CASE REPORT

Primary intracranial melanoma in a child with a giant congenital melanocytic naevus and normal MRI

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SUMMARY

We present a case of a 10-year-old girl with a giant congenital melanocytic naevus, and malignant cerebral melanoma.

BACKGROUND

To our knowledge this is the first report describing an intracranial malignant melanoma with no association with leptomeningeal disease (LMD) and normal MRI screening.

CASE PRESENTATION

A 3-day-old female neonate was referred to our laser unit following an emergency caesarean section for bradycardia at term. She was found to have a giant congenital melanocytic naevi (CMN) which covered 70–80% of her body and a further 100–200 smaller satellite naevi (figure 1). Ultrapulsed CO₂ laser ablation of the pigment was carried out for the first time when she was 2 months with further treatments over the next 6 years (table 1).

Multiple biopsies performed at this time demonstrated benign congenital melanocytic naevus. She was up to date with vaccinations, required no regular medications and had no known drug allergies. There was no family history of note.

She suffered no persistent neurological problems and met all her developmental milestones. However, at 2 months she suffered an episode of frothing of the mouth after a general anaesthetic and postoperative codeine phosphate, which resolved spontaneously. Neurological examination and developmental milestones remained normal. T1-weighted MRI postgadolinium axial images (figure 2) were reported as being normal. At 6 years she had a further MRI to investigate a 6-month period of lethargy, dizziness, global weakness, feeling limp and possible loss of consciousness. A fluid-attenuated inversion recovery (FLAIR) image: T1 coronal flair, axial T2, T1 3D volume, precontrast and postcontrast (figure 3) was reported as normal with no signs of LMD. Development and neurological examination remained normal and she received one further UCO₂ laser treatment for her CMN.

Three years later she developed headaches, vomiting and blurred vision and she was found to have papilloedema but an otherwise normal neurological examination. An urgent T2-weighted MRI and FLAIR was grossly normal except a 6 mm non-specific T2 hyperintense (figure 4). This was a vague enhancement and a common area to see vascular enhancement and was reported as non-specific. Lumbar puncture revealed opening pressures of 40 cm H₂O and cytology did not reveal any

malignant cells. Her case was discussed at the neuro-oncological multidisciplinary team and she was thought to have benign intracranial hypertension. Persistent headaches lead to initiation of furosemide and acetazolamide. However, she continued to have headaches, blurred visions and nausea, and 3 weeks later had a lumbar peritoneal shunt inserted.

Four months later she represented with worsening headaches, and a subsequent coronal FLAIR MRI brain revealed a solid cerebellar mass (figure 5). She was also found to have diffuse intracranial leptomeningeal enhancement (Figure 6). There was also a further intradural nodule anterolateral to the spinal cord at C1 with some pial enhancement of the dorsal surface of the thoracic spinal cord. There was no evidence of hydrocephalus.

TREATMENT

Attempted surgical resection revealed a large, haemorrhagic, black intra-axial cerebellar lesion, too extensive to completely excise. Histopathological analysis demonstrated primary malignant melanoma. Genetic coding was carried out revealing an activating C.181c>A(p.Glu61Lys) mutation on codon 61 of the neuroblastoma RAS viral (v-ras) oncogene homolog (NRAS) gene. The matched blood and cutaneous biopsies did not demonstrate any melanoma.

She was started on temozolamide and whole brain radiotherapy. But despite this, developed right arm weakness and urinary retention within 3 months. Follow-up MRI of her spine revealed widespread disease. She died 1 month later.

DISCUSSION

Neurocutaneous melanosis (NCM) is a rare congenital disorder, characterised by the presence of large

Figure 1 Clinical photographs of a neonate with a giant congenital melanocytic naevus in an axial distribution over the trunk.

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Table 1 Laser treatment regimen and outcomes

Treatment	Age	Area	Dose	Outcomes
1	2/12	L upper back and nasal tip	Ultrapulsed CO ₂ laser: CPG (1, 9, 5) 4 passes: energy 250 mJ, power 25 W	Frothing at mouth following codeine
MRI at 2 months: following episode of frothing at the mouth following a general anaesthetic and codeine phosphate				
2	5/12	Whole lower back lumbro sacral—punch biopsies	Ultrapulsed CO ₂ laser: CPG (1, 8, 5), 4–5 passes, energy 250 mJ, power 30 W	
3	9/12	Lower back	Ultrapulsed CO ₂ laser: CPG (1, 8, 5) 4–5 passes, energy 250 mJ, power 30 W	
4	12/12	Lower back and satellite lesions:	Ultrapulsed CO ₂ laser: 300 mg, 30 W Ultrapulsed CO ₂ laser 225 mJ, power 30 W	
5	14/12	Ant abdomen nose tip and right middle finger	Ultrapulsed CO ₂ laser: CPG (1, 8, 5), energy 250 mJ, power 35 W	
MRI at age 6 to investigate lethargy, dizziness and global weakness and possible loss of consciousness				
6	6 6/12	Left foot, leg, hand and finger, right thigh	Ultrapulsed CO ₂ laser: CPG (1, 8, 5), energy 175 mJ, power 35 W	Hypertrophic scar

