Co-presentation with both ANCA and anti-GBM antibodies

Dr mojgan mortazavi

Professor of nephrology

Isfahan kidney diseases research center

Isfahan university of medical sciences

80 y/o man with Renal Failure and Double Seropositive for ANCA and Anti-GBM Ab

Lab data:
BUN: 56mg/dl
Cr:7.3 mg/dl
ca:9.2
WBC:4100
Hb:8.5 g/dl
Plt:75000
Hco3:15.2
LfT: NL

- Urinalysis:
- Blood ++
- Pr +
- RBC: 10-15
- WBC:5-7
- CAST RBC:1

Kidney sonography:

- Lengths of Rt.kidney :98mm Lt kidney:108 mm

Past medical history:

