

CASE REPORT

WAARDENBURG SYNDROME TYPE I WITH IRIS AND RETINAL COLOBOMA

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ABSTRACT

We present a rare case report, Waardenberg syndrome type I, and ocular abnormalities related to the disease. A Boy, 11 months, presented with blue and hole in inferior iris. Patient also controlled to pediatric and ENT department according to his global developmental delayed, and unresponsiveness to sound stimulus since birth. Patient presented with dystopia canthorum, bilateral iris coloboma, brilliant blue iris, and retinal coloboma. Others systemic condition were skin hypopigmentation, bilateral sensorineural hearing lost, and global developmental delay equal to 6 months old baby. According to manifestations, this supporting diagnosis for Waardenberg syndrome type I. The management consists in treating the symptoms accordingly. Careful follow up and work up is important to improve patient quality of life

Keywords : *Waardenberg syndrome, iris coloboma, retinal coloboma*

INTRODUCTION

Waardenburg syndrome is rare genetic Abnormalities caused by absence of melanocytes in the skin, hair, eyes, and the stria vascularis of the cochlea, and classified as a disorder of neural crest cell development. The prevalence was 1/42.000 -1/1.000.000 depend on the type of syndrome. It is inherited as autosomal dominant, autosomal recessive, either sporadic (Pingault, 2010).

Waardenburg syndrome classified into four types. Clinical manifestation are hypopigmentation iris, or heterochromia, white forelock since birth or before 30 years old, dystopia canthorum, and sensory neural hearing lost. In some conditions ocular manifestation could be followed by blepharophimosis, *synophrys*, lagophthalmus, lacrimal mucocele, and hypopigmentation on eyelashes, choroid, and retina (Boparai, 1979; Shields, 2013). We report, 11 month old boy with characteristic feature of waardenburg syndrome type 1 along with iris and retinal coloboma.

CASE REPORT

A boy, 11 months old, non consanguineous marriage was referred to our clinic (Ophthalmology department, Soetomo General Hospital, Surabaya) from pediatric and ENT department because hypopigmentation on his both iris. In pediatric and ENT department, patient was followed up for his global developmental delayed, and sensory neural hearing lost. Family history didn't indicate same condition with patient. (Pasien adalah pasien RSUD dr soetomo, belum pernah dipublishkan sebelumnya di jurnal lain. Persetujuan ada di rekam medik rumah sakit rsud dr soetomo)

On general examination we noticed patients could not sit by his self, decreased respond to sound stimulus, and skin hypopigmentation in his neck (Figure 1). On ocular we noticed dystopia canthorum (with W index= 2.48), bilateral iris coloboma, brilliant blue iris

(Figure 2). His binocular refractive revealed 1 cpcm (59 cm)/ 1 cpd, similar to 6/180 both eyes, streak retinoscopy was +2.00 D on both eyes. posterior segment examination show retinal coloboma without involvemnet optic nerve (Figure 3).

Patient had global developmental delayed, personal social equal to 7 month old, intestinal disorders, and MRI also did not show any abnormalities.



Figure 1. Skin Hypopigmentation on neck
(Apakah hasil foto sendiri? IYA)



Figure 2. Distopia canthorum with brilliant blue iris and iris coloboma (Iya)

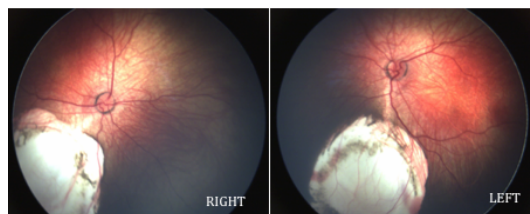


Figure 3. Retinal Coloboma (Iya)

fine motoric equal to 6 months old, language equal to 6 months old, and gross motoric equal to 5 months old. Patient also performed karyotype analysis, and showed 46 XY. Audiometry examination showed sensory neural hearing lost. Patient did not have any upper limbs defect, and cranial skeletal abnormalities.

