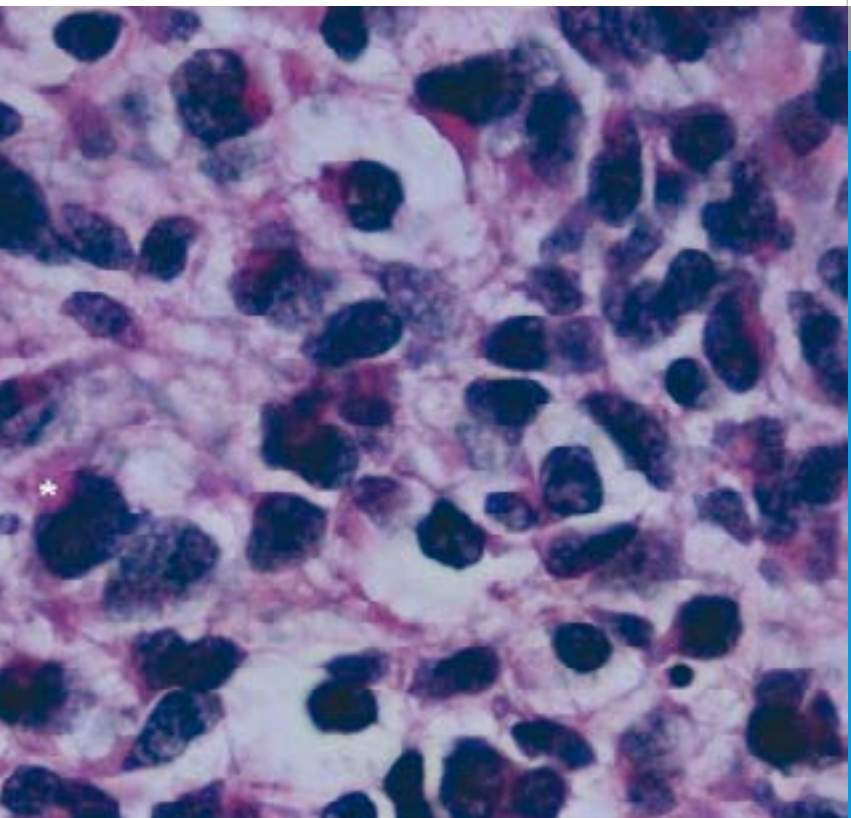
SWISS SOCIETY OF NEONATOLOGY

Neonatal macrocephaly: cerebral PNET or neuroblastoma as an infrequent cause



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A male newborn was delivered at 38 1/7 weeks by secondary C-section because of arrest of dilation. Because of a positive Group B Streptococcus swab and PROM for 36 hours, perinatal ampicillin was administered. The antenatal history was uneventful and three ultrasound examinations at 7, 21 and 30 weeks, respectively, were reported as normal. Head circumference on ultrasonography was 193.7 mm at 21 3/7 weeks (P 10-50) and 279 mm (P 10-50) at 30 5/7 weeks. The Apgar scores were 6/5/5 at 1/5/10 minutes, respectively. The child was intubated at 8 minutes of age because of poor respiratory effort.

Birth weight was 3080 g (P 50), length 53 cm (P 90-97), head circumference 39.5 cm (P >97, + 3.5 SDs). Vital signs on admission: HR 158 bpm, RR 40 bpm, BP 64/42 mmHg. The physical examination showed a wide and tense anterior fontanel, splayed sutures without external bruising or swelling. Pupils were bilaterally 3 mm, isoreactive. The general tone was lowered, but he moved all extremities spontaneously and symmetrically.

Initial neurological imaging was performed by ultrasonography and showed a large intraparenchymal mass in the right cerebral hemisphere, predominantly hyperechoic with some anechoic areas, a compressed right lateral ventricle and a massively dilated right lateral temporal horn with a transverse diameter of 50 mm, as well as an enlarged and laterally displaced

right frontal horn (Fig. 1). The right frontal mass extended down into the anterosuperior aspect of the dilated third ventricle. The ventricular walls appeared echogenic, and some areas of increased echogenicity were seen within the lateral ventricles consistent with blood. Contralaterally, a dilated left lateral ventricle with a transverse diameter of 27 mm at the foramen Monroi was noted. Midline shift to the left and some downward compression on the right tentorium was seen, with a normal fourth ventricle.

For further investigation a CT scan (Fig. 2A and 2B) was performed. A 44 x 40 mm mass was identified in the right frontal lobe and crossing the midline. The mass had an irregularly marginated and hypodense centre with peripheral rim enhancement. A 6 mm midline shift to the left was seen. Massive hydrocephalus was present. The biventricular diameter of the lateral ventricles was 80 mm. The other findings described previously were confirmed.

A right sided subdural hemorrhage, posterior to the parietal lobe, was seen and this tracked posteriorly along the falx and along the tentorium. Some white matter hypodensity was noted within the left parietal lobe around the ventricles which may have represented transependymal flow. A low density extra- axial collection was seen posterior to the left cerebellum consistent with an old left subdural hematoma. The interpretation was that the mass most likely was a te-

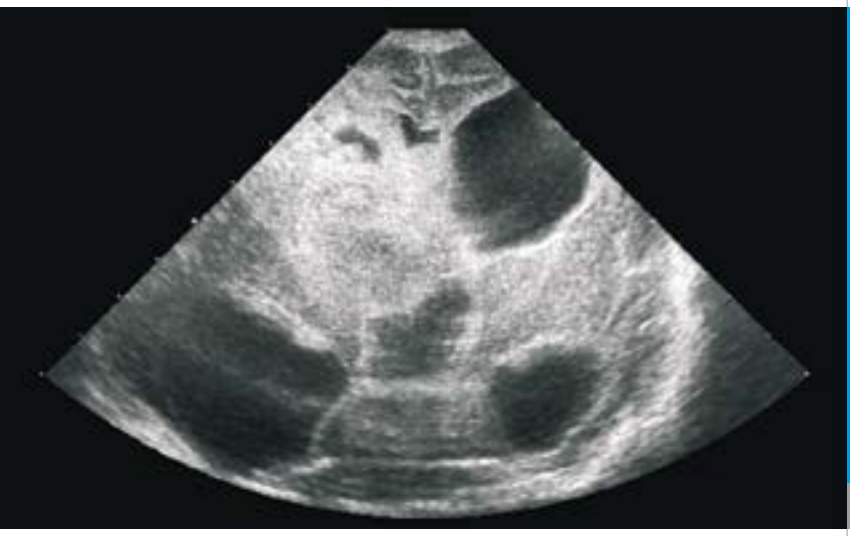


Fig. 1

Initial head ultrasound.

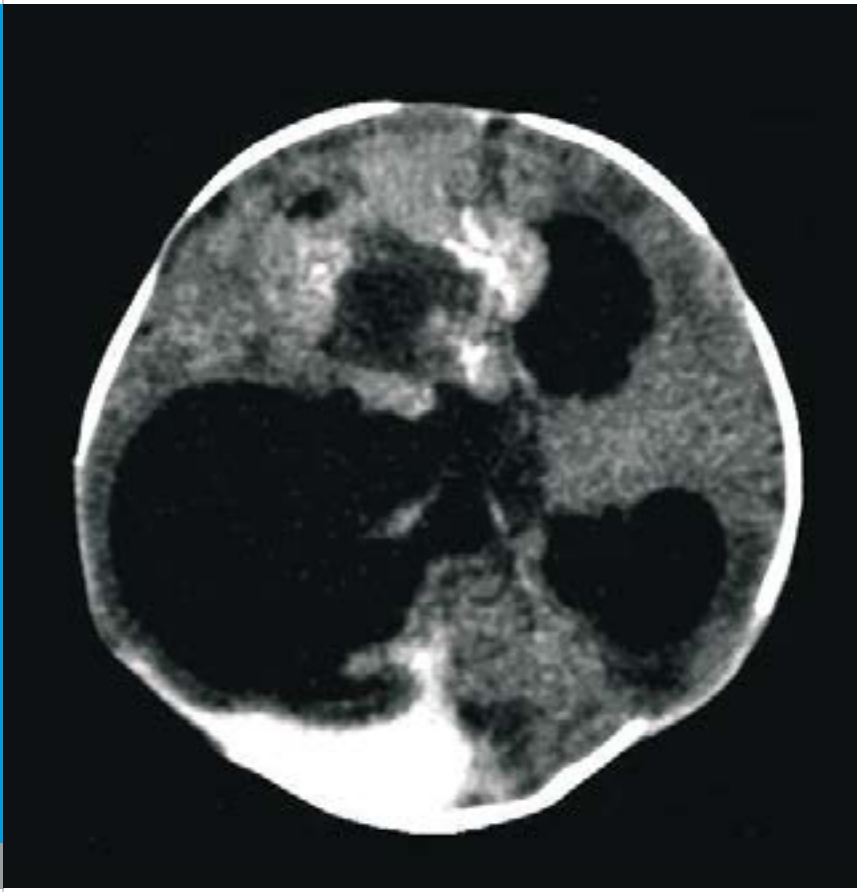


Fig. 2A

Head CT without contrast.

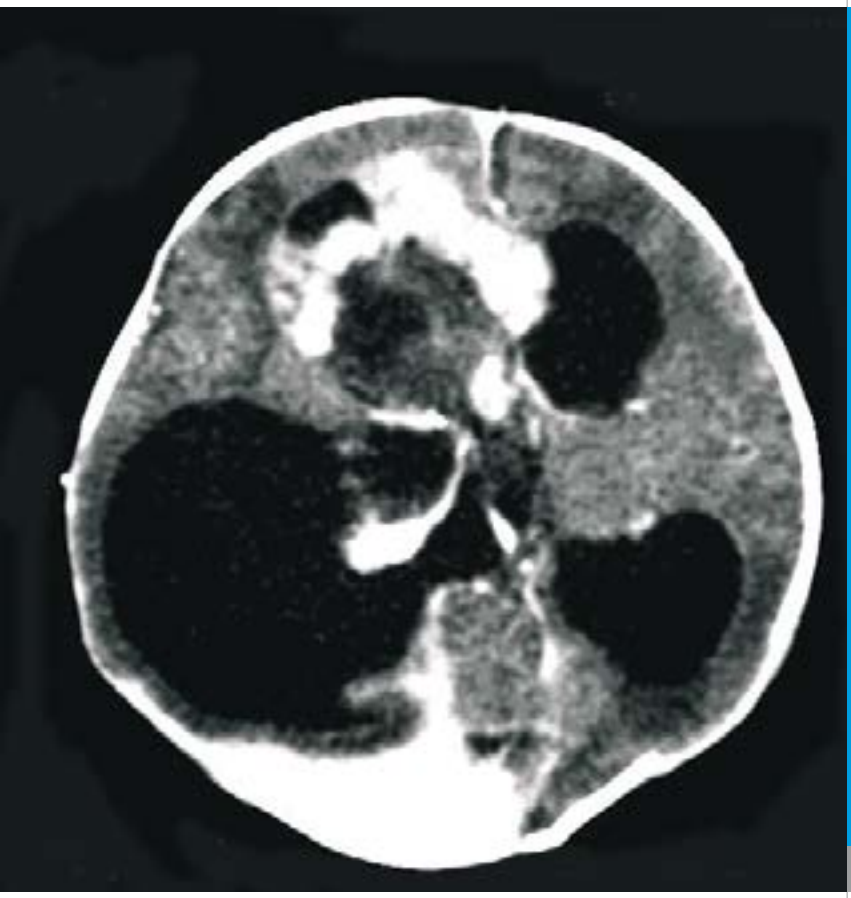


Fig. 2B

Head CT with contrast.

ratoma or a PNET, with occlusive hydrocephalus and acute right subdural hematoma posterior to the parietal lobe and old left subdural hematoma posterior to the left cerebellum.

A head MRI (Fig. 3) was performed and showed communicating hydrocephalus likely on the basis of previous intraventricular hemorrhage ("tentorial block") and a tumor cantered in the right frontal horn with associated hematoma.

The baby was taken to the operating room for decompression and biopsy. Intraoperatively, a ventricular tap was performed, as the brain was very tight. The CSF was xanthochromic. The cytology revealed degenerative cells of favorable lymphoid origin as a reactive component, but no definite evidence of malignant cells. After ventriculotomy, the tumor was accessed. It was brownish- black, soft, friable, suckable and moderately vascular with areas of prior hemorrhage. In the area of the foramen Monroi, it was attached to the chorioid plexus. A partial resection was achieved.

