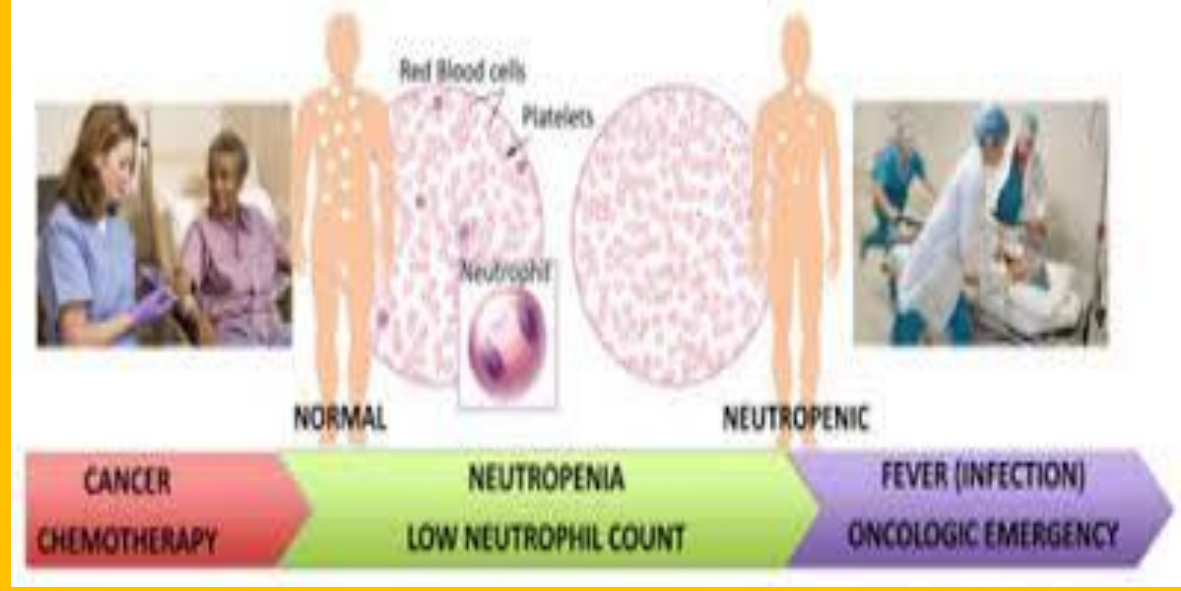
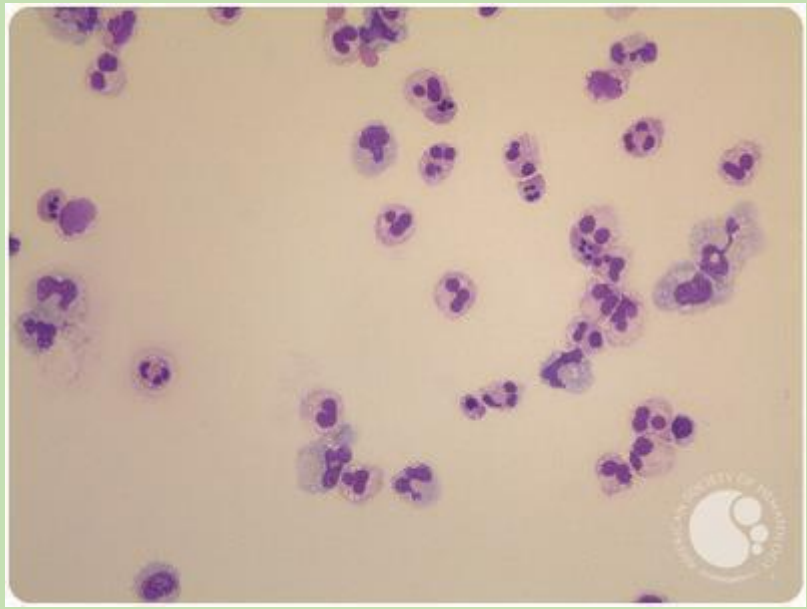


Neutrpenia & factor 7 deficiency

دکتربابک عبدالکریمی
هماتولوژیست آنکولوژیست کودکان
دانشگاه علوم پزشکی لرستان

Case presentation:

- A 10 y boy with severe neutropenia(resolve by GCSF) and recurrent bleeding tendency(factor 7=37%)
- +Osteopenia(causes recurrent pathologic FX in long bones)



آزمایشگاه تشخیص طبی سیمرغ

میدان انقلاب اسلامی-خ کارگر شمالی- خ نصرت غربی-پلاک ۳۷

تلفن : ۴۰۶۶۱۰۴۵

شماره پذیرش : ۳۶-۱۲ تاریخ پذیرش : ۱۴۰۰/۱۲/۰۱ پزشک معالج : سرکار خانم دکتر لیلا مرادی

نام مراجعه کننده : آقای محمدامید عبداله زاده سن : ۱۳ سال

Hematology

Test	Result	Unit	Reference Range	Differential	
Complete Blood Count					
W.B.C	*L 2.95*	*x10*3/micL*	*3.9 - 11.5*	*Neutrophils*	*(L) 6 %*
R.B.C	*H5.39*	*x10*6/micL*	*3.9 - 5.3*	*Lymphocyte*	*(H) 79 %*
Hemoglobin	*15.2*	*x10*3/micL*	*12.8 - 16*	*Monocyte*	*(H) 15 %*
Hematocrit	*44.4*	*x10*3/micL*	*37 - 46*		
M.C.V	*82.4*	*fL*	*77 - 92*		
M.C.H	*28.2*	*pg*	*25 - 34*		
M.C.H.C	*34.2*	*g/dL*	*34.2 - 35.7*		
Platelet Count	*197*	*x10*3/micL*	*170 - 450*		
RDW-CV	*13.7*		*13 - 15.5*		

H=High L=Low

Reference ranges are according to the age and sex of the patient.

