Esophagus Cancer and IgA Deficiency in a Patient with Dubowitz Syndrome: A Case Report

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Dubowitz syndrome was first described in 1965 by the English physician Dr. Victor Dubowitz. This genetic disorder causes growth retardation both before and after birth. It is primarily diagnosed through the distinctive facial features of affected individuals, including a small triangular-shaped face with a high forehead and wide-set, slitted eyes. The main method of diagnosis is through identification of facial phenotype. Esophageal mass biopsy revealed squamous cell carcinoma type. Both malignancy and IgA deficiency have been reported literature in patients with Dubowitz syndrome. However, Esophagus cancer has not been reported among the malignant tumors. Herein, we reported a patient with Dubowitz syndrome, IgA deficiency and Esophagus cancer.

Key words: Dubowitz syndrome, Esophagus cancer, IgA deficiency

INTRODUCTION

Dubowitz syndrome is a rare genetic disorder characterized by microcephaly, growth retardation and a characteristic facial appearance (small, round, triangular shaped with a pointed, receding chin, a broad, wide-tipped nose, and wide-set eyes with drooping eyelids). Symptoms vary among patients, but other characteristics include a soft, high pitched voice; partial webbing of fingers and toes; palate deformations; genital abnormalities; eczema; hyperactivity; preference for concrete thinking over abstract; language difficulties and aversion to crowds [1]. The pathogenesis of the disease is yet to be identified and no medical tests can definitively diagnose the disease [2]. The main method of diagnosis is through identification of facial phenotype. Since it was first described in 1965 by an English physician Victor Dubowitz, over 140 cases have been reported worldwide. A majority of cases have been reported from the United States, Germany, and Russia, and it appears to affect all ethnicities and genders equally [3]. We here report on a Dubowitz syndrome patient with Esophagus cancer due to microcephaly, pre/postnatal growth retardation and a characteristic facial appearance, eczema and IgA deficiency.

CASE REPORT

A 24 year-old male patient was seen in the outpatient clinic due to growth retardation, recurrent respiratory infection, recurrent diarrhea, and sputum. He was born from first degree cousin marriage with 1900 gr birth weight and 43 cm birth height after an unfollowed up full term pregnancy. In his postnatal period he had a history of poor feeding, frequent vomiting, chronic diarrhea, frequent otitis media and delayed teeth eruption. He left public primary school due to mild mental retardation. Three years ago he was seen in the pulmonary clinic and his laboratory studies revealed IgA deficiency, bronchiectasis in lungs His physical examination revealed a cachectic appearance. His length was 150 cm, his weight was 32 kg and head circumference was 44.5 cm. Head and neck examination revealed microcephaly, sparse hair, facial asymmetry, long and triangular face, deep set eyes, strabismus, micropthalmi, perioral fullness, thin upper lip, prominent lower lip, missing teeth, hypertrophic adenoids, micrognathia, prominent and dysplastic ears. 2x3 cm diameter and irregular borderline nevus and diffuse seborheic dermatitis. Respiratory system examination showed pectus excavatum and bilateral ronchi in ausscultation. In his cardiovascular system examination 2-3/6 systolic murmur in mitral region and 2/6 diastolic murmur in tricuspid region were recorded. Echocardiography revealed 2+ mitral insufficiency and 3+ tricuspid insufficiency. In his abdominal examination 5 cm hepatomegaly with totally 18 cm liver length was observed. Abdominal ultrasonography revealed hepatosplenomegaly, solid mass 4x3 cm in liver and bilateral pleural efussion. Extremity examination revealed 4/5 muscle force in all extremities. Lung CT showed diffuse overventilated cystic bronchiectasis areas in the right lung lower segments. An upper gastrointestinal endoscopic examination showed fragile, ulcerated, vegetan mass originating from the lower

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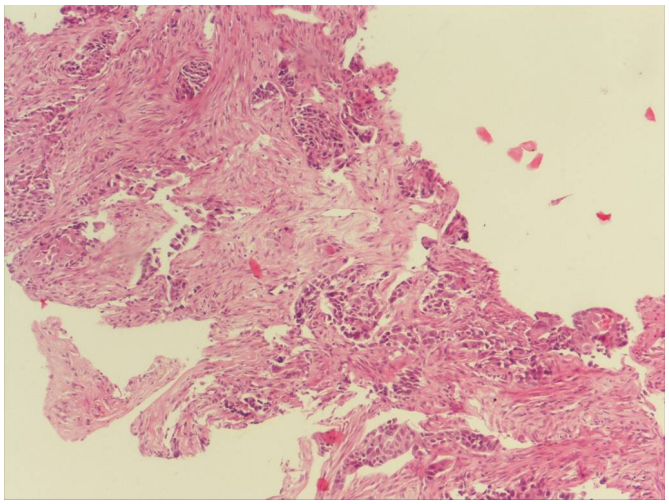

Figure Squamous cell carcinoma infiltration (H-E x40)

esophageal and invading throughout the cardia The histopathological diagnosis was squamous cell carcinoma (figure). Patient was diagnosed as metastatic Esophagus carcinoma and we started chemotherapy protocol for the patient. However, we stopped the chemotherapy due to nephrotoxicity and ototoxicity. Four months later the patient died due to respiratory insufficiency. Chromosome analysis revealed normal karyotype.

DISCUSSION

In 1965 Dubowitz reported 4 patients with a malformation syndrome characterized by intrauterine growth retardation, short stature, microcephaly, mild mental retardation with behavior problems, eczema, and unusual and distinctive facies. Various minor malformations, such as pilonidal dimples, submucous clefts, high-pitched voice and sparse hair, were also observed [1]. Thuret *et al.* [4] reported the cases of 2 caucasian sisters who, in addition to other features, had repeated infections and recurrent ulcerative stomatitis. They suffered from recurrent neutropenia. One had complete IgA deficiency with elevated IgM levels; the other had low values of both IgA and IgG with an increased level of IgM. An increased rate of chromosomal breakage was demonstrated in both.

Eczema may be resolved with age, however occasional flareups. Asthma, headaches, and seizures may also be observed. Mild mental retardation was present. Tsukahara and Opitz [5] reviewed clinical information on 141 individuals with Dubowitz syndrome, 105 reported since 1965, and 36 previously unreported. They suggested that facial anomalies are perhaps the most diagnostic feature of the physical signs. Microcephaly was present in 112 of the patients, blepharophimosis in 60, and ptosis in 53. They considered a prominent round tip of the nose noted in 17 of their 34 cases to especially characteristic of the Dubowitz syndrome at a young age. In the total of 141 patients, normal appearance was found 15 times.

The frequency of malignant tumors may be increased in the Dubowitz syndrome. Sauer *et al.* [6] were described Two own cases of Dubowitz syndrome in two sisters are described, one of them with hypogammaglobulinemia and neuroblastoma, the other one with complete IgA deficiency and malignant lymphoma in 1977. Grobe [7] was described a child with Dubowitz syndrome and acute lymphatic leukemia. Dubowitz syndrome in a newborn, who has embryonal rhabdomyosarcoma and chromosomal breakage, was reported by Al-Nemri *et al.* in 2000 [8]. Andrade-Machado *et al.* [9] reported Dubowitz syndrome, polymyositis and aleucemic myeloblastic leucemia. A propensity to malignant disorders has been known in Dubowitz syndrome. Here, we described the first case of Dubowitz syndrome with IgA deficiency and Esophagus cancer.

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