Histology (Fig. 4-7) revealed the typical findings of a PNET with the presence of "little blue cells" and electronmicroscopy (Fig. 8) showed the neuronal differentiation by exposing the neurosecretory granule and the microtubules. A cytogenetic analysis showed an abnormal clone with structural rearrangement involving chromosome 1 and 15 and tetraploidy with un-

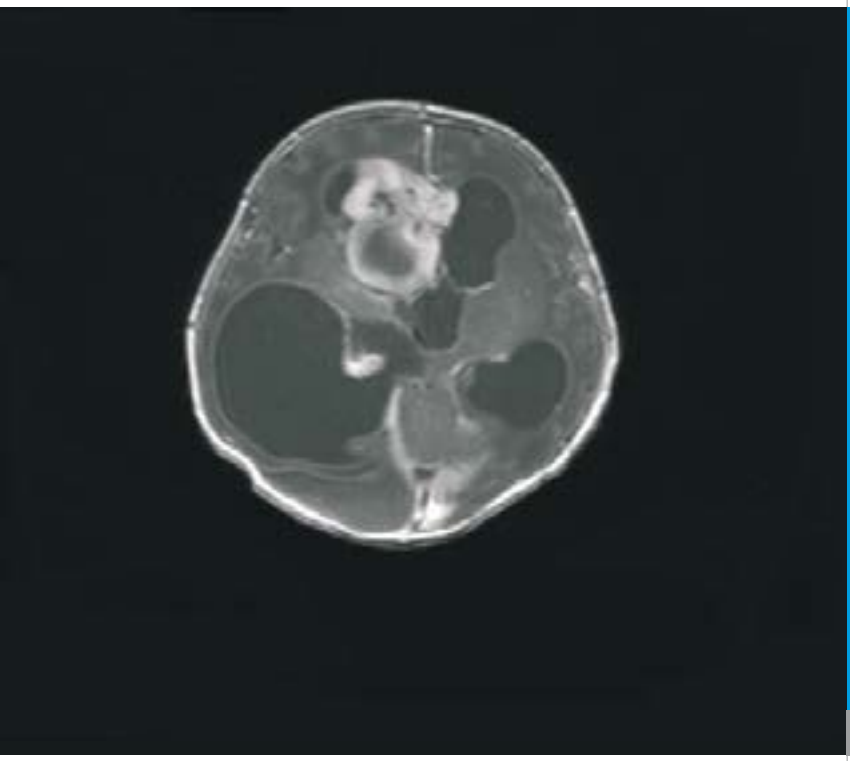


Fig. 3

Head MRI (T1-weighted image).

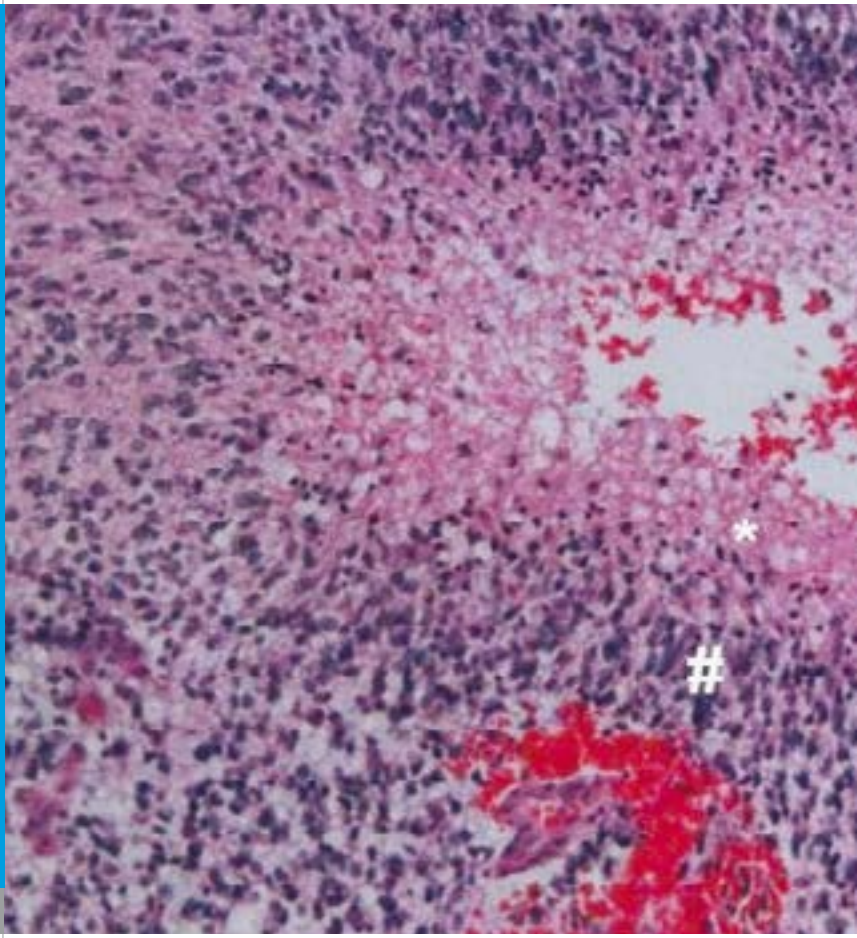
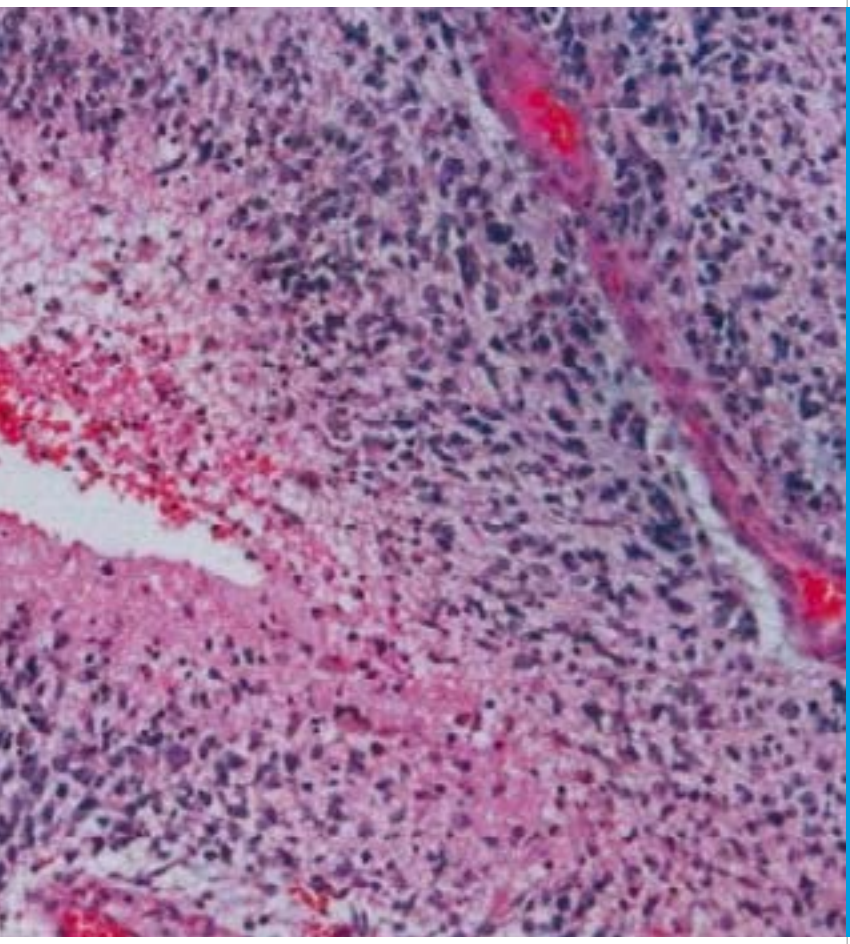


