Familial Neurogenic Tumors: Review Questions

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QUESTIONS

Choose the single best answer for each question.

Questions 1 and 2 refer to the following case study.

A 14-year-old boy presents with reported difficulty seeing the chalkboard at school. Upon examination, there are large, brownish spots on his skin and a central field scotoma.

1. **Which of the following should be strongly considered as a possible etiology in this patient?**
   (A) Li-Fraumeni syndrome
   (B) Neurofibromatosis type 1 (NF1)
   (C) Neurofibromatosis type 2 (NF2)
   (D) Tuberous sclerosis
   (E) Turcot's syndrome

2. **What other potential findings might be expected on physical examination of this patient given the possible etiology?**
   (A) Ashleaf spot
   (B) Freckling in the axillary region
   (C) Opacities in the posterior aspect of the lens
   (D) Retinal angioma
   (E) Skin pits on the palms and soles

3. **Which of the following familial tumor syndromes is associated with bilateral vestibular schwannomas?**
   (A) Li-Fraumeni syndrome
   (B) NF1
   (C) NF2
   (D) Tuberous sclerosis
   (E) Turcot's syndrome

4. **An infant is brought to the emergency department with a history of seizures manifest by flexor and extensor myoclonus. On physical examination, a hypomelanotic macule is noted on the infant's back. Which of the following syndromes should be considered?**
   (A) Li-Fraumeni syndrome
   (B) NF1
   (C) NF2
   (D) Tuberous sclerosis
   (E) Turcot's syndrome

5. **A 10-year-old boy enters the emergency department after having a tonic clonic seizure. His past medical history includes treatment for a rhabdomyosarcoma at age 6 years. A computed tomography scan of the brain shows an enhancing lesion with a necrotic center in the left frontoparietal lobe. Which of the following familial tumor syndromes should be considered?**
   (A) Cowden's syndrome
   (B) Gorlin's syndrome
   (C) Li-Fraumeni syndrome
   (D) Tuberous sclerosis
   (E) Turcot's syndrome

(turn page for answers)

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ANSWERS AND EXPLANATIONS

1. **(B) NF1.** The most recognizable clinical feature of NF1 is the appearance of café au lait spots. These spots are brownish in color and appear prior to adulthood. Café au lait spots occur in 95% of NF1 patients and are frequently the first indication of this genetic disorder.[1] Clinical criteria for the diagnosis of NF1 includes café au lait spots. In addition, optic gliomas also are a frequent manifestation in these patients; there is a 25% incidence of this type of glioma in NF1 patients. Tuberous sclerosis, NF2, Li-Fraumeni syndrome, and Turcot's syndrome are not associated with café au lait spots.
2. **(B) Freckling in the axillary region.** Freckling in the axillary region is one of the specific clinical criteria of NF1; other criteria include neurofibromas (≥ 2 or 1 plexiform), 2 or more Lisch nodules, a distinctive osseus lesion or thinning of the long bone cortex with or without pseudoarthritis, and a first-degree relative with NF1. As noted above, café au lait spots are the hallmark of the disorder, and optic glioma occurs frequently. Lens opacities occur in NF2. Retinal angiomas are found in Von Hippel-Lindau Syndrome, ashleaf spot occurs in tuberous sclerosis, and skin pits on palms and soles are a manifestation of Gorlin syndrome.
3. **(C) NF2.** The hallmark of NF2 is the appearance of bilateral vestibular schwannomas. These tumors most often occur on the vestibular portion of the eighth cranial nerve and typically are benign. Like NF1, NF2 is associated with specific diagnostic criteria including: the presence of multiple types of central nervous system tumors (eg, meningioma, glioma, neurofibroma, schwannoma) cerebral calcification, and posterior subcapsular lens opacity. Tuberous sclerosis, NF1, Li-Fraumeni syndrome, and Turcot's syndrome are not associated with bilateral vestibular schwannomas.
4. **(D) Tuberous sclerosis.** Tuberous sclerosis (or tuberous sclerosis complex) is associated with seizures that typically begin in infancy. The flexor/extensor myoclonus may indicate infantile spasms, which are associated with hypsarrhythmia on electroencephalogram. Of all infants experiencing this seizure disorder, 50% have tuberous sclerosis.[2] The hypomelanotic macule may be shaped like a leaf and thus has been deemed an "ashleaf spot"; this is the most common lesion associated with this disease.
5. **(C) Li-Fraumeni syndrome.** Li-Fraumeni syndrome is a familial cancer syndrome that was first identified in families with rhabdomyosarcoma. The most common nervous system tumor is a malignant glioma. These tumors often occur in patients younger than 14 years. Other malignancies that have been associated with this syndrome include other soft tissue sarcomas, premenopausal breast cancer, osteosarcoma, and leukemias. This combination of tumors has not been observed in any of the other syndromes noted.

REFERENCES

1. Kandt RS. Tuberous sclerosis complex and neurofibromatosis type 1: the two most common neurocutaneous diseases. Neurol Clin 2002;20:941–64.
2. Kwiatkowski DJ, Short MP. Tuberous sclerosis. Arch Dermatol 1994;130:348–54.