CPG, computerised pattern generator.

of multiple congenital melanocytic cutaneous naevi associated with intracranial leptomeningeal melanocytosis.¹ The diagnosis of NCM can be made when: the projected adult size of the cutaneous lesion is more than 20 cm, or there are multiple lesions or both; there is no evidence of cutaneous melanoma and there is no evidence of meningeal melanoma.²

Figure 2 T1-weighted MRI at 2 months old. Normal postaxial gadolinium image.

Figure 3 Fluid attenuated inversion recovery MRI at 6 years old. Normal axial image.

Giant lesions (GCN) (≥ 20 cm) (Kopf), and those associated with satellites have a greater risk of undergoing malignant transformation to melanoma.^{3–4} In view of this some authors⁵ advocate MRI imaging of brain and spine in patients with more than one CMN lesion, in order to detect possible LMD and cause for developmental delay.

Melanocytes originate from neural crest, and are normally found within the stratum basale of the epidermis, pia mater and other sites of ectoderm origin. Cases of NCM MRI with temporal lobe pigmentation or temporal lobe malignant melanoma,⁶ abnormal leptomeningeal enhancement without malignant degeneration, and with intraparenchymal melanin

Figure 4 T2-weighted MRI at 10 years: axial image showing 6 mm non-specific T2 hyperintense focus in the right pons at the middle cerebellar peduncle.

Figure 5 Fluid attenuated inversion recovery MRI: axial Image showing midline T2 hyperintense peripherally based, well-defined, enhancing cerebellar mass.

deposition without detectable leptomeningeal melanosis⁷ have been reported. This is the first case of primary intracranial melanoma with normal MRI findings at 2 months and 6 years, including no previously detected LMD or NCM.

Characteristic MRI findings of T1 shortening indicative of melanotic rests within the brain or meninges are due to (1) paramagnetic metal scavenging of melanoma cells resulting in a spontaneous high signal of melanin on T1-weighted images and/or (2) stable free radicals (indolesemiquinones and semiquinones) within the melanin pigment which affect a shortening of T₁ and T₂ relaxation times. Increased melanisation of the

Figure 6 T1-weighted MRI: coronal postgadolinium image demonstrating diffuse leptomeningeal disease with evidence of cerebrospinal fluid loculation in the fissures involving both supra and infratentorial compartments.

anterior temporal lobes and amygdala, cerebellum, thalamus and/or base of the frontal lobe¹ correlates with the normal distribution of melanocytes within the leptomeninges.³

Detection of NCM and early malignancy is difficult. Pitfalls include: (1) leptomeningeal enhancement is not pathognomonic for leptomeningeal melanosis and can be seen in infectious, inflammatory and malignant processes of the central nervous system (CNS). (2) There is limited evidence on the detection rates in MRI and whether cytology aids this. In a study comparing MRI with cytology for detection of LMD⁸ only 32% patients with known LMD were diagnosed correctly based on cerebrospinal fluid cytology, spinal MRI or both. (3) Differentiation between benign and malignant parenchymal melanocytosis on MRI is difficult.¹ (4) The absence of meningeal enhancement does not exclude the diagnosis of neurocutaneous melanosis or malignant melanoma.⁹ (5) Screening MRI scans should be performed before myelination can interfere with visualisation of the leptomeningeal melanin deposits.¹⁰

The question then arises as to if screening with MRI should be carried out, when, and how frequently, and if it should be carried out in isolation or with additional lumbar puncture and cytological sampling.

In conclusion, as detection rates with MRI and cytology are limited and the risks of developing intracranial melanoma are much greater in patients with CMN. In any child with signs of raised intracranial pressure NCM must be considered. Unfortunately, the prognosis remains poor once CNS symptoms occur.⁴ Around 100 cases of neurocutaneous melanosis have been reported. To our knowledge this is the first report of primary intracranial melanoma with no previous signs of neurocutaneous melanosis and normal MRI.

Learning points

- ▶ Giant congenital melanocytic naevi (≥ 20 cm) and those associated with satellites have a greater risk of undergoing malignant transformation to melanoma.
- ▶ Melanocytes originate from neural crest, and are normally found within the stratum basale of the epidermis, pia mater and other sites of ectoderm origin and therefore melanoma can occur in any of the sites from this embryological origin.
- ▶ In children with giant congenital melanocytic naevus and signs and symptoms consistent with raised intracranial pressure, leptomeningeal disease or neurocutaneous melanosis must be considered.

Competing interests None.

Patient consent Obtained.

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