Discussion

Waardenburg syndrome is auditory pigmentary syndrome which first describe in 1947 and 1950 by Waardenburg and Klein. This genetic condition was caused by abnormal differentiated from neural crest pluripotent cell during embryogenesis. During embryogenesis, blastomere differentiated into three of layer, ectoderm, mesoderm, and endoderm. Neural system was generated from ectoderm, and developed into neural crest, and neural tube. Cell on neural tube was an origin from central neural system, including retina. Whereas, neural crest was an origin for peripheral neuron, endocrine cell, bone, cartilage, and connective tissue which are important on melanocyte synthesis. Melanocyte not only used within pigment production on skin, hair, and iris, but also it is used to regulated fluid potassium gradient between ear plasma membrane and endolymph. This fluid managed sound signal transduction on hair cell. This condition was an underlying causes on pathophysiology of the disease (Osawa, 2009).

Waardenburg syndrome classified into 4 type, manifestation of the disease depending on its type (Tabel 1). Most common type of this syndrome were waardenburg syndrome type 1 and type 2. Waardenburg syndrome type 1 was autosomal dominant spectrum that affected PAX3 gene, chromosome 2, band 2q35- 2q36.1. In China population, mutation affected on S209X gene, in Europe mutation affected on R223S gene, others reported mutation on MIFT gene in chromosome 2, and SOX10 gene, chormosome 22. Waardenburg

syndrome type 1 diagnosed when patient fulfill 2 major criteria, or 1 major criteria and 2 minor criteria. Major criteria are, sensory neural hearing lost, hypopigmentation iris, white forelock (hair hypopigmentation), and dystopia canthorum (waardenburg index > 1.95). Minor criteria are, skin hypopigmentation, broad/ high nasal root, hypoplasia alae nasi, synophrys, and premature graying of hair (before 30 years old) (Dumayas, 2015).

Waardenburg syndrome type 2 is a condition inherited as autosomal dominant or autosomal recessive. Main manifestation in this syndrome are congenital hearing lost, and heterochromia iris. Difference manifestation between type 1 and type 2 is absence dystopia canthorum on type 2. Some condition follow in waardenburg syndrome type 2 are hypogonadotropine, hypogonadism, anosmia, lacrimal gland and parotis gland hypoplasia (Dumayas, 2015). Waardenburg syndrome type 3 or Klein Waardenburg syndrome, could be sporadic or autosomal dominant inheritance (Pingalut, 2010). Manifestation could be follow by cleft palate, hypoplasia musculoskeletal system, disturbance lower extremities development, and joint abnormalities. Waardenburg syndrome type 3 was similar to type 1, but in type 3, musculoskeletal deformity is present (Kniffin, 2014). Waardenburg syndrome type 4 or shah waardenburg syndrome reported as autosomal dominant or autosomal recessive. This type is the most rare condition among others type. Sometimes this type of syndrome followed by hirschprung disease, severe short stature, scoliosis, mild developmental delayed, ear formation hypoplasia, and peripheral neuropathy (Dumayas, 2015).

Genetic anomaly classified into five category, which are single gene disorder, somatic gene disorder, chromosomal disorder, mitochondrial disorder, and multifactorial. Waardenburg syndrome classified into single gene disorder. Although we could not

evaluated gene disorder in this patient (because limitation on genetic analysis facilities), supporting data and examination result showed patient fulfill criteria for waardenburg syndrome type 1. Patient fulfill three major criteria, and one major criteria. One publication reported waardenburg syndrome followed by bilateral congenital cataract as unusual entity (Vichare and Bhargava, 2013). Coloboma iris and retina was also rare condition following the syndrome. Management consists in treating the symptoms accordingly. Patient has been followed up for his sensory neural hearing lost, and has been planned to use hearing aid. In pediatric department, patient had been stimulated for his global developmental delayed routinely. Ocular follow up was necessary to evaluate ocular manifestation according to the disease.

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