Fig. 4

Areas of necrosis (*) and the palisade arrangement of the cells around the area of necrosis (#) (x50, H&E).



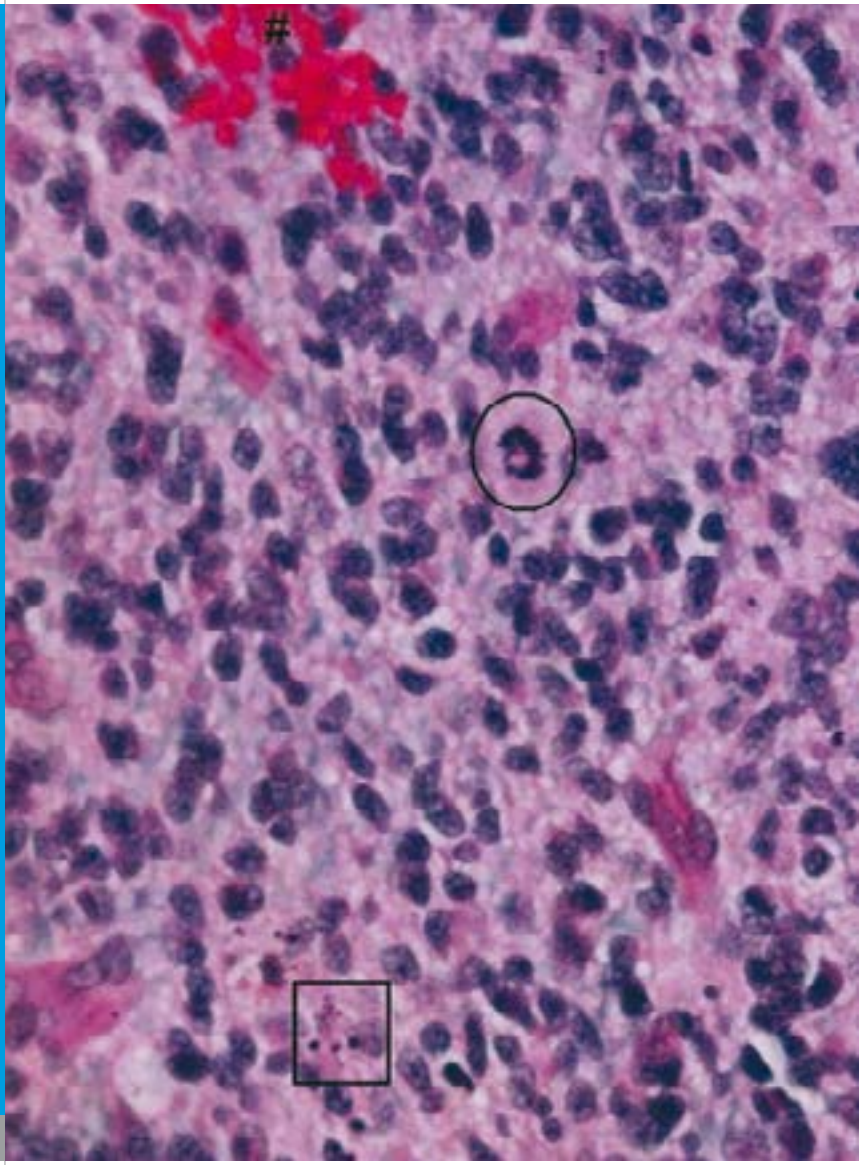
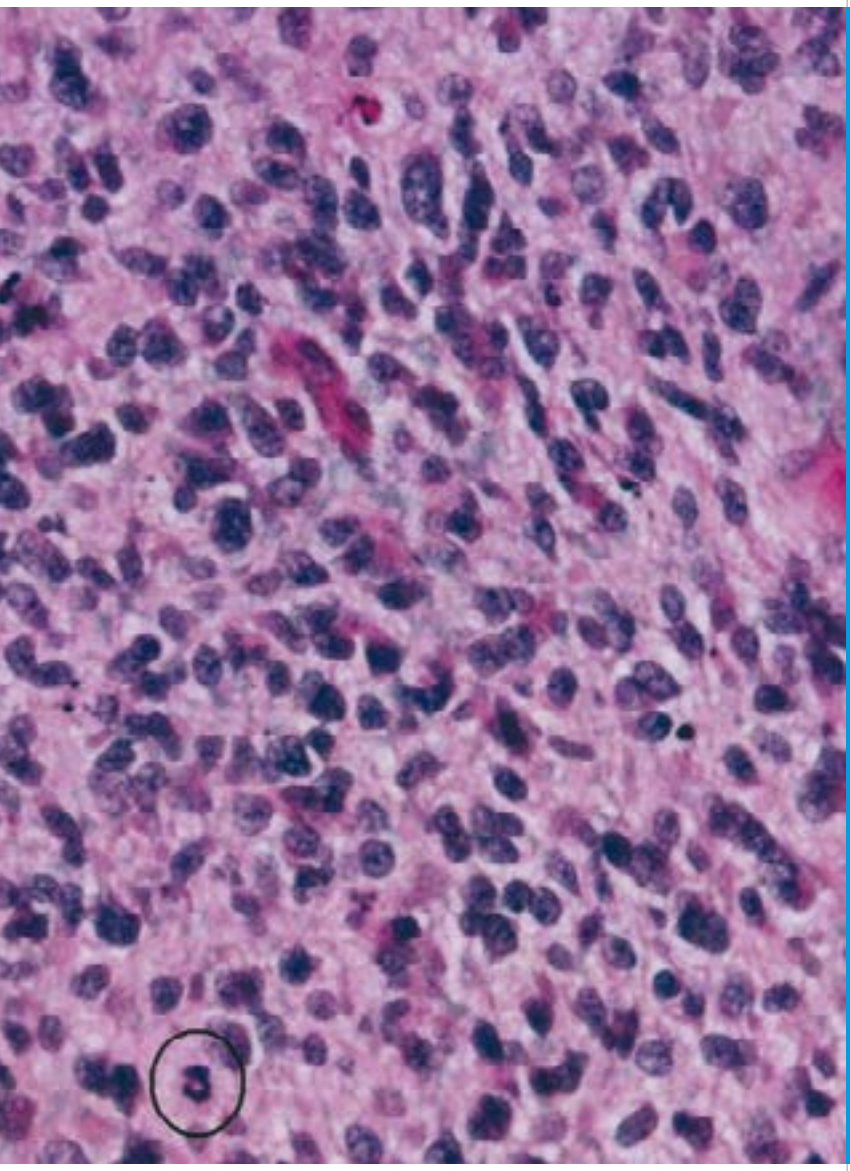


