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A Rare Case with Werner's Syndrome was Developed Cirrhosis due to Steatohepatitis During of Follow-up Period

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Abstract: Werner's syndrome is a rare autosomal recessive, hereditary systemic disease with progeroid features, usually presenting in adolescence. Its clinical manifestations are short stature, scleroderma-like skin changes, cataracts, premature aging of the face, gray hair, genital hypoplasia and endocrinological abnormalities. Cirrhosis is an extremely rare manifestation of Werner's syndrome. It has been reported in <4% of patients. A 31-year old man, with Werner's syndrome, he had been followed the last presention for liver failure were evalueted and cirrhosis was diagnosed due to steatohepatitis by liver biopsy. In 1999 initial diagnosis; cataracts, DM, short stature, and genital hypoplasia were found. In 2002 was showed steatohepatitis by liver biopsy which was performed for the persisting high liver transaminases. In 2007 developed gray hair, high-pitched voice, hypergonadotropic hypogonadism and osteopenia. He was a month ago had been hospitalised for nausea and vomiting with hematemesis. He was admitted to our hospital performed in the upper gastrointestinally endoscopy by the depertmant of gastroenterologia was found esophageal varices and to them was performed band ligation. Laboratory investigations and the imaging methods were showed as chronic liver disese. It was not found for other causes of chronic liver disease. In coclusion, here, we want to present a case with Werner's syndrome who had cirrhosis due to steatohepatitis during of follow-up period in our clinic.
Keywords: Werner's syndrome, Steatohepatitis, Cirrhosis.

INRODUCTION

Werner's syndrome (WS) is a rare autosomal recessive disease. It is also known as progeria adultorum and pangeria. Werner's syndrome was first described by Otto Werner at 1904 that juvenil cataracts, short stature, scleroderma-like skin alterations, premature aging of the face, gray hair and genital hypoplasia [1]. It was added later endocrinological abnormalities and predisposition to sarcoma and carcinoma. Myocardial infarction and cancer are the most common causes of death [2]. But, cirrhosis is an very rare manifestation of WS. Here, we reports a case with WS was developed cirrhosis due to steatohepatitis during of follow-up period.

Written informed consent has been obtained from the patient for publication of the case report.

CASE REPORT

We previously reported two siblings with Werner syndrome (WS) that we followed since our the initial diagnosis [3]. They were at 20 and 16 years of ages at their first diagnosis. Elder sister was died after 13 years follow up due to sudden cardiac arrest at 33 years old. She had had characteristics of WS such as diabetes mellitus (DM), cataracts, genital hypoplasia, short stature, osteopenia, gray hair, high-pitched voice and hepatosteatosis. Its brother who had been followed the last presention for liver failure were evalueted and cirrhosis was diagnosed due to steatohepatitis by liver biopsy. In 1999 initial diagnosis; cataracts, DM, short stature, and genital hypoplasia (micropenis and right cryptorchidism) were found. In 2002 was showed steatohepatitis by liver biopsy which was performed for the persisting high liver transaminases. In 2007

developed gray hair, high-pitched voice, hypergonadotropic hypogonadism and osteopenia.

The living second case is now 31 years-old. He was a month ago had been hospitalised for nausea and vomiting with hematemesis. He was admitted to our hospital performed in the upper gastrointestinally endoscopy by the depertmant of gastroenterologia was found esophageal varices and to them was performed band ligation. Laboratory investigations performed in our clinic revealed the following results: Hb 9.4 g/dL, MCV 75 fL, WBC 4000 µL, Plt 103000 µL. Serum electrolytes and thyroid function tests were within normal ranges. Blood analysis showed glucose 201 mg/dL total protein 7.1 g/dL, albumin 2.8 g/dL, ferritin 5.4 ng/dL, HbA1c 7.0%, PT 14.6 second, AST 59 U/L (0 to 40), ALT 30 U/L (0 to 41), ALP 63 U/L (38 to 126), GGT 40 U/L (11 to 49), protein electrophoresis was showed as hyper gammaglobuline (γ 40.15%) with broad-based monoclonal spike. It was not found for other causes of chronic liver disease.

Abdominal doppler ultrasonography was showed the portal vein diameter 10 mm, long axis of the spleen 130 mm. An abdominal CT showed splenomegaly, intra-abdominal minimal free fluid and liver was consistent with chronic liver disease. A liver biopsy was performed and revealed cirrhosis due to steatohepatitis (Fig. 1 and 2).

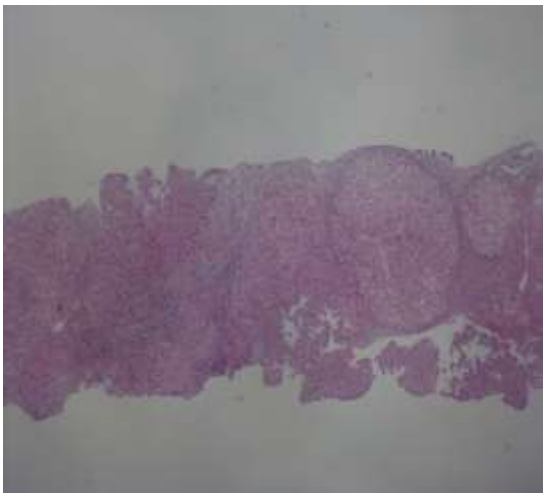

Fig. 1: Microscopically, liver is replaced by regenerative nodules surrounded by fibrous bands (Hematoxyline& Eosin (HE), x40)

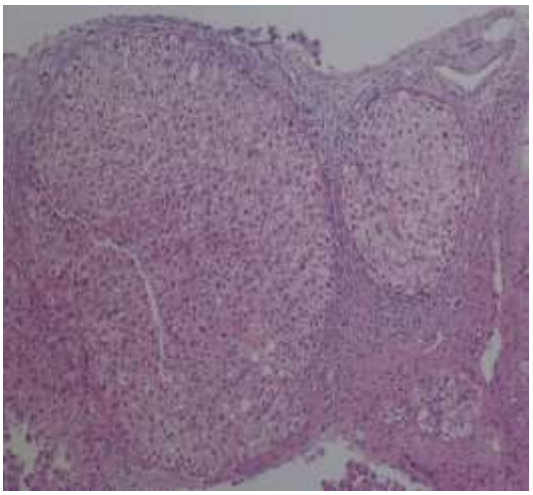

Fig. 2: High power appearance of regenerative nodules (HE, x400)

DISCUSSION

Werner's syndrome is a rare autosomal recessive systemic disease it was seen with short stature, scleroderma-like skin changes, cataracts, premature aging of the face, gray hair, genital hypoplasia, osteoporosis, diabetes mellitus [1-3]. The diagnosis of WS can be confirmed by detection of biallelic WRN muthagenic variants, identified in approximately 90%. An updated of WS in 2014; it is reported that mutation in the RECQL2 gene, is responsible for the syndrome [4]. The gene is also implicated in the normal aging process. This is most likely the result of a founder mutation in the Japanese population [5]. Approximately 91% of affected individuals have all four cardinal signs, that are bilateral ocular cataracts 99%, premature graying and/or thinning of scalp hair 100%, characteristic dermatologic pathology 96%, short stature 95% [6]. The clinical diagnosis may be further supported by the presence of the following signs and symptoms: Thin limbs 98%, pinched facial features 96%, osteoporosis 91%, voice change 89%, hypogonadism 80%, type 2 DM 71%, soft tissue calcification 67%, neoplasm(s) 44%, atherosclerosis 30% [7].

In our Werner cases; all these symptom and funding were observed except neoplasm. In our living case with cirrhosis due to steatohepatitis exluded other causes of cirrhosis such as hepatitis B or C, alcohol abuse, Wilson sydrome, autoimmun hepatitis. Cirrcosis in WS be seen very rare finding in literature and it was reported as case reports [8].

Metabolic disorders such as liver dysfunction, hyperlipidemia, insulin resistance and regional increase of intra-abdominal fat due to WS may complicate and cause NASH [9]. Furthermore, over production of types I and III collagen and nonalcoholic steatohepatitis secondary to insulin resistance and dyslipidemia

possibly contribute to cirrhosis in WS [10]. Our patient admitted with the hemorragia of esophageal varices and he is still following by the both endocrinology and gastroenetrologia departments.

CONCLUSION

The case of presented is very rare condition in WS that circcosis due to steaohepatitis. Therefore, we want to present this case during of follow-up period in our clinic.

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