

Diabetes Update

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Dear Doctor,

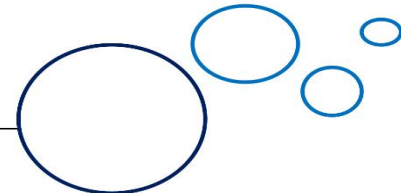
Greetings from Micro Labs Limited. We are happy to bring you **“DIABETES UPDATE”** which contains latest and interesting news in the field of Diabetes and Endocrinology.

- “Clonal hematopoiesis: A New Risk for Type 2 Diabetes in Hypercholesterolemia”
- DXA and QCT Evaluation of Bone Mineral Density in Adult Type 1 Diabetes Mellitus Patients.
- Relationship between Cardiac Function and Diabetic Retinopathy Severity in Type 2 Diabetes Patients
- A case of 19-year-old with young-onset diabetes who developed Purtscher-like retinopathy

Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in

Looking forward to your valuable feedback

Best Regards,
Medical Team, Micro Labs Limited



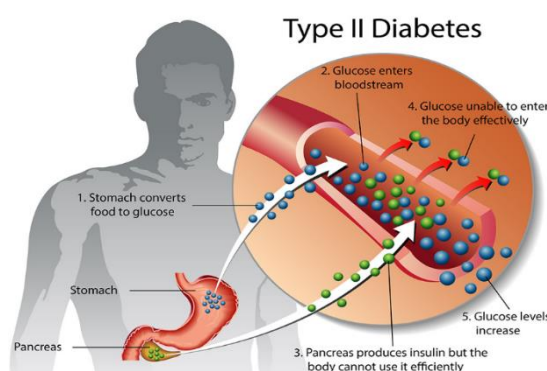
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“Clonal hematopoiesis: A New Risk for Type 2 Diabetes in Hypercholesterolemia”

INTRODUCTION

Clonal hematopoiesis of indeterminate potential (CHIP) is described as the somatically-driven growth of hematopoietic stem cells (HSCs) in the absence of any hematologic malignancy. Increased cardiovascular disease, ageing, and insulin resistance have all been related to CHIP ⁽¹⁾. Atherosclerosis and cardiovascular disease are both strongly correlated with type 2 diabetes. Type 2 Diabetes is associated with ageing, just like CHIP. An increased risk of hematologic malignancy has been linked to type 2 diabetes, according to a meta-analysis ⁽²⁾. Since these results indicate that CHIP may have some relationship with type 2 diabetes, this study looked at the connection between CHIP and type 2 diabetes.



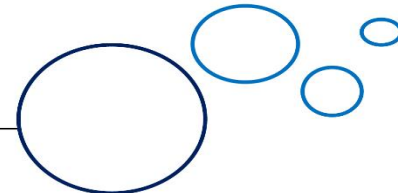
A major risk factor for diabetes is the interaction with Clonal hematopoiesis of indeterminate potential (CHIP) and high Low Density Lipoprotein (LDL) cholesterol.

METHODS

The retrospective cohort study was conducted on 4,047 subjects aged greater than or equal to 40 years with more than one of the risk factors for cardiovascular disease. Targeted gene sequencing was performed by isolating genomic DNA from peripheral blood to detect CHIP. During the follow-up period, the incidence of new-onset type 2 diabetes was assessed.

RESULTS

Six hundred and thirty-five (635) participants (15.7%) of the total had CHIP. The incidence of new-onset diabetes was substantially greater in CHIP carriers than in persons without CHIP over the median follow-up of 5.1 years (11.8% vs. 9.1%). CHIP considerably increased the chance of developing new-onset diabetes in a univariate study, but it had no effect in a multivariate analysis. For newly diagnosed type 2 diabetes, only LDL cholesterol shown a significant association with CHIP. CHIP significantly raised the risk of diabetes in the group with hyper-LDL cholesterolemia, but not in the group with non-hyper-LDL cholesterolemia



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(FIGURE 1). The risk of developing diabetes was almost double for patients with CHIP and hyper-LDL cholesterolemia compared to persons without CHIP and with low LDL cholesterol.

DISCUSSION

The current study showed that in those with high LDL cholesterol, CHIP increased the probability of developing type 2 diabetes for the first time. When combined, CHIP and LDL cholesterol significantly increased the likelihood of type 2 diabetes developing for the first time. In comparison to non-CHIP carriers in the non-hyperLDLC group, CHIP carriers were twice as likely to develop new-onset type 2 diabetes in the hyperLDLC group⁽²⁾. A synergistic impact on the onset of type 2 diabetes may be produced by LDL cholesterol and CHIP, which increase macrophage activation via the inflammasome. Increased cholesterol levels may promote hematopoietic stem cell growth and activation^(3,4).

CONCLUSION

In participants with high LDL cholesterol in particular, the presence of CHIP constituted a major risk factor for new-onset type 2 diabetes. According to these findings, a major risk factor for diabetes is the interaction with CHIP and high LDL cholesterol.

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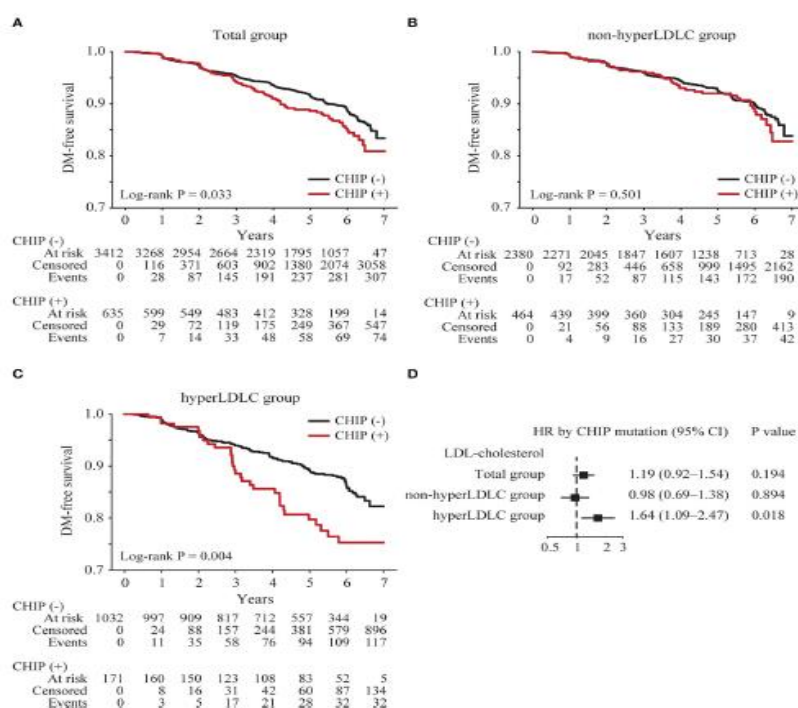
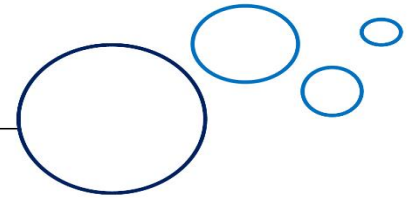


Figure 1 A) Type 2 diabetes risk based on the presence of CHIP. For the entire group of participants (n = 4,047), Kaplan-Meier curves were displayed. B) Low LDL cholesterol (non-hyperLDLC group) participants C) participants with elevated LDL cholesterol (hyperLDLC group) D) In the whole group, non-hyperLDLC group, and hyperLDLC group, the multivariate Cox regression model was examined after controlling for age, sex, BMI, and family history of diabetes.



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DXA and QCT Evaluation of Bone Mineral Density in Adult Type 1 Diabetes Mellitus Patients

INTRODUCTION

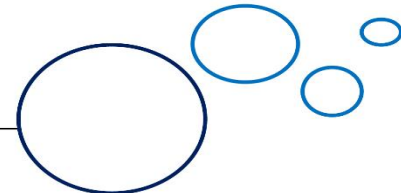
Type 1 diabetes complications have recently been related to an elevated risk of bone fracture ⁽¹⁾. In comparison to the general population, the risk of hip fracture is thought to be three to six times higher affecting people of all sexes and ages. One of the key risk factors for fractures at the spine and hip is low bone mineral density (BMD), and T1DM patients were shown to have lower BMD than nondiabetics ⁽²⁾.

Quantitative computed tomography(QCT) had a better sensitivity than Dual X-ray absorptiometry(DXA) in identifying abnormal BMD levels and could be useful in assessing the risk of fracture in individuals with uncomplicated type 1 diabetes mellitus(T1DM)

BMD measurement is crucial for diagnosing osteoporosis, evaluating fracture risk, and evaluating the success of treatment. The most reliable approach for diagnosing osteoporosis at the moment is Dual X-ray absorptiometry (DXA), however quantitative computed tomography (QCT) is more sensitive to BMD change since it can measure volumetric BMD. The therapeutic use of QCT in the therapy of osteoporosis justifies continued study despite the drawback of the considerably greater radiation dosage compared to DXA ⁽³⁾. This study analyzed BMD using both DXA and QCT in uncomplicated young adult patients with T1DM and sex- and age-matched controls, and to evaluate the effectiveness of these two techniques in identifying unusual results in these groups.

METHODS

The single-centre, case-control study was conducted on 118 patients with type 1 diabetes mellitus (T1DM) for more than 5 years. They had a mean age of 30.12 years and 55% were females. None of the participants had micro- or macro vascular complications(T1DMG). BMD



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was measured at the lumbar spine using a Hologic Discovery QDR Series Densitometer.

Absolute BMD values (in g/cm²) and Z-scores were obtained due to the young age of the participants. Total LS BMD(L1-L4)

was calculated, and L1, L2, AND L3 vertebrae were compared separately with QCT measurements for region of interest (ROI) selection. According to the International Society for Clinical Densitometry (ISCD) definition, a Z-score of -2.0 or lower indicated BMD below the expected range for age, while a Z-score above -2.0 was considered within the expected range. QCT measurements were conducted using a Toshiba Aquilion 16- slice CT device and a solid QCT phantom. Three lumbar vertebrae(L1-L3) were scanned using 120Kv, 100maS, and 1mm slice thickness. Trabecular BMD was measured using QCT PRO 4.2.3 software, following ISCD guidelines. BMD-score above -2.0 were considered within the expected range, while-scores of -2.0 or lower indicated values below the expected range of age. Blood samples were taken while fasting to assess beta-crosslaps (-crosslaps), a marker of bone resorption, and total procollagen type 1 amino-terminal propeptide (TP1NP), a marker of bone production. Blood samples were then kept at 80°C until analysis. The enzyme-linked immunosorbent test or Elisa, was used to assess both markers. SPSS version 25 was used for all data analysis.

RESULTS

In T1DMG, BMD measured by DXA was significantly lower than the control group(CG) at total lumbar spine(LS) and L1, L2, and L3 vertebrae. Male participants with T1DM had significantly lower

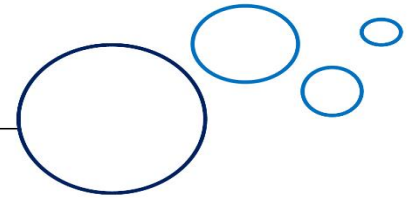
BMD values at these sites compared to sex-matched controls, while the difference in BMD values for females did not reach statistical significance (TABLE 1). When compared to CG, QCT BMD readings for all studied vertebrae were considerably lower in T1DMG. Males with

TABLE 1 - LS MEASUREMENTS BY DXA

Variable LS		All		Males		Females	
		T1DM (n = 118)	CG (n = 94)	T1DM (n = 53)	CG (n = 42)	T1DM (n = 65)	CG (n = 52)
TOTAL	BMD (g/cm2)	1.06	1.10	1.05	1.12	1.06	1.07
	Z-score	0.11	0.65	-0.20	0.64	0.36	0.66
L1	BMD (g/cm2)	1.01	1.06	1.01	1.09	1.00	1.03
	Z-score	0.10	0.65	-0.29	0.49	0.42	0.81
L2	BMD (g/cm2)	1.08	1.11	1.07	1.14	1.08	1.09
	Z-score	0.43	0.90	0.04	0.83	0.75	0.97
L3	BMD (g/cm2)	1.08	1.12	1.07	1.15	1.09	1.10
	Z-score	0.15	0.63	-0.10	0.72	0.35	0.55

TABLE 2 - BMD MEASUREMENTS BY QCT

Variable QCT		All		Males		Females	
		T1DM (n = 118)	CG (n = 94)	T1DM (n = 53)	CG (n = 42)	T1DM (n = 65)	CG (n = 52)
L1	BMD (g/cm3)	180.82	192.83	171.35	199.53	187.55	188.54
	Z-score	0.0	0.61	-0.43	0.52	0.33	0.74
L2	BMD (g/cm3)	178.88	189.64	169.21	195.37	185.12	186.76
	Z-score	0.19	0.79	-0.13	0.78	0.63	0.89
L3	BMD (g/cm3)	175.30	189.11	166.67	193.19	182.34	185.90
	Z-score	-0.10	0.57	-0.34	0.61	0.24	0.42



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T1DM had significantly lower BMD values at all vertebrae compared to controls, while females showed no significant difference (TABLE 2). QCT detected more T1DMG patients with BMD values below the expected range compared to DXA. β -Crosslap values were significantly lower in T1DMG compared to CG, and this was observed in both sexes. In T1DMG, BMI showed a positive correlation with DXA Z-scores and QCT BMD. HbA1C levels in T1DMG were negatively correlated with QCT BMD measurements at all vertebrae but had no correlation with DXA BMD. In T1DMG, TP1NP and β -Crosslaps were both substantially and adversely linked with the length of diabetes. Age at diabetes diagnosis showed a significant negative correlation with TP1NP in T1DMG. In T1DMG, negative correlations were found between β -Crosslaps and total BMD(DXA) at LS, as well as with L1, L2, AND L3(QCT). No correlations were found with BMI or HbA1c.

DISCUSSION

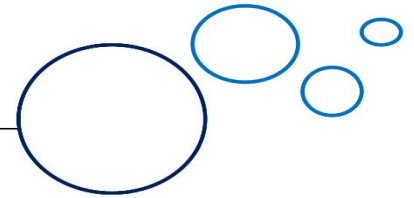
In present study BMD measured by DXA was significantly lower than the control group(CG) at total lumbar spine(LS). At all the analyzed vertebrae, QCT BMD values were considerably lower in T1DMG ⁽²⁾. Females with BMI >25 kg/m² had substantially lower Lumbar Spine (LS) T-score values by DXA compared to QCT ⁽⁴⁾. In present study QCT had a better sensitivity than DXA in identifying abnormal BMD levels in individuals with uncomplicated T1DM. similar study demonstrated that QCT is more sensitive than DXA in detecting osteoporosis and QCT may prevent BMD overestimation by DXA linked to spinal degeneration, aortic calcification, and other lesions ⁽⁵⁾.

CONCLUSION

In individuals with uncomplicated T1DM, QCT had a better sensitivity than DXA in identifying abnormal BMD levels and could be useful in assessing the risk of fracture in these individuals. DXA (The clinical gold standard for BMD measurements) may be able to detect the diabetes-related lower BMD in these patients prior to their diagnosis. Proper evaluation and management of reduced BMD in T1DM patients are essential to minimize the risk of fractures and improve bone health.

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Relationship between Cardiac Function and Diabetic Retinopathy Severity in Type 2 Diabetes Patients

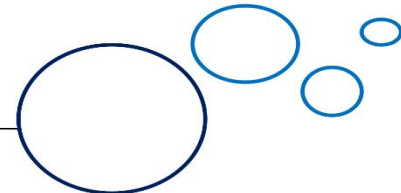
INTRODUCTION

There are 415 million individuals worldwide who have diabetes mellitus, making it a global epidemic. Diabetes patients are more likely to develop serious complications specific to the disease (such as neuropathy, nephropathy, and retinopathy) as well as other conditions with similar pathophysiologies or complications (such as cardiovascular disease, dementia, psoriasis, non-alcoholic steatohepatitis, metabolic syndrome, and cancer). Diabetic retinopathy (DR) is one of the most prevalent consequences of diabetes. It produces progressive changes in the microvasculature that result in retinal ischemia, neovascularization, altered retinal permeability, and macular oedema. It should be noted that the main reason for blindness in working-age adults is diabetic retinopathy⁽¹⁾. Patients with type 2 diabetes mellitus (T2DM) are at a higher risk of mortality from cardiovascular disease (CVD)⁽²⁾ and the risk of CVD increases steadily with increasing fasting plasma glucose levels, even before reaching levels sufficient for a diabetes diagnosis⁽³⁾. Diabetic retinopathy and myocardial damage's interaction contributes to the larger discussion on the link between micro- and macrovascular diabetic complications. Thus clinical study was performed to investigate the relationship between cardiac function and diabetic retinopathy severity.

Proliferative retinopathy was linked to Left ventricle hypertrophy independently. Additionally, severe retinopathy was significantly correlated with abnormal electrocardiogram results.

METHODS

A retrospective Study was conducted on 790 patients with T2DM and preserved left ventricle (LV) ejection fraction. Medical records were used to extract demographic and clinical information. With the patient resting in the lateral decubitus position, every patient got a thorough transthoracic echocardiographic evaluation. From an ophthalmologist's fundoscopy, retinal diseases were discovered. Retinopathy stages were divided into four categories: no retinopathy, early nonproliferative DR, moderate to severe nonproliferative DR, and proliferative DR. Myocardial conduction function was evaluated using the ECG. The structure



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and functionality of the myocardium were assessed using echocardiography. Utilizing SPSS version 26.0, statistical analysis of the data was performed.

RESULTS

Based on the presence of retinopathy, a total of 790 patients were divided into three groups: those without DR (NDR, n=475), those with nonproliferative DR (NPDR, n=247), and those with proliferative DR (PDR, n=68). Patients with nonproliferative or proliferative retinopathy showed a higher prevalence of

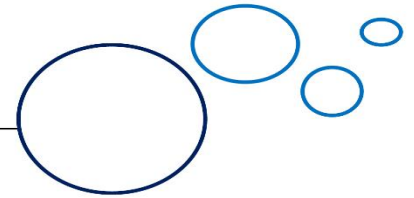
TABLE 1 - Comparing echocardiographic indices in T2DM patients according to retinopathy status.

Indices	Total (n = 790)	NDR (n = 475)	NPDR (n = 247)	PDR (n = 68)	P value
IVST (mm)	10:19	10:00	10:42	10:66	<0.001
LAD (mm)	35:57	35:30	35:78	36:65	0.001
LV ESD (mm)	31:26	31:54	30:78	31:03	0.001
LV EDD (mm)	44:74	45:13	44:11	44:26	<0.001
LV EDV (ml)	74:42	76:21	71:59	72:19	<0.001
LV ESV (ml)	31:39	32:16	30:19	30:41	0.001
LV EF (%)	58:15	58:17	58:12	58:06	0.938
LVFS (%)	30:19	30:20	30:22	30:06	0.893
E velocity (cm/s)	55:50	54:28	56:73	59:50	0.258
A velocity (cm/s)	67:21	61:61	74:55	79:40	<0.001
E/A ratio	0:85	0:90	0:78	0:76	<0.001
Stroke volume (ml)	43:17	44:07	41:81	41:79	<0.001
E/A ratio < 1, n (%)	659 (84.6)	367 (78.3)	228 (94.2)	64 (94.1)	<0.001

LV: left ventricular; IVST: interventricular septal thickness; LAD: left atrial diameter; LV ESD: LV end-systolic dimension; LV EDD: LV end-diastolic dimension; LV EDV: LV end-diastolic volume; LV ESV: LV end-systolic volume; LVEF: LV ejection fraction; LVFS: LV fractional shortening.

females, longer diabetes duration, older age, higher blood pressure, lower eGFR, elevated cholesterol levels, and increased prevalence of hypertension and diabetic nephropathy. The Doppler echocardiographic data in TABLE 1 showed no difference in LV ejection fraction(LVEF) or fractional shortening across retinopathy groups. However, cardiac parameters related to LV structural changes were significantly different in patients with nonproliferative or proliferative retinopathy compared to those without retinopathy.

The E/A ratio <1 was prevalent in patients with retinopathy, and its values were lower in nonproliferative or proliferative cases. Patients with nonproliferative or proliferative retinopathy showed higher heart rates and longer PR and QTC intervals. They also had a higher prevalence of PR interval >200 ms and QTC interval > 440 ms compared to those without retinopathy. The multiple linear regression analysis for clinical variables associated with the electrocardiogram parameters showed that the DR stage remained independently associated with heart rate ($\beta = 1.593$), PR interval ($\beta = 4.666$), and QTC interval ($\beta = 8.807$). LV geometry parameters (IVST, left atrial diameter, LV EDV, and stroke volume) showed significant



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correlation across retinopathy groups. Diastolic function indicators (A velocity, E/A ratio, and E/A ratio <1) also demonstrated the same result.

DISCUSSION

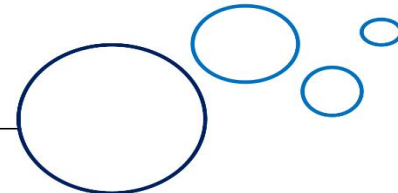
This study analyzed the correlation between retinopathy severity and cardiac structure and function in T2DM patients. Results showed that worsening cardiac indices were significantly correlated with more severe retinopathy in asymptomatic patients with preserved LVEF⁽²⁾. Based on these findings, the study by S. Bonapace et al. indicated that diabetic retinopathy and microvascular heart disease might not be entirely separate. Microangiopathy may play a crucial role in developing cardiac dysfunction or share a common fundamental pathway with these disorders⁽⁴⁾. Previous studies have suggested that PR and QT interval prolongation in diabetic retinopathy patients require early attention to prevent cardiovascular events. However, there is limited data analyzing the correlation between electrocardiogram abnormalities and DR stage in patients with diabetic micro- and macroangiopathy⁽⁵⁾.

CONCLUSION

The study concluded that most T2DM patients had asymptomatic LV diastolic dysfunction, and proliferative retinopathy was linked to LV hypertrophy independently. Additionally, severe retinopathy was significantly correlated with abnormal electrocardiogram results in these patients. The presence of retinopathy in T2DM patients with preserved LVEF holds clinical importance, indicating the need for further cardiac evaluation by clinicians.

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A case of 19-year-old with young-onset diabetes who developed Purtscher-like retinopathy

INTRODUCTION

Purtscher's retinopathy is a rare angiopathy, that is documented in patients with a history of severe trauma and other systemic disorders⁽¹⁾. Purtscher like retinopathy (PLR) is identified when linked with conditions like pancreatitis, renal failure and autoimmune disorders. A fundoscopic examination reveals Purtscher fecken, a characteristic intraretinal whitening, bilateral peripapillary cotton wool patches, and retinal haemorrhages. There is just one instance of PLR linked to diabetic retinopathy, and diabetes is not a known risk factor⁽²⁾. This study reported a case of PLR in a patient with multiple diabetic complications and a 17q12 chromosomal deletion- linked maturity-onset diabetes of the young 5 (MODY5).

Patients with poorly managed diabetes should be evaluated for Purtscher-like retinopathy (PLR)

CASE PRESENTATION

A 19-year-old Hispanic male with a history of insulin-dependent type II diabetes experienced sudden painless vision loss in both eyes for a week, along with bilateral lower extremity weakness, inability to walk, and urinary and bowel incontinence. He had undergone bilateral toe amputations for diabetic foot infections three months before and had cataract extraction with intraocular lens implantation at the age of 15. The patient had a history of multiple hospitalizations, including intensive care unit admissions due to poorly controlled diabetes. On examination, the best-corrected visual acuity was significantly worse than his baseline of 20/20. Retinal screening from three months prior showed normal optic disc and vessels with some macular aneurysms and trace cotton wool spots (Fig 1 A). Peripapillary cotton wool patches and a few flame haemorrhages

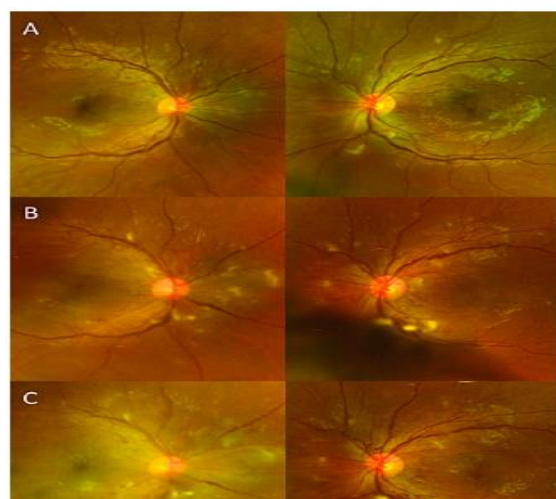
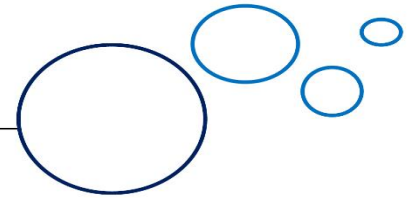


FIGURE 1 Dilated fundus images of a patient with retinopathy similar to Purtscher's. A) Diabetic retinal examination- There was no sign of diabetic retinopathy 3 months previous to the initial presentation. Bilateral 20/20 best corrected visual acuity was present at this time. B) Photographs of dilated fundi multiple cotton wool spots and intraretinal haemorrhages were found 2 weeks after the beginning of acute painless vision loss, which was compatible with Purtscher-like retinopathy. Comparing bilaterally to 20/200, visual acuity was substantially worse. C) Fundus examination after one month showed persistent peripapillary cotton wool spots bilaterally, visual acuity was poor.



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without neovascularization were discovered on a dilated fundus examination (Fig 1B). A comparison with baseline optical coherence tomography (OCT) showed new significant areas of subretinal and intraretinal macular fluid bilaterally. Fluorescein angiography indicated retinal arteriole staining and leakage in a peripapillary distribution with multifocal filling defects and capillary nonperfusion. The ophthalmic examination suggested Purtscher-like retinopathy. After admission to the pediatric intensive care unit, further evaluation revealed multi-organ complications of diabetes, including bilateral diabetic foot ulcers with recurrent toe osteomyelitis, sensorimotor neuropathy, neurogenic bowel and bladder, and a genetic deletion on chromosome 17q12. A follow-up ophthalmic examination showed no improvement in visual acuity or resolution of cotton wool spots (Fig 1C). An intravitreal injection of antivascular endothelial growth factor led to partial resolution of retinal edema, but visual acuity remained poor.

DISCUSSION

A case of Purtscher like retinopathy was reported in a 19-year-old male with young-onset diabetes. No published cases of related ocular problems were identified and this syndrome is only observed in 1% of diabetics. It's probable that PLR and sudden-onset bilateral vision loss were caused by an inflammatory reaction brought on by recurring osteomyelitis and bilateral foot infections. Following a presumably related vasculitic mechanism, viral diseases have been linked to PLR ⁽³⁾. The 17q12 deletion in this patient made him more likely to grow up with diabetes and associated consequences ⁽²⁾. Reduced birth weight, gout, diabetic syndrome, and renal cysts are all linked to this particular chromosomal locus loss ⁽⁴⁾.

CONCLUSION

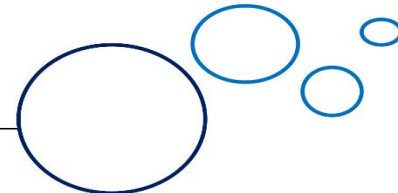
Patients with poorly managed diabetes should be evaluated for Purtscher-like retinopathy (PLR) which might be a consequence of diabetes. Our case indicates that diabetes is a risk factor for PLR.

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