive of cells that fall off from an epithelium.

Medulloepithelioma: This is a highly pleomorphic, highly aggressive but rare tumor. It is seen in infants and children. Although the present case has epithelial-papillary like features that can be found in medulloepithelioma, the nuclear pleomorphism in this case is not high and practically rule out the possibility of medulloblastoma.

Medulloblastoma: Medulloblastoma tends to occur in young children and infants and they occur in the cerebellum. The cells in cytologic preparations appear as small blue cell tumor with a minimal rim of cytoplasm. Many of the nuclei are naked. In general the nuclei are relatively monotonous but a higher degree of variation in nuclear size can be appreciated in the cytologic preparations than frozen sections or paraffin sections. Typically, the nuclei have a dirty "salt and pepper" suggestive of neuroendocrine differentiation. Nuclear groove can be seen in some nuclei. Medulloblastoma do not arrange in papillary structures as in this case. The tumor cells in this case has too much cytoplasm and the nuclei lacks the characteristic "salt and pepper" neuroendocrine appearance.

Pilocytic astrocytoma: They are common benign pediatric brain tumors and the cerebellum is the most common site. Similar to other astrocytic tumors, pilocytic astrocytomas has long cytoplasmic processes on cytologic preparation. The nuclei are also low-grade. Pilocytic astrocytoma do not arrange in papillary structures as illustrated in this case.

Ependymoma: Similar to other glial neoplasms, ependymoma typically have elongated cytoplasmic process. However, their perivascular arrangement often lead to vaguely arranged papilla-like structures but they are usually not as distinct as in the choroid plexus papilloma being shown here. There is an
uncommon variant of papillary ependymoma that may be confused with choroid plexus papilloma on frozen sections. However, the papillary ependymoma cells still maintain the typical elongated cytoplasmic structure like in other glial neoplasm. In contrast, the cells in this case has short, stub shaped cytoplasm rather than elongated cytoplasm in glial neoplasms.

34. B. Secretory Meningioma.

In this cytologic preparation, there are many bubble like structure with a centrally located eosinophilic globules (🔍). These structures are several times the size of the nuclei that is present in this photo. The morphology of the nuclei is bland overall. In addition, some nuclei have pseudonuclear inclusions (🔍). The cytoplasm of these cells are amphophilic and granular. These features are highly suggestive of a secretory meningioma.

Metastatic adenocarcinoma: Although metastatic adenocarcinoma cells tend to have intracytoplasmic inclusions and those in mucin producing ones and signet ring cell adenocarcinoma can be large, the bubbly structures here are several times the size of a nuclei. This is too large for metastatic adenocarcinoma. In addition, the blend nuclear morphology and the pseudonuclear inclusions are more compatible with a meningioma.

Metastatic melanoma: The large bubbly globules and the bland nuclei go against metastatic melanoma. Psuedonuclear inclusion, however, can be seen in metastatic melanoma.

Glioblastoma and oligodendroglioma: The large bubbly globules go against a diagnosis of glial neoplasm including glioblastoma and oligodendroglioma.