Fig. 5

Small blue cell tumor. Representative photomicrograph of the highly cellular tumor with two mitotic cells (circles), erythrocytes (#) and karyorrhectic remnants of nuclei (square) (x200, H&E).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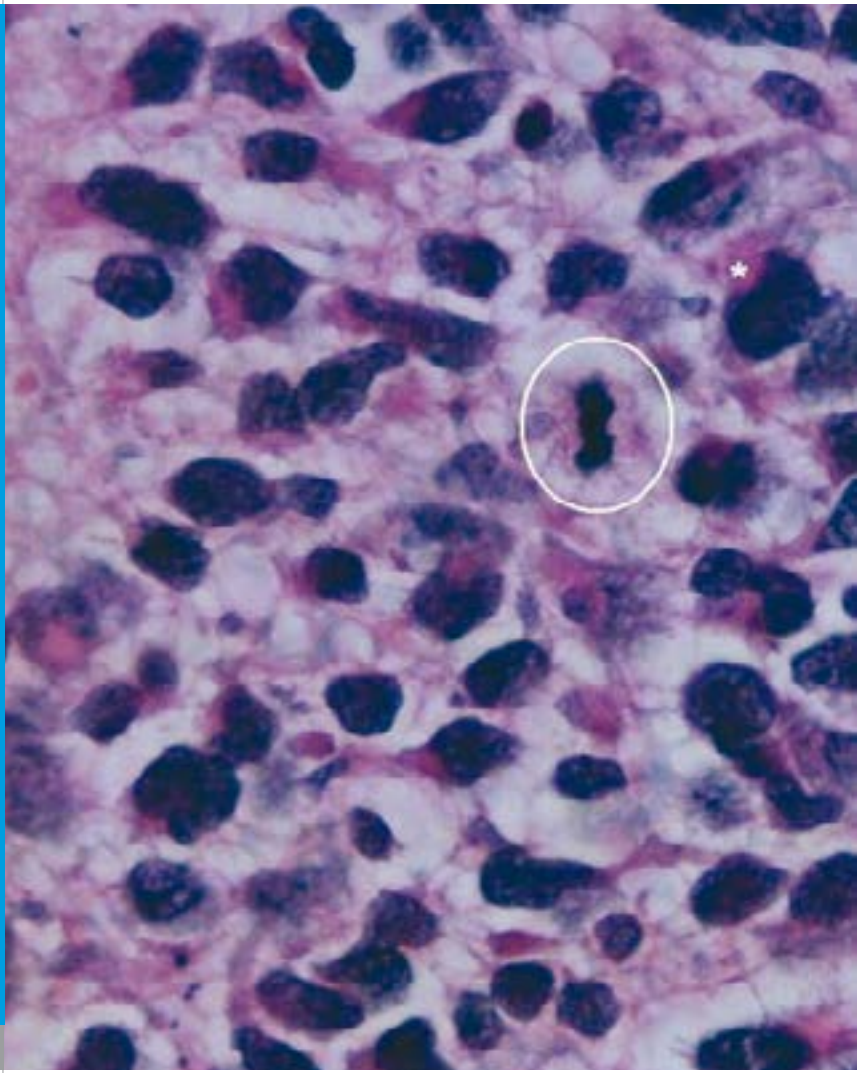
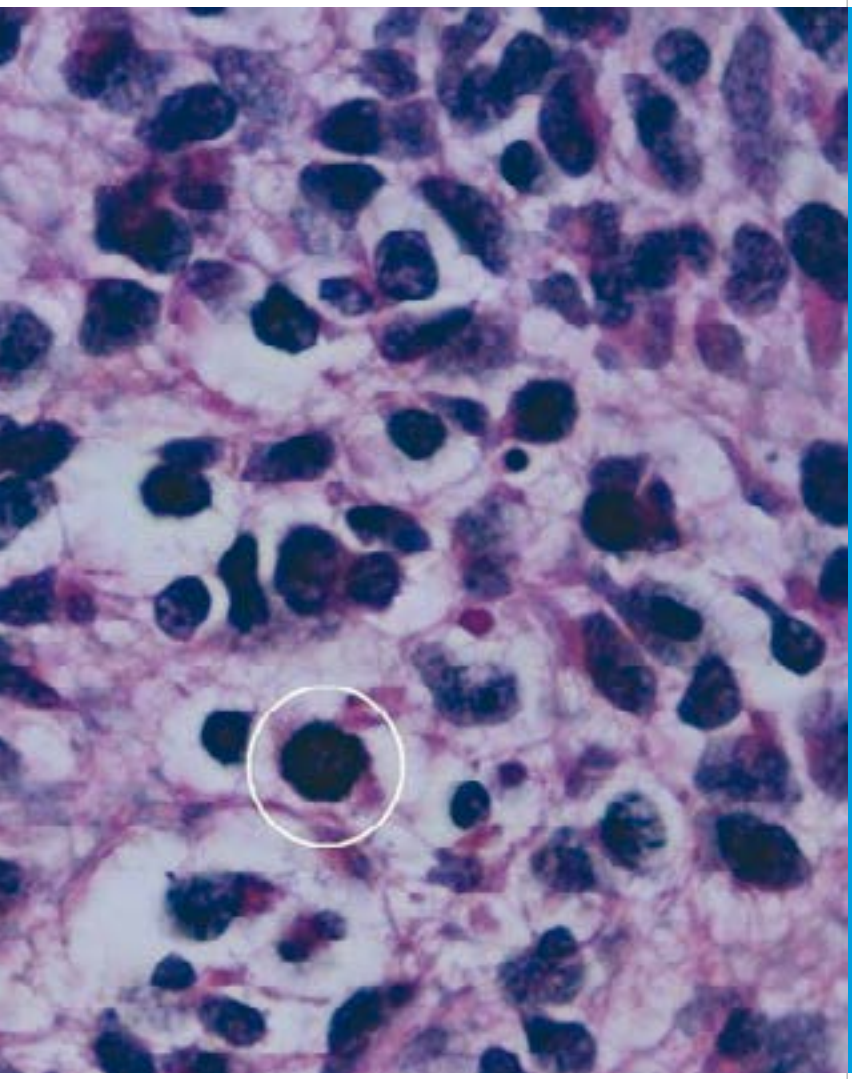


Fig. 6

High power photomicrograph showing the tumor cells which have a high nuclear-cytoplasmic ratio, small oval or hyperchromatic nuclei with a small eccentric mass of eosinophilic cytoplasm (*). The tumor is mitotically active and 2 mitotic figures are present in this photomicrograph (x400, H&E).



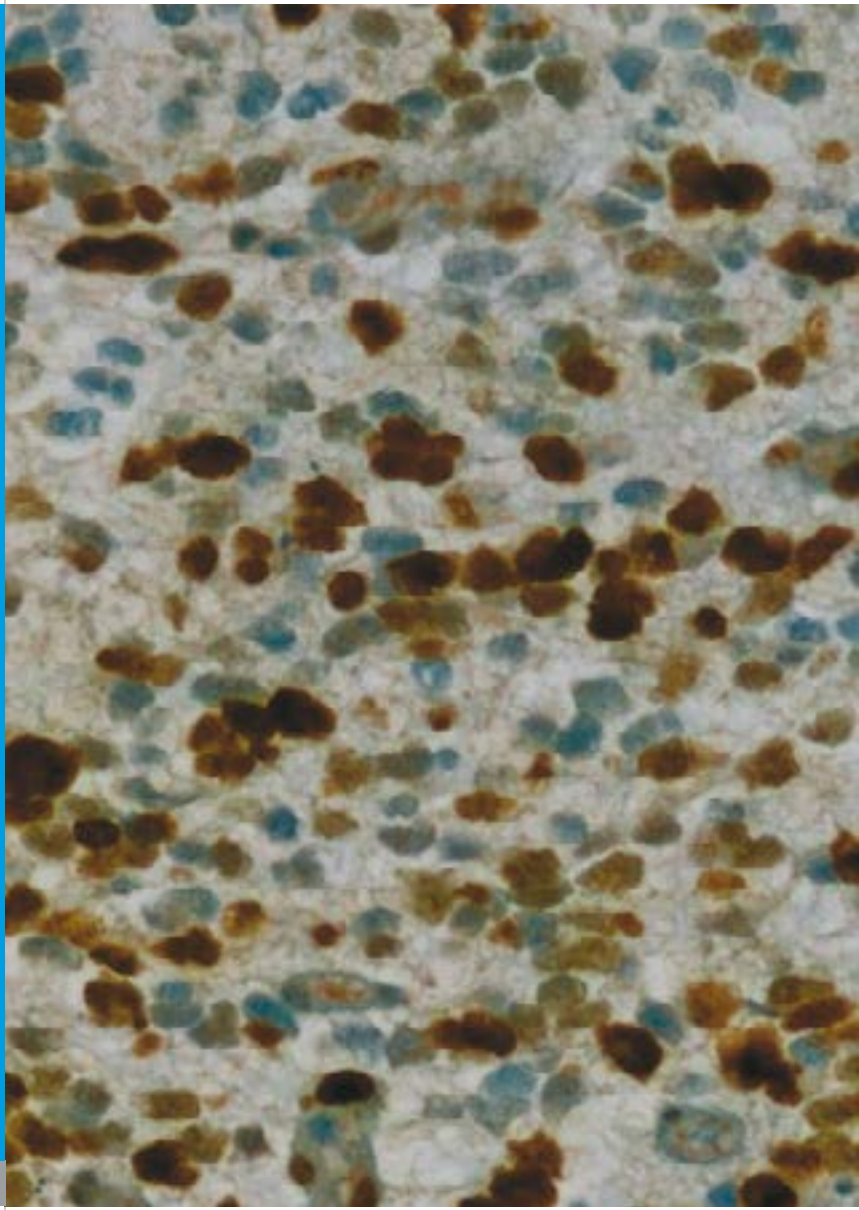
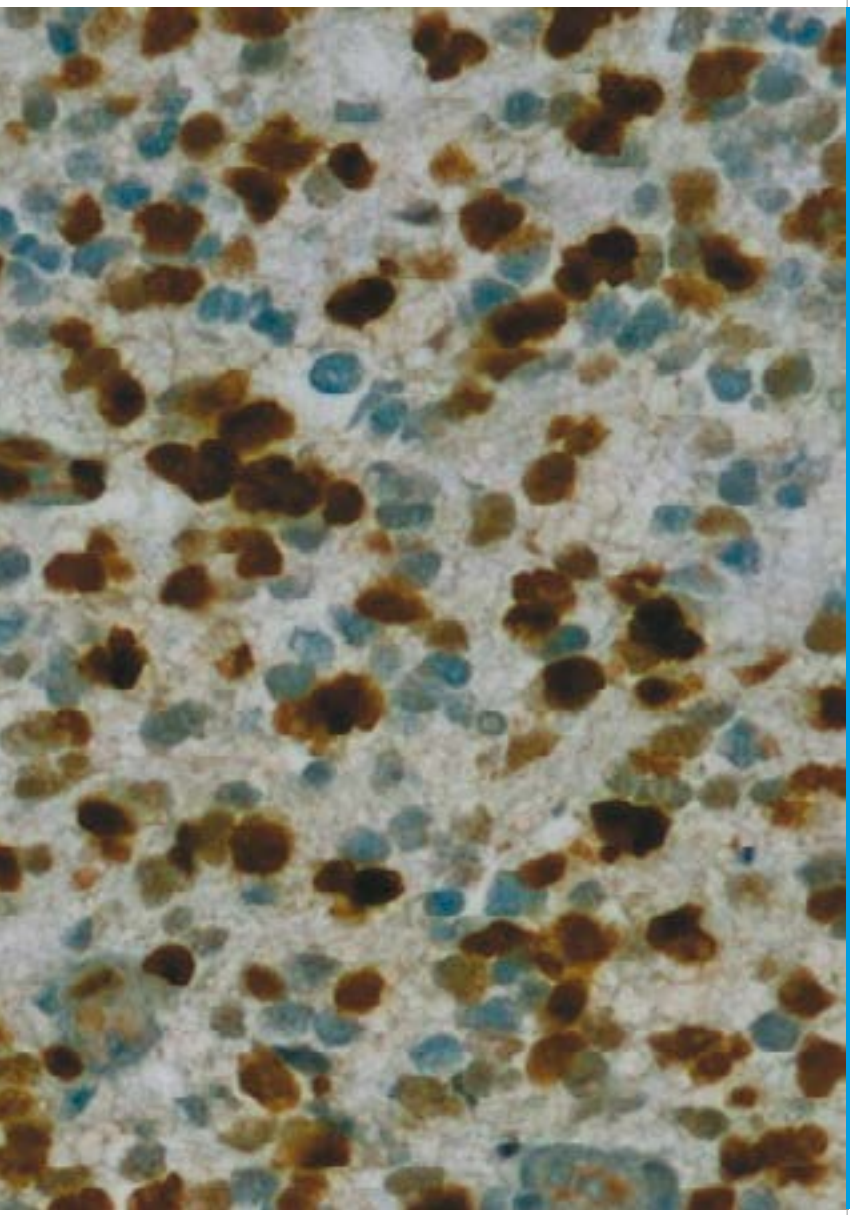


Fig. 7

Visualization of a high proliferation index. Immunohistochemical stain for Ki-67 stains cell in proliferation brown (x200, KI-67).



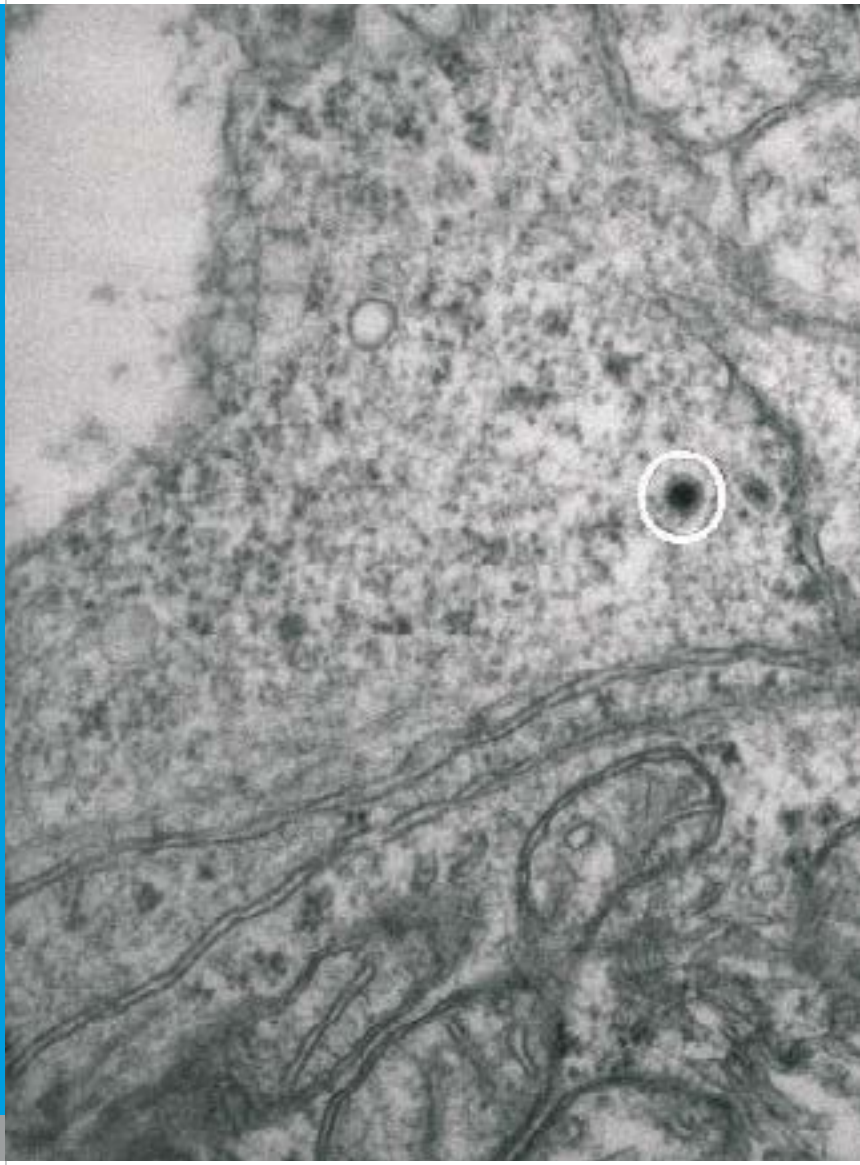
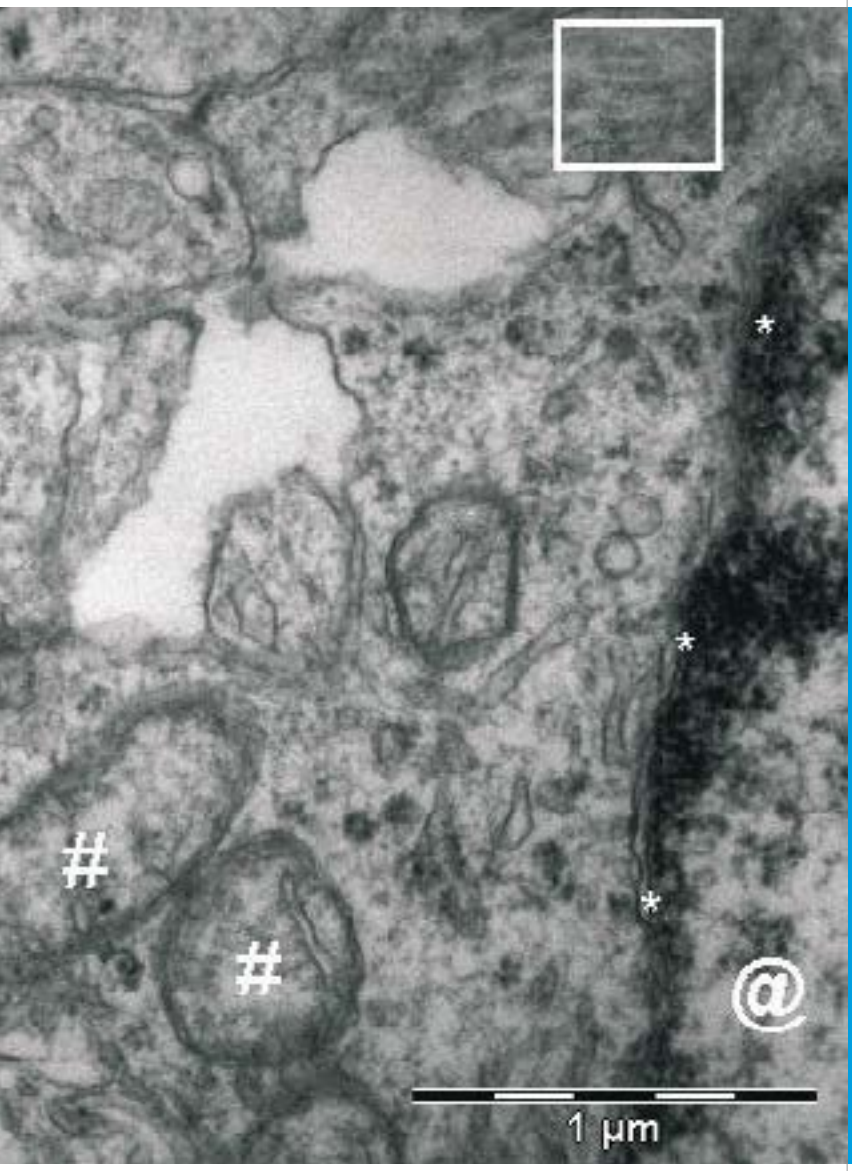


Fig. 8

EM picture showing neurosecretory granule (circle) in cytoplasm of tumor cell and microtubules (square), indicative of neuronal differentiation. Mitochondria (#), nuclear membrane (*) and nucleus (@).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92, XXYY, ?t (1;15) (p36; q24) / 46, XY / 92, XXYY). This abnormality was similar to a previously reported reciprocal translocation in a neuroblastoma cell line (1). Unfortunately the cells could not be cultured for further analysis.

Our patient was placed under the Baby POG protocol 9233 A I and II after the first partial resection at day 2 of life. At 1 month of age, a left ventriculo-peritoneal shunt had to be inserted. The cause of the hydrocephalus was a post-operative intraventricular hemorrhage. At 2 months of age, tumor progression was suspected because of an increase of the head circumference and confirmed on a follow-up MRI. The therapy regimen was changed to the POG protocol 9233 B. At 4 months of age the treatment was changed to the Head Start II protocol, Regimen A (Headstart II: A Phase II study of two alternative intensive induction chemotherapy followed by consolidation with myeloablative chemotherapy and autologous stem cell rescue with or without subsequent radiation therapy for children less than 10 yrs of age newly diagnosed with malignant brain tumors), of which he completed to date 4 of 5 courses. At 6 months of age, a 2nd tumor debulking was performed and a fenestration between the drained left lateral and the right lateral ventricle was successfully done. A follow-up CT scan at 7 month did not show any hydrocephalus or hemorrhage.

The incidence of neonatal brain tumors varies in the literature between 1.4 and 3.6 per 100,000 live births (2,3). Perinatal brain tumors tend to be supratentorial, in contrast to those in older children. The most commonly reported findings in a review of 250 cases of published congenital brain tumors were macrocephaly (28.7%), hydrocephalus (17.3%), detection by imaging pre- or postnatally (12.2%) and stillbirth (10.4%) (4). Macrocephaly can be caused by the tumor mass itself or the concomitant hydrocephalus. The latter is caused by ventricular compression or by hemorrhage from the tumor. The incidence of hemorrhage from perinatal brain tumors is reported between 14 and 18% (4, 5). More frequent causes of hemorrhage in term neonates include trauma, coagulopathy and hypoxia.

In an older review of 230 cases, 23 patients had an associated anomaly of various and nonspecific type (5). PNETs are associated with the Li-Fraumeni syndrome (germline mutation of the p53 tumor suppressor gene).

The polymorphic radiological aspect can be explained by the macroscopical findings showing an inhomogeneous texture with hemorrhage, old and new necrosis; and the microscopical diagnosis of areas with neuronal and astrocytic differentiation. The cytogenetic analysis revealed a previously described translocation.

CONCLUSION

Neonatal brain tumors are rare. They differ in their mostly supra-tentorial location compared to older children. The more common types of perinatal intracranial malignancies in decreasing order are teratomas, astrocytomas, chorioid plexus neoplasias, medulloblastomas (cerebellar PNETs), craniopharyngeomas and meningiomas. Once the cerebral (5.6%) and the cerebellar incidence are combined, the intracranial PNETs are ranked third in frequency with 13.2%.

The most frequent clinical signs are macrocephaly and hydrocephalus. Although neoplasias are not the most frequent causes of these findings, they should be considered in the differential diagnosis. Once initial head ultrasound is performed, the presumed diagnosis has to be aggressively investigated with further imaging and surgical decompression as well as histological sampling has to be performed.

Despite rapid diagnosis and aggressive treatment, overall survival remains poor. In the survivors, a considerable portion has neurological sequelae due to extensive surgical resection or chemotherapy.

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