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Case Study

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A CASE OF ADULT ONSET AUTOIMMUNE TYPE 1 DIABETES WITH AGE OF ONSET AT 56 YEARS.

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JUN aged 58 years presented with history of frequent hypoglycemic episodes. She had history of diabetes since 2 years since February 2021. There is no family history of diabetes. At diagnosis her random blood glucose was 400 mg/dl. She was started on premix insulin 10-0-10 and continued for 1.5 years. She went to a local doctor one month back and he had stopped insulin, started oral drugs. The patient developed diabetic ketoacidosis and she was admitted for treatment.

The patient was referred to Karnataka institute of endocrinology and research on 16-2-2023. She came with history of frequent episodes of hypoglycemia. She had the following features –

BMI 20.06
Waist circumference -78 cms
Duration of diabetes – 2 years
No family history of diabetes
BP – 129/84 mm
CVS – NAD
RS – NAD
Per abdomen – NAD.
Investigations –
FPG-180 MG/DL
PPPG- 263 MG/DL
HBA1c-11.4%
Total cholesterol-161mg/dl
LDL-128 mg/dl
HDL-69.2 mg/dl

Triglycerides-128 mg/dl
VLDL – 26 mg/dl
Serum creatinine – 0.6 mg/dl
TSH- 1.14 micro IU/ml.

Fasting C-pepide – 0.070 nanogram/ml
GAD ANTIBODIES ->2000 IU/ML.
Serum sodium-135 meq/l
Serum potassium-4.02 meq/l
Serum chloride -102.4 meq/l
Liver function tests –
Serum total bilirubin – 0.3 mg/dl.
Dirct bilirubin – 0.2 mg/dl.
Indirect bilirubin – 0.1 mg/dl.
Total serum protein – 7 grams/dl
Serum Albumin – 3.8 grams/dl
Serum globulin – 3 grams/dl
A/G ratio -1
SGOT -42U/L, SGPT -36 U/L, GGT – 16U/L, Alkaline phosphatase – 72IU/L
Urine glucose 4+, ketone bodies – negative,
Urine microalbumin/creatinine – 44 mg/gram.

Diagnosis - Adult onset type 1 diabetes with age of onset at 56 years.

The points which help in diagnosis of type 1 diabetes –

1. No family history of diabetes.
2. History of diabetic ketoacidosis on stopping insulin.
3. Fasting C-pepide – 0.070 nanogram/ml
4. GAD antibodies - >2000 IU/ML.

This patient was apparently normal before the age of 56 years which is surprising in spite of having GAD antibody titers of more than 2000. She could have at least developed latent autoimmune diabetes in adults.

Discussion- Type 1 diabetes mellitus results from a T-cell-mediated destruction of pancreatic beta islet cells, resulting in rapid progression to absolute insulin deficiency. Of patients newly diagnosed with type 1

diabetes, 80% are positive for GAD or IA2 antibodies,[1] whereas 20% are antibody negative at the time of diagnosis. The risk of developing diabetes over a 10-year period, on the basis of positive GAD and IA2 antibody tests, is three times greater with a family history of type 1 diabetes in a first-degree relative. [2] The incidence of anti-islet cell autoantibodies is 31% in type 1 diabetes, 6% in non-type 1 diabetes and 8–9% in unaffected first-degree relatives of people with type 1 diabetes.

This case highlights an important diagnostic point, that types 1 or 1a diabetes should be considered in adult patients who present with particularly rapid-onset hyperglycaemia. In this case, there was no evidence of other associated autoimmune conditions. Coeliac disease is known to occur in up to 10% of patients with type 1 diabetes, [3] and there is a strong association between type 1 diabetes and autoimmune thyroiditis.[4] Although there have been numerous immunological markers identified in types 1 and 1a diabetes,[5] the commercially used assays that are acceptably sensitive and specific for the condition are the anti-GAD and anti-IA2 antibodies. Early detection of autoimmune diabetes mellitus in adults ensures appropriate treatment of the condition and early establishment of euglycaemia,[6] which supports a legacy effect of blood glucose control,[7] and reduction in the risk of complications such as diabetic nephropathy and retinopathy.

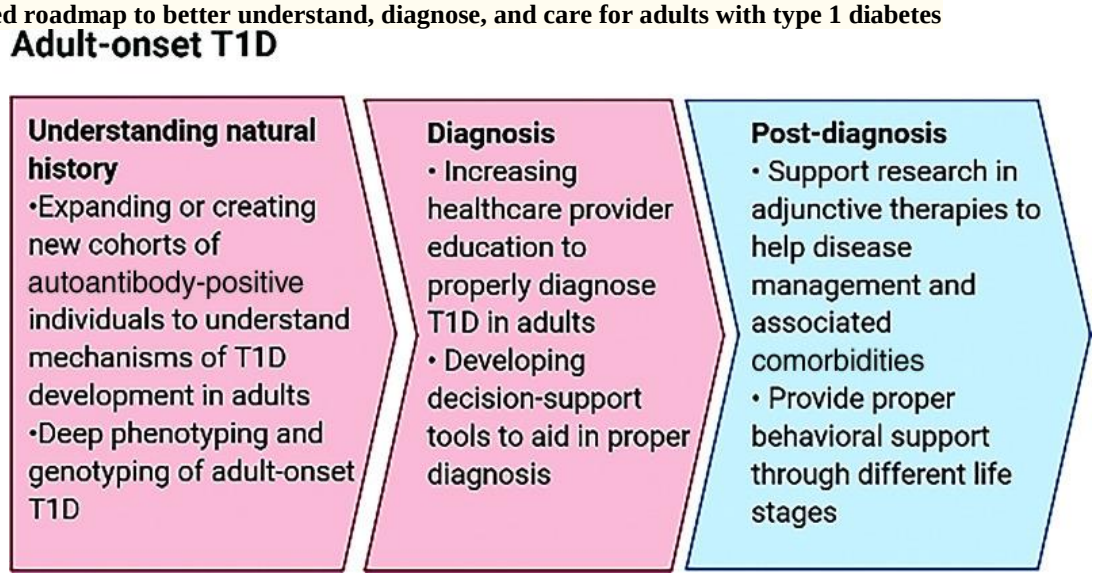
Although it is possible to predict the development of type 1 diabetes through human leukocyte antigen (HLA) genetic predisposition and the appearance of islet cell autoantibodies,[8,9] none of the treatments trialed to date have been able to arrest the progressive loss of insulin secretion resulting from destruction of beta islet cells.[10] Further research has enabled identification of another major islet autoantigen, zinc transporter-8 (ZnT8), which is associated with beta islet cell secretory granules. Antibodies against ZnT8 are found in about 70% of patients with type 1 diabetes and may predict the development of the disorder, thereby providing an opportunity to treat patients before the onset of autoimmune beta cell destruction.[11]

Type 1 diabetes is commonly diagnosed in childhood, but ~ 25% of people with type 1 diabetes are diagnosed as adults, some even as late as the ninth decade of life.[12] About 10% of adults initially diagnosed with type 2 diabetes are found to have pancreatic autoantibodies associated with type 1 diabetes.[13]

The clinical characteristics of youth-onset type 1diabetes and type 1diabetes with onset in adulthood can differ, with potential consequences concerning management later in life.[14] Individuals with detectable C-peptide levels, which are more common early in the course of the disease and with onset of type 1 diabetes in adulthood, have better clinical outcomes and can achieve lower A1C levels with less serious hypoglycemia than those without detectable C-peptide concentrations.[15,16] An earlier onset of type 1 diabetes is also associated with a longer burden of disease and more diabetes-related complications in the aging population. Lower quality of life in adults with type1 diabetes is related to worse glycemic control, the presence of chronic complications such as renal disease, and a history of severe hypoglycemia.[17,18] All of these factors are important to consider in individualizing management plans for older adults with type 1 diabetes.

A case of elderly woman aged 96 years diagnosed as type 1 diabetes was reported by Hiroshi Yamaguchi et al in Japan.[19]

Proposed roadmap to better understand, diagnose, and care for adults with type 1 diabetes



Adult-onset type 1 diabetes is more common than childhood-onset type 1 diabetes, as shown from epidemiological data from both high-risk areas such as Northern Europe and low-risk areas such as China. In

southeastern Sweden, the disease incidence among individuals aged 0–19 years is similar to that among individuals 40–100 years of age (37.8 per 100,000 persons per year and 34.0/100,000/year, respectively).[12] Given that the comparable incidence spans only two decades in children, it follows that adult-onset type 1 diabetes is more prevalent. Similarly, analysis of U.S. data from commercially insured individuals demonstrated an overall lower incidence in individuals 20–64 years of age (18.6/100,000/year) than in youth aged 0–19 years (34.3/100,000/year), but the total number of new cases in adults over a 14-year period was 19,174 compared with 13,302 in youth.[20] Despite the incidence of childhood-onset type 1 diabetes in China being among the lowest in the world, prevalence data show similar trends across the life span. From 2010–2013, the incidence was 1.93/100,000 among individuals aged 0–14 years and 1.28/100,000 among those 15–29 years of age versus 0.69/100,000 among older adults.[21] In aggregate, adults comprised 65.3% of all clinically defined newly diagnosed type 1 diabetes cases in China, which is similar to estimates using genetically stratified data from the population-based UK Biobank using a childhood-onset polygenic genetic risk score (GRS).[22]

Older adults with type 1 diabetes are a heterogeneous group and have not been well studied. With long-duration diabetes, hypoglycemia is common, regardless of A1C level. Individualized treatment plans using more complex insulin regimens and lower glycemic goals with frequent SMBG are recommended in healthy older adults. For individuals with poor health status and frailty, modifications are suggested. Older adults should be assessed for hypo- and hyperglycemia; hypertension; physical disabilities; vision, hearing, and cognitive impairments; pain; social support; urinary incontinence; polypharmacy; depression; nutritional deficits; fall risk; and the need for social services. The treatment plan should focus on minimizing hypoglycemia and serious hyperglycemia and should address identified physical, emotional, and social challenges to enhance safety and quality of life. In the future, new insulin preparations and technological advances are expected to contribute to better therapeutic approaches for this growing population.

It is also pertinent to consider the psychological effects of a diagnosis of type 1 diabetes in adulthood. Significant changes across all areas of life are generally required and the condition has the potential to affect work and family life. As with other chronic disease diagnoses, patients would be expected to experience the usual stages of bereavement, and GPs play a pivotal role in supporting these patients to overcome the grief of the diagnosis. Beyond accurate and timely diagnosis of the condition, education and instilling confidence in the adult patient newly diagnosed with type 1 diabetes is critical to the patient's ability to self-manage. Indeed, there is a need not only for counselling and support from the GP, but also the consideration of additional counselling from allied health professionals such as psychologists for optimal support and patient outcomes.

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