Checked by:

راهنمائی مسئول فنی برای پزشک و بیمار :

Lab Director : Dr .T . Ghazanfari Dr . A. Jelveh

آزمایشگاه تشخیص پزشکی سیمرغ ۶۶۴۲۶۸۹۱

NOOR Pathology Lab

Dr. A. Aliepour MD AP-CP

آزمایشگاه پاتوبیولوژی نور

انجام آزمایشات تشخیص پزشکی، پاتولوژی و سیتولوژی

دکتر اصغر علیپور متخصص پاتولوژی آناتومیک و بالینی

شماره پذیرش : ۱۲-۱۸۲۵ تاریخ پذیرش : ۱۳۹۳/۱۲/۰۹ تاریخ جوابدهی : ۱۳۹۳/۱۲/۱۷ پزشک معالج : آقای دکتر بابک عبدالکریمی

نام مراجعه کننده : آقای محمدامید عبداله زاده سن : ۷ سال شماره پاتولوژی : P-94-19094

SPECIMEN : Bone marrow biopsy & Aspiration

CLINICAL DATA : Neutropenia

GROSS DESCRIPTION:
Received specimen in formalin in one container labeled as " BMB " consists of 0.5 cm needle shaped bone tissue with 5 aspiration slides & 2 PBS.

MICROSCOPIC DESCRIPTION:
PERIPHERAL BLOOD:
RBC Morphology: Mild aniso-poikilocytosis
WBC: Neutr: 3%, Lymph:92%, Mono: 5%
Plt: Mild decreased

BONE MARROW ASPIRATTON:
There are numerous hematopoietic cells in different stages of maturation. The erythroid series are prominent. The myeloid series shows decrease maturation.

TREPHINE BONE BIOPSY:
Section shows fragment of bone marrow and intertrabecular marrow spaces. The intertrabecular spaces containing polymorphic marrow population with about 80% cellularity. The myeloid , erythroid, lymphoid and megakaryocytic series are present. The erythroid series are prominent. The myeloid series shows decreased maturation & hypoplasia.

DIAGNOSIS:

Bone marrow aspiration and trephine biopsy:
-Myeloid hypoplasia in marrow & peripheral neutropenia
-Relative erythroid hyperplasia

Note: Both familial abnormalities & acquired disease (such as drug reactions and viral disease) could shows above pattern. A constellation of clinical and pathological charecteristics is necessary to reach a correct diagnosis.

Pathologist
A. Alipour MD AP CP

خرم‌آباد-پل‌شهدا-ابتدای کوچه‌مخابرات تلفن : ۲۲۳۲۹۳۹

IN THE NAME OF GOD
ISFAHAN UNIVERSITY OF MEDICAL SCIENCES
SAYEDAI-SHOHADA HOSPITAL
FLOWCYTOMETRY

NAME: MOHAMMAD OMID
AGE: ABDOLLAHZADEH
SEX: 5
Male
SAMPLE: BMA

PATIENT NO:92-A-493
DATE: 1392/05/29
VIABILITY: GOOD
Doctor: KARGAR

CYTOCHEMICAL STAINING

MYELOPEROXIDASE:
PERIODIC ACID SHIFF:

	MARKER	Lymph	Gran	Mono	Total
COMMON ALL ANTIGEN	CD10	31%			
PAN B-CELL	CD19	52%			
MONOCYTE/GRANOLOCYTE	CD13		39%		
B-CELL	CD20	55%			
LEUKOCYTE COMMON ANTIGEN	CD45	83%			
LEUKOCYTE COMMON ANTIGEN	CD45		76%		
MONOCYTE/GRANOLOCTE	CD33		98%		
HEMATOPOIETIC PRECURSOR CELL	CD34	15%			
STEM CELL FACTOR RECEPTOR	CD117		2.3%		
TERMINAL DESOXITRANSFERASE	TdT	3%			
MHC Class II	HLA-DR	59%			
ALPHA CHAINE BETA-2 INTEGRINE	CD11b		92%		
LOW EXPRESSION CD45/CD117	CD45/CD117		0.5%		

COMMENTS:BMA immunophenotyping reveals [illegible]ion of lymphoid cells about 12% which are positive for CD10, CD19, CD20 that are more compatible with hematogones .
Close follow up of the patient is recommended.

مرکز آموزشی درمانی حضرت سید الشهدا (ع)
دکتر میترا حیدر نور
متخصص کلینیکال و آناتومیکال پاتولوژی

M.Heidarpour MD.ACP

A.KAZEMI-Technologist
M.Sc of Hematology

Noor Specialized Clinical& Anatomical Lab .
Dr.ASGHAR ALIEPOUR MD AP CP
KHORAMABAD, SHOHADA BRIDGE, MOKHABERAT STREET -Tel:33332939-Fax:33333814

آزمایشگاه تخصصی تشخیص پزشکی وپاتولوژی نور
دکتراصغرعالیه پورمتخصص پاتولوژی آناتومیکال و کلینیکال
خرم آباد: پل شهدا، ابتدای کوچه مخابرات تلفن:۳۳۳۳۲۹۳۹
فکس: ۳۳۳۳۳۸۱۴

شماره پذیرش: ۱۲-۱۸۲۹ تاریخ پذیرش: ۱۳۹۳/۱۲/۰۹ پزشک معالج:
نام مراجعه کننده: آقای محمدامید عیداله زاده سن: ۷ سال

Hematology2

Test	Result	Unit	Normal Range
CD10	12		
CD45	96		
CD33	10		
CD34	<1		
CD13	3		

Comment : Please see the attached file for details

DR. Aliepour MD. AP CP

Specimen ID: P94-1850
Collected: Clinic
Received date: 10.12.94
Report date: 10.12.94
Clinical information:

Patient: Mohammad Omid Abdollah zadeh
Age: 7 years
Medl Code:
Phone #:
Source of Tissue/ Specimen: Bone Marrow

Physician: Noor Lab
Specialty: Referral Lab
Viability: >90%

Interpretation / Diagnosis: Markedly diluted / Hypocellular marrow. Immunophenotyping & cytomorphology results were consistent to Blast (5%) & CD10+CD19 dual positive cells. Immunophenotyping of acute leukemias should be considered for definitive diagnosis.

Stem-Cell associated Markers	%	Comments	B-Cell Associated Markers	%	Comments
CD34 (Myeloblast Cell)	<1		CD19 (Pan-B)	26	
CD117 (Promonocyte Cell)			CD10 (CALLA)	12	

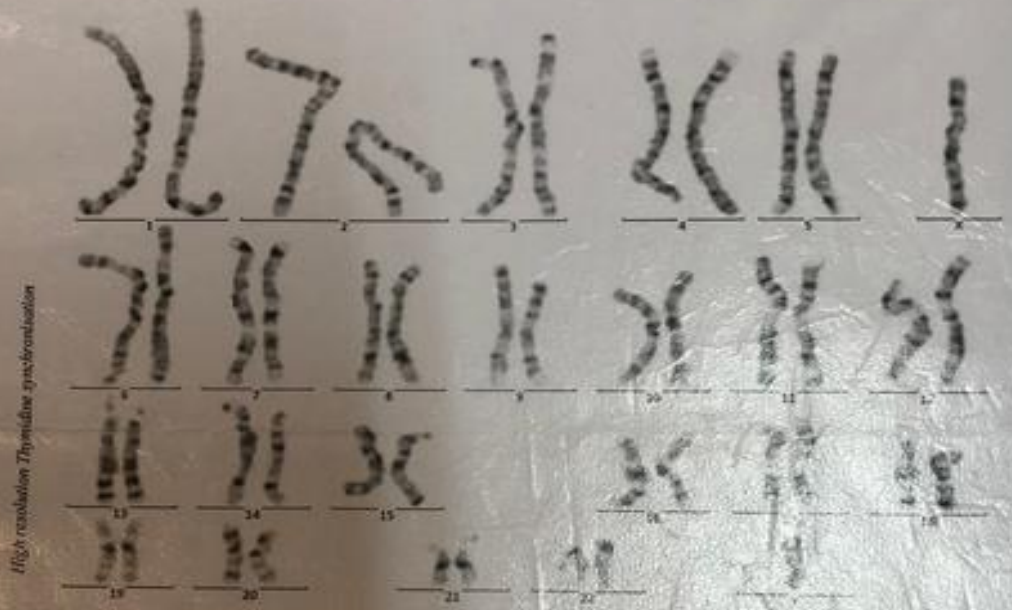
Kariminejad – Najmabadi Pathology & Genetics Center
62 Fourth St, Hasan Seyf Ave,
Sanat Sq, Shahrak Gharb, Tehran 14667-13713
Tel: (+9821) 88363955, 88370838
Fax: (+9821) 88083575
Founded: Summer 1979
Email: lab@irangenepath.com

مرکز پاتولوژی و ژنتیک کریمی نژاد – نجم آبادی
تهران، شهرک غرب، میدان صنعت،
خیابان حسن سیف، کوچه چهارم، شماره ۲
کد پستی: ۱۴۶۶۷-۱۳۷۱۳
تلفن: ۸۸۳۶۳۹۵۵ - ۸۸۳۷۰۳۳۸ (۰۹۸۲۱)
فکس: ۸۸۰۸۳۵۷۵ (۰۹۸۲۱)
تاسیس: تابستان ۱۳۵۸

Lab Ref: PBx10328-1/ 950021201

Reported: 1395/01/25
Received: 1395/01/15
Object: Blood - Heparin
Age :8 Years
Sex : Male
Clinical Data: Rule in/out Fanconi anemia
First cousin parents

نام : محمد امید عبداله زاده
پزشک معالج : –



Twenty metaphase spreads were studied from routine culture, 100 spreads from culture prepared with addition of two concentrations of mitomycin C and were compared with 100 spreads from age related normal control. 4 breaks and 1 radial rearrangement were detected in 4 cells in culture of proband, yielding an average of 0.06 breaks per metaphase; while 2 breaks and 1 radial rearrangement (average of 0.04/metaphase) in 3 cells were detected in normal control. From cytogenetic point of view breakage more or equal to 10 fold of control is clinically significant. Analysis at 500-550 band resolution revealed no chromosome aberration.

Conclusion: **46,XY compatible with apparently normal male from cytogenetic point of view**

Comment: Study of chromosome breakage following clastogenic agents has been shown to have false negative and false positive results. The cause of false negative results may be 1. mosaicism as a result of gene reversion and 2. the overlap of breakage range between normal and affected individuals specially when using Mitomycin C. Therefore close correlation with clinical profile is necessary in interpretation of the results.
Subtle genetic changes beyond the technical limits of the preparation and low-level mosaicism are potentially possible in cases with apparently normal karyotype.

Supervisor In Charge

Clinical Advisor

M.H. Karimi Nejad, M.D.
Prof. of Pathology & Genetics

خلاصه بررسی ژنتیکی

نام و نام خانوادگی بررسی شونده: محمد امید عبداله زاده | **جنسیت:** مذکر | **تاریخ تولد:** ۱۳۸۷/۰۸/۱۰

همکار محترم ارجاع دهنده: جناب آقای دکتر عبدالکریمی | **تاریخ پذیرش:** ۱۳۹۷/۰۸/۲۹ | **تاریخ گزارش:** ۱۳۹۷/۱۲/۲۵

بررسی های صورت گرفته:
بررسی کلیه نواحی اگزونی شناخته شده *(Whole Exome Sequencing)* به روش تعیین توالی نسل دوم *(NGS)*

خلاصه نتایج و تفسیر:

در بررسی صورت گرفته، نمونه مورد بررسی دارای یک واریانت در یک ژن مرتبط با بیماری‌های نزدیک به فنوتیپ ذکر شده توسط پزشک محترم می‌باشد:

- یک واریانت missense بصورت همی‌زیگوت (با جزئیات ذکر شده در گزارش اصلی) در ژن ***WAS*** شناسایی گردید. این ژن به عنوان عامل بیماری‌های ***X-linked severe congenital neutropenia, Intermittent X-linked thrombocytopenia, X-linked thrombocytopenia*** و ***Wiskott-Aldrich syndrome*** با توارث وابسته به X مغلوب گزارش شده است. این تغییر تاکنون به عنوان جهش بیماری‌زا گزارش نشده است. بنابر بررسی‌های صورت گرفته (شامل فراوانی جمعیتی و آنالیزهای بیوانفورماتیک) و بر اساس دستورالعمل ACMG، این تغییر را می‌توان در گروه ***Variant of Uncertain Significance (VUS)*** طبقه‌بندی نمود.

- طبق دستورالعمل‌های جاری، واریانت‌های با طبقه‌بندی VUS را نمی‌توان مبنای تصمیم‌گیری‌های بالینی/تشخیصی از جمله تشخیص پیش از تولد قرار داد. طبیعتا بررسی‌های بیشتر (شامل بررسی این واریانت در سایر افراد خانواده/شجره و مطالعات عملکردی) جهت تعیین دقیق بیماری‌زا بودن یا نبودن این واریانت ضروری می باشد. در این راستا با در نظر گرفتن توارث وابسته به X مغلوب بیماری‌های حاصل از ژن ***WAS***، در صورت ناقل (هتروزیگوت) بودن مادر برای واریانت فوق، بررسی دایی (ها) و نمونه در دسترس از پدر بزرگ مادری از نظر واریانت فوق، جهت تفسیر دقیقتر واریانت لازم می باشد.

*****

- علاوه بر واریانت فوق، در نمونه مورد بررسی، یک واریانت دیگر به صورت هتروزیگوت در ژن ***DHX38*** یافت شد. بر اساس دستورالعمل ACMG، این تغییر را می‌توان در گروه ***pathogenic*** طبقه‌بندی نمود. این ژن به عنوان عامل بیماری ***Retinitis pigmentosa-84*** با توارث اتوزومی مغلوب گزارش شده است. با توجه به هتروزیگوت بودن محمد امید عبداله زاده، ایشان به بیماری مذکور مبتلا نمی باشد، ولی بررسی والدین ایشان، جهت تعیین وضعیت آنها برای این واریانت قبل از بارداری بعدی توصیه می‌گردد. در صورتی که والدین هر دو برای این واریانت یا هرگونه واریانت *pathogenic* یا *likely pathogenic* دیگر در این ژن ناقل باشند، احتمال ۲۵ درصد برای ابتلا فرزند در هر بارداری برای بیماری مذکور را باید مد نظر داشت. همچنین مشاوره ژنتیک و بررسی ناقل بودن احتمالی در برادران و خواهران فرد بیمار، و در صورت تایید ناقل بودن والد/والدین، در برادران و خواهران ایشان نیز توصیه می‌شود. این بررسی‌ها باید قبل از بارداری صورت گیرند. طبیعتا اهمیت این امر در صورت ازدواج خویشاوندی در این افراد بیشتر خواهد بود.

*****

- واریانت‌های گزارش شده، حاصل بررسی به روش NGS بوده است و با روش مولکولی دیگری تایید نشده‌اند. لذا لازم است نسبت به تایید این واریانت‌ها با یک روش مولکولی دیگر اقدام شود

- ضروری است توجه گردد که در این مرحله، امکان انجام تشخیص پیش از تولد برای بیماری فرزند مبتلا، در این خانواده وجود ندارد. لذا توصیه می‌گردد والدین و سایر افراد در معرض خطر در خانواده/شجره، تا اتمام کامل بررسی های لازم و تعیین تشخیص و جهش (های) عامل، از بارداری پرهیز نمایند.

نشانی: خیابان کارگر شمالی - بالاتر از تقاطع فاطمی کارگر - نبش کوچه اشراقی - پلاک ۱۳۲۴ - طبقه اول
تلفن: ۲۷۶۸ ۶۶۹۰ ۲۱ ۹۸+ کد پستی: ۱۴۱۱۸۹۳۴۸۷

Iranian Comprehensive Hemophilia Care Center543 Felestin Ave.Tehran,Iran.Tell:88898742-4

Member of UKNEQAS United Kingdom National Quality Assessment service

04-294

تاریخ پذیرش : 1400/04/16 پزشک معالج : آقای دکتر محمدرضا بقایی پور

آقای محمدامید عبداله زاده — سن : 13 سال

Coagolation Laboratory(Factor Assay)

Test	Result	Unit	Normal Range
F VII Activity (1-Stage method) L	37	%	50 - 150

L=Low

M.Jazebi MSc.

Dr. Hamidreza Jamali

آزمایشگاه مرکز درمان جامع هموفیلی ایران

تهران، خیابان فلسطین شمالی، زرافشت، پلاک ۵۴۳ تلفن ۸۸۸۹۸۷۴۲-۴

Iranian Comprehensive Hemophilia Care Center543 Felestin Ave.Tehran,Iran.Tell:88898742-4

۰۳-۱۰۶ اشتراک : ۹۵۸۹۷۳۸۲ تاریخ پذیرش : ۱۳۹۶/۰۳/۰۶ پزشک معالج : آقای دکتر حمیدرضا جمالی

آقای محمد امید عبداله زاده — سن : ۹ سال

Coagolation Laboratory(Factor Assay)

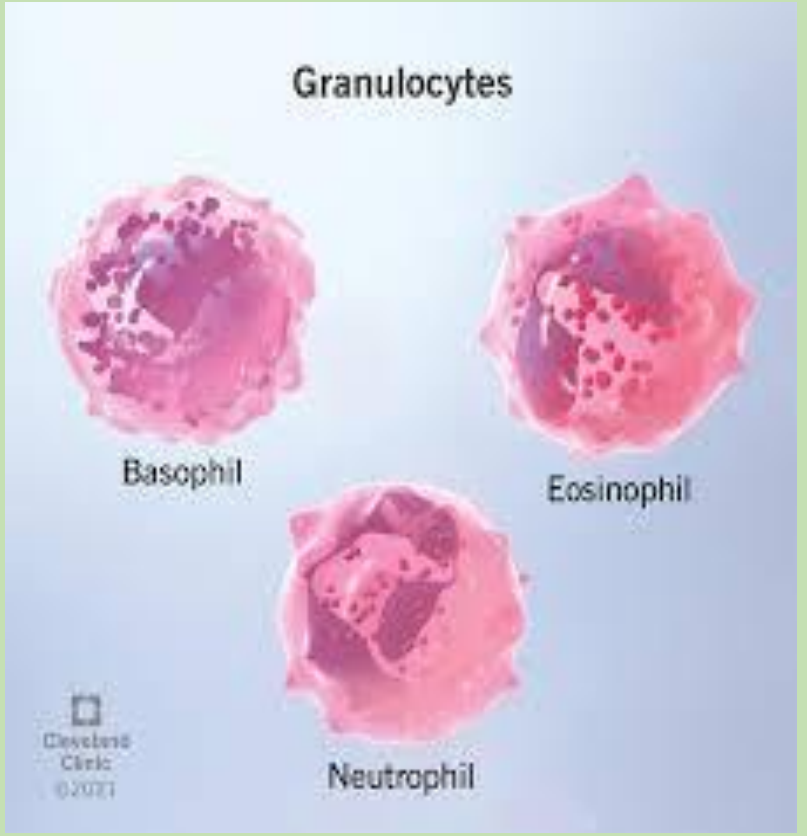
Test	Result	Unit	Normal Range
F VIII Activity (1- Stage method)	98	%	50 - 150
vWF Activity (RiCof method)	89	%	50 - 150
vWF Antigen (Turbidimetric method)	101	%	50 - 150
F IX Activity (1-Stage method)	92	%	50 - 150
F XI Activity (1-Stage method)	98	%	50 - 150
F XII Activity (1-Satge method)	79	%	50 - 150

M.Jazebi MSc.

Dr. Hamidreza Jamali

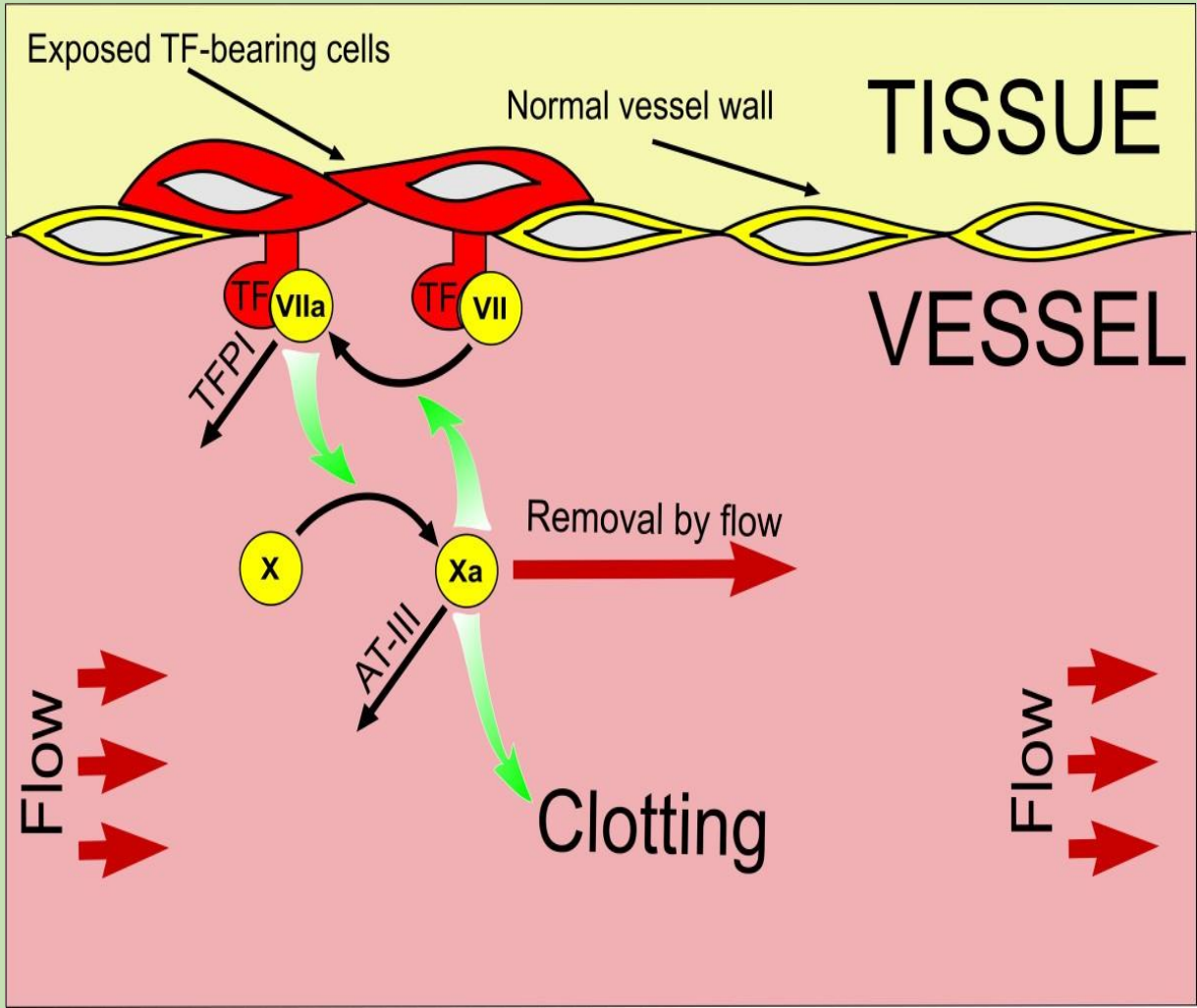
Key questios about this case:

- 1.what is his diagnosis?
- 2.is WAS correct diagnosis for this patient?
- 3.what cause of osteopenia in this patient?
- 4.what is correlation between factor 7 deficiency and neutropenia?



tissue factor & factor 7

- Tissue factor (TF) is **a transmembrane receptor for Factor VII/VIIa (FVII/VIIa)**.
- TF also called **CD142** or **plt TF** or **coagulation facctor 3**
- It is constitutively expressed by **cells surrounding blood vessels.**
- The endothelium physically separates this potent "activator" from its circulating ligand FVII/FVIIa and prevents inappropriate activation of the clotting cascade.



CASE REPORT

A novel mutation in Wiskott-Aldrich gene manifesting as macrothrombocytopenia and neutropenia

Daniel Lee[2],
Abdullah Haddad[3],
Prerna Mewawalla[4]

Correspondence to Dr Mais Arwani, dr.arwani@gmail.com, mais_arwani@yahoo.com

Summary
Wiskott-Aldrich syndrome (WAS) is a rare X-linked disorder, described as a clinical triad of microthrombocytopenia, eczema and recurrent infections. Different mutations in WAS gene have been identified, resulting in various phenotypes and a broad range of disease severity, ranging from classic WAS to X-linked thrombocytopenia and X-linked neutropenia. WAS in some cases can be fatal without haematopoietic stem cell transplantation early in life. In this particular case, we present a novel mutation with a unique presentation. An 18-year-old man incidentally found to have **macrothrombocytopenia and neutropenia** at 16 years of age later found to be **hemizygous for c. 869T>C (p.Ile290Thr) mutation in WAS gene**. The late presentation, absence of other manifestations of WAS and presence of macrothrombocytopenia, rather than microthrombocytopenia, which is usually a characteristic finding in WAS, misled the initial diagnosis. On review of literature, **this mutation has not been reported as causing WAS.**

http://dx.doi.org/10.1136/bcr-2018-225123

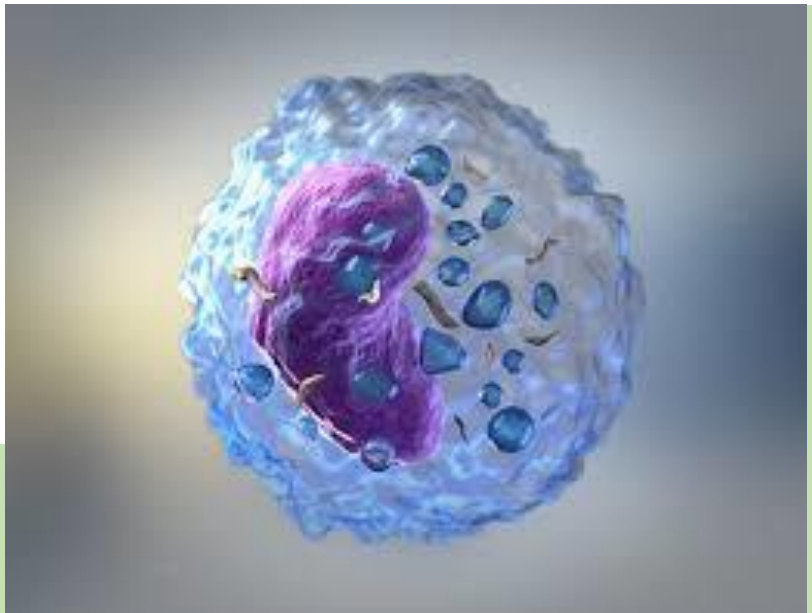
X-Linked Neutropenia with a I294T Mutation of the Wiskott-Aldrich Syndrome Gene.

Melanie M. Cotter, MD,

Blood (2006) 108 (11): 1278.
https://doi.org/10.1182/blood.V108.11.1278.1278

X-linked neutropenia (XLN, OMIM #300299) is a rare cause of severe congenital neutropenia and was first described in a three-generation Belgian family with 5 affected members. Reported features of XLN include severe congenital neutropenia and monocytopenia with recurrent bacterial infections, a decreased CD4/CD8 ratio and bone marrow maturation arrest at the promyelocyte/metamyelocyte stage. In the Belgian family, a **L270P *WAS* mutation** was identified, causing constitutive activity of the Wiskott-Aldrich-syndrome protein (WASP) toward actin polymerisation (Devriendt et al. Nat.Genet. 2001). Here, we report the clinical phenotype of a second large family with XLN and with a **I294T *WAS* mutation**. In this three-generation family, 10 affected males (7–45 y) and 8 female carriers were identified. Variable non-cyclic neutropenia is present in affected males (0.2–3.3*10^9/L in those not on G-CSF; 0.1–1.0*10^9/L on G-CSF). Five of 10 affected males in the I294T family have monocytopenia. A consistent feature in all cases is a reduced NK cell number. In fact, 3 of 3 tested L270P cases also had reduced NK cell counts. The severity of the clinical phenotype is variable without apparent correlation with the degree of neutropenia. Five of 10 affected males are receiving treatment with G-CSF because of recurrent infections. Four of 10 are reported healthy in the absence of G-CSF. One case with a borderline neutrophil count (2.4*10^9/L) is not on G-CSF, despite recurrent infections. In addition, two males with a history of recurrent infections, at least one of whom had neutropenia, died of infectious causes at age 5 and 18 years.

Platelet counts are variably reduced in affected males, but with normal platelet volume. No consistent abnormalities in CD4/CD8 ratio are found. Available bone marrows have revealed no myelodysplastic features or cytogenetic abnormalities. Of note, female carriers show intermediate findings in neutrophil, platelet and NK cell counts. Only 1 female carrier is known with recurrent upper respiratory and ear infections and is treated with G-CSF. The T916C mutation we found in exon 9 of *WAS*, has recently been described (Ancliff et al. Blood online 2006) and results in a I294T mutation of the WASP GTPase-binding domain (GBD). The I294T GBD-VCA construct has a lower melting temperature (36°C) as measured by circular dichroism spectroscopy (78°C for wild-type). In the absence of Cdc42, I294T GBD-VCA is nearly completely active toward the Arp2/3 complex, contrary to wild-type GBD-VCA, but similar to the L270P construct. Thus, these data provide new and independent genetic evidence that mutations that disrupt the auto-inhibitory domain of WASP are the cause of XLN. In addition, based on this largest XLN kindred to date, reduced NK cell counts appear a consistent feature. None of the affected males presented with myelodysplasia. Finally, female carriers have moderately reduced neutrophil counts, mostly without clinical consequences. Thus, the presence of mild neutropenia in potential female carriers does not rule out the possibility



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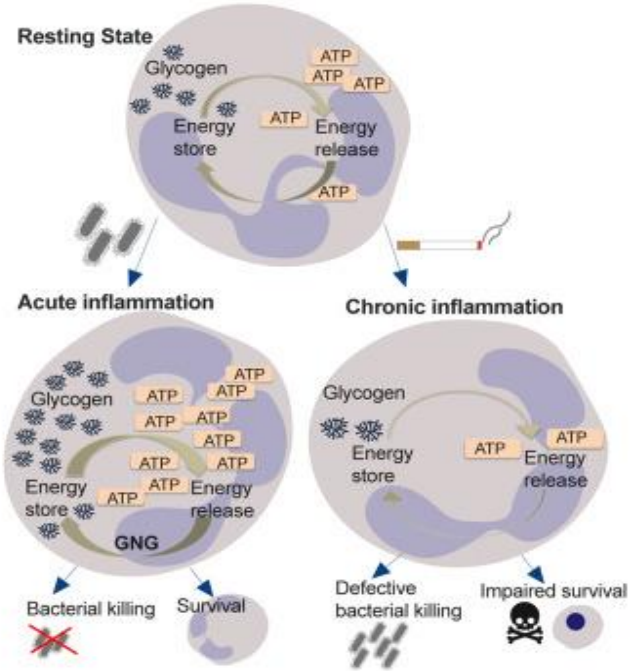
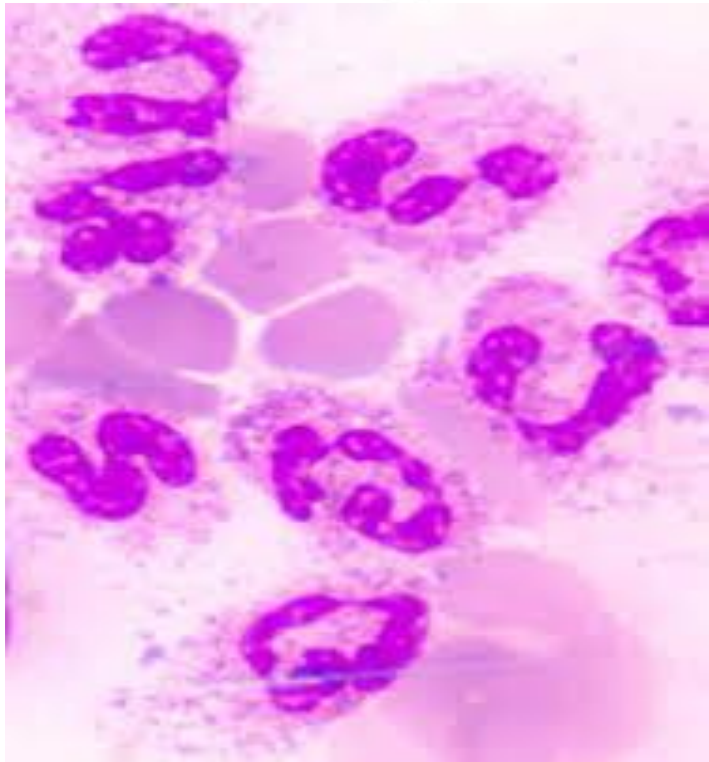
Tissue factor-positive neutrophils bind to injured endothelial wall and initiate thrombus formation

Roxane Darbousset[1], DOI: 10.1182/blood-2012-06-437772

For a long time, blood coagulation and innate immunity have been viewed as interrelated responses. Recently, the presence of leukocytes at the sites of vessel injury has been described. Here we analyzed **interaction of neutrophils, monocytes, and platelets in thrombus formation** after a laser-induced injury in vivo. Neutrophils immediately adhered to injured vessels, preceding platelets, by binding to the activated endothelium via leukocyte function antigen-1-ICAM-1 interactions. Monocytes rolled on a thrombus 3 to 5 minutes postinjury. The kinetics of thrombus formation and fibrin generation were drastically reduced in low tissue factor (TF) mice whereas the absence of factor XII had no effect. In vitro, TF was detected in neutrophils. In vivo, the inhibition of neutrophil binding to the vessel wall reduced the presence of TF and diminished the generation of fibrin and platelet accumulation. Injection of wild-type neutrophils into low TF mice partially restored the activation of the blood coagulation cascade and accumulation of platelets. Our results show that the interaction of **neutrophils with endothelial cells is a critical step preceding platelet accumulation for initiating arterial thrombosis in injured vessel**s. Targeting neutrophils interacting with endothelial cells may constitute an efficient strategy to reduce thrombosis.





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The emerging role of neutrophils in thrombosis—the journey of TF through NETs

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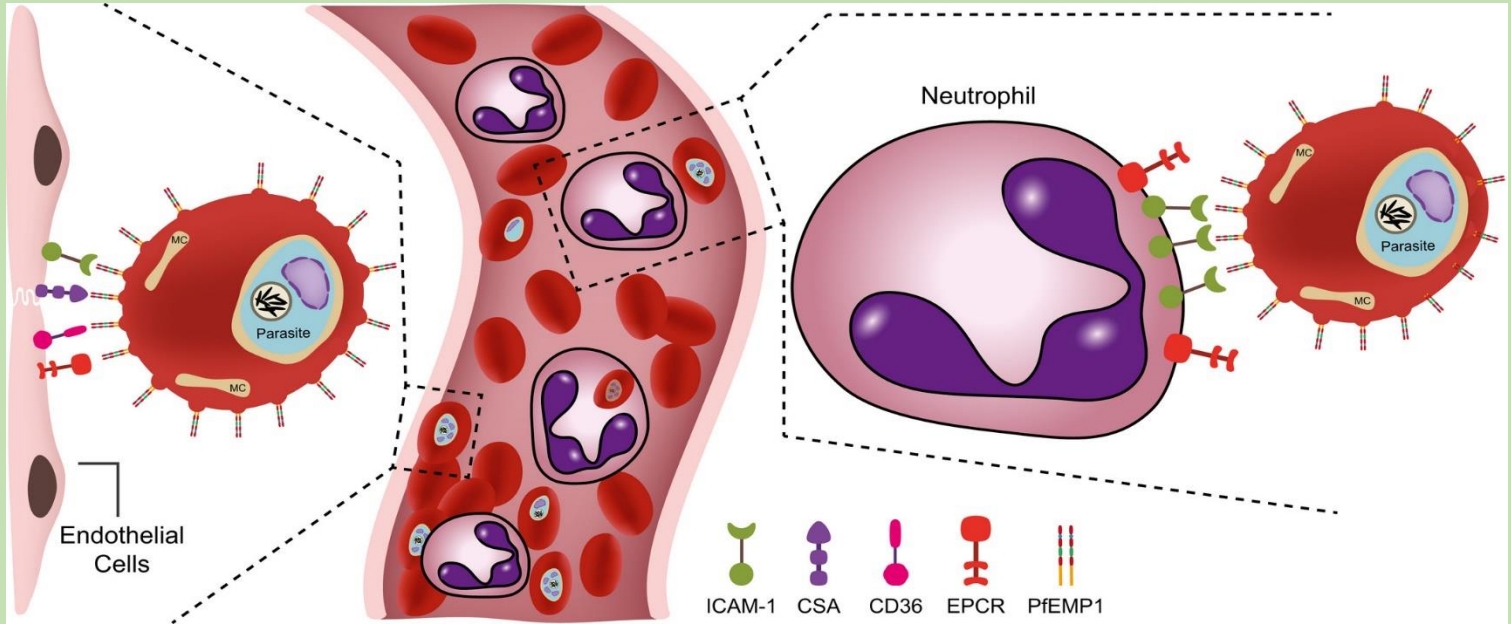
The production of TF by neutrophils and their contribution in thrombosis was until recently a matter of scientific debate. Experimental data suggested the *de novo* TF production by neutrophils under inflammatory stimuli, while others proposed that these cells acquired microparticle-derived TF. Recent experimental evidence revealed the critical role of neutrophils in thrombotic events. Neutrophil derived TF has been implicated in this process in several human and animal models. Additionally, neutrophil extracellular trap (NET) release has emerged as a major contributor in neutrophil-driven thrombogenicity in disease models including sepsis, deep venous thrombosis, and malignancy. It is suggested that NETs provide the scaffold for fibrin deposition and platelet entrapment and subsequent activation. The recently reported autophagy-dependent extracellular delivery of TF in NETs further supports the involvement of neutrophils in thrombosis. Herein, we seek to review novel data regarding the role of neutrophils in thrombosis, emphasizing the implication of TF and NETs.

Keywords: neutrophil extracellular traps, thrombosis, tissue factor, neutrophil, coagulation cascade

Probably diagnosis:

- **Deficiency of TF-positive neutrophil (CD142)**

- **Defenite treatment for neutropenia & coagulation disorder severity:**
  - **Allogenic HSCT**



باتشکر از توجه شما