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DICER1 Mutations

Individuals with *DICER1* syndrome have an increased chance to develop several different types of tumors. The tumors most commonly seen in individuals with a *DICER1* mutation are pleuorpulmonary blastoma and cystic nephroma.

The penetrance (likelihood to develop a tumor if one has a mutation) of *DICER1* mutations is unknown, but is thought to be low. *DICER1*-related tumors typically develop before the age of 40, with many tumors occurring in childhood.

DICER1Cancer/Tumor Risks

- **Pleuropulmonary Blastoma (PPB):** PPB is a rare childhood lung tumor that begins in or around the lungs. The tumor can be benign or malignant.[1] The majority of PPBs are diagnosed before the age of 12, but rare occurrences have been reported in older children and young adults.[2]
- **Cystic Nephroma and Wilms Tumor:** Cystic nephroma is a benign kidney tumor. Rarely, cystic nephroma may progress to anaplastic sarcoma of the kidney. Cystic nephroma appears to have the highest incidence before the age of 4 years.[3,4] *DICER1* syndrome also includes an elevated risk of Wilms tumor, a type of cancer that starts in the kidney.
- **Ovarian Sertoli-Leydig Tumors (SLCT):** SLCT are testosterone secreting ovarian tumors. About 10-30% of SLCT are malignant (cancerous). The age range of risk is from early childhood through ~45 years.[1,3]
- **Ciliary Body Medulloepithelioma**: These are tumors of the eye that can be either benign or malignant.
- **Nasal Chondromesenchymal Hamartoma (NCMH):** NCMH are benign tumors that grow high inside the nose. This usually only occurs in early infancy. It may cause breathing difficulties and interfere with the development of the eyes.[5]
- **Thyroid Goiters, Cysts, and Hyperplasia:** *DICER1* mutations are associated with an increased risk for thyroid cysts, multi-nodular goiter and hyperplasia. These are all benign growths on the thyroid gland. By the age of 40 years, the cumulative incidence of multi-nodular goiter or thyroidectomy was 75% in women and 17% in men with *DICER1* syndrome.[6]
- **Embryonal Rhabdomyosarcoma (EMRS) of Cervix, Bladder, Ovary:** EMRS most commonly occur in pubertal and post-pubertal women.[7,8]
- **Pineoblastoma and Pituitary Blastoma:** Pineoblastoma are malignant tumors of the pineal gland. Pituitary blastoma are tumors of the pituitary gland and is typically seen in children 2 and under and often presents with Cushing syndrome, ophthalmoplegia (weakness of eye muscle) or diabetes insipidus. The incidence of these tumors within *DICER1* syndrome is rare (<1% incidence).[3]

DICER1 Surveillance and Management Recommendations

Cancer/Tumor Type	Surveillance/Management Recommendations[3]
Pleuropulmonary Blastoma (PPB)	• Initial chest CT between 3 and 6 months of age. The follow-up interval for screening should be determined based on initial findings. ◦ If normal, chest CT between 2.5 and 3 years of age • Consider chest radiographs every 6 months until 8 years of age and annually from age 8-12 years.

Cystic Nephroma Wilms Tumor	• Consider biannual abdominal ultrasound until age 8 and annually thereafter.
Ovarian Sertoli-Leydig Tumors Embryonal Rhabdomyosarcoma	• Consideration of annual or semiannual pelvic ultrasound throughout early and late childhood and adulthood. • Abdominal ultrasound could be performed at the same time to look for cystic nephroma or renal tumor.
Ciliary Body Medulloepithelioma	• Meeting with an ophthalmologist may help to detect to these tumors early on. • Treatment may include surgery.
Nasal Chondromesenchymal Hamartoma	• Ear, nose, and throat (ENT) evaluation with nasal endoscopy is suggested for persistent symptoms of nasal obstruction. • Treatment may involve removal of the tumor.
Thyroid Goiters, Cysts, and Hyperplasia	• Consider thyroid ultrasound with assessment for regional adenopathy starting at age 8 years. Repeat every 3 years if normal. • If nodules are seen, routine follow-up per standard pediatric endocrinology guidelines is recommended.
Pineoblastoma Pituitary Blastoma	• The role of surveillance brain MRI is controversial. Consider urgent brain MRI if there are symptoms of intracranial pathology.

Research

- The NIH has a research study and registry for individuals who have *DICER1* gene mutations or are at increased risk for *DICER1* gene mutations, more information on these initiatives may be found at https://ppb.cancer.gov/ and http://ppbregistry.org.

Implications for Family Members/Reproductive Considerations

- First-degree relatives (i.e., parents, siblings, and children) have a 50% chance to inherit the familial *DICER1* mutation. Second-degree relatives (i.e., nieces/nephews, aunts/uncles, and grandparents) have a 25% chance to inherit the familial mutation.
- For carriers of a known mutation, assisted reproduction (with or without egg or sperm donation), pre-implantation genetic testing, and prenatal diagnosis options exist.
- All family members are encouraged to pursue genetic counseling to clarify their risks. Family members can visit www.FindAGeneticCounselor.com to find genetic services near them.

References

1. Schultz KA, Pacheco MC, Yang J, et al. Ovarian sex cord-stromal tumors, pleuropulmonary blastoma and DICER1 mutations: a report from the International Pleuropulmonary Blastoma Registry. *Gynecologic oncology.* 2011;122(2):246-250.
2. The International Pleuropulmonary Blastoma (PPB) / DICER1 Registry. https://www.ppbregistry.org/. Accessed.
3. Schultz KAP, Rednam SP, Kamihara J, et al. PTEN, DICER1, FH, and Their Associated Tumor Susceptibility Syndromes: Clinical Features, Genetics, and Surveillance Recommendations in Childhood. *Clinical cancer research : an official journal of the American Association for Cancer Research.* 2017;23(12):e76-e82.
4. Doros L, Schultz KA, Stewart DR, et al. DICER1-Related Disorders. *GeneReviews.* 2014.

5. Priest JR, Williams GM, Mize WA, Dehner LP, McDermott MB. Nasal chondromesenchymal hamartoma in children with pleuropulmonary blastoma--A report from the International Pleuropulmonary Blastoma Registry registry. *International journal of pediatric otorhinolaryngology.* 2010;74(11):1240-1244.
6. Khan NE, Bauer AJ, Schultz KAP, et al. Quantification of Thyroid Cancer and Multinodular Goiter Risk in the DICER1 Syndrome: A Family-Based Cohort Study. *The Journal of clinical endocrinology and metabolism.* 2017;102(5):1614-1622.
7. Dehner LP, Jarzembowski JA, Hill DA. Embryonal rhabdomyosarcoma of the uterine cervix: a report of 14 cases and a discussion of its unusual clinicopathological associations. *Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc.* 2012;25(4):602-614.
8. Doros L, Yang J, Dehner L, et al. DICER1 mutations in embryonal rhabdomyosarcomas from children with and without familial PPB-tumor predisposition syndrome. *Pediatric blood & cancer.* 2012;59(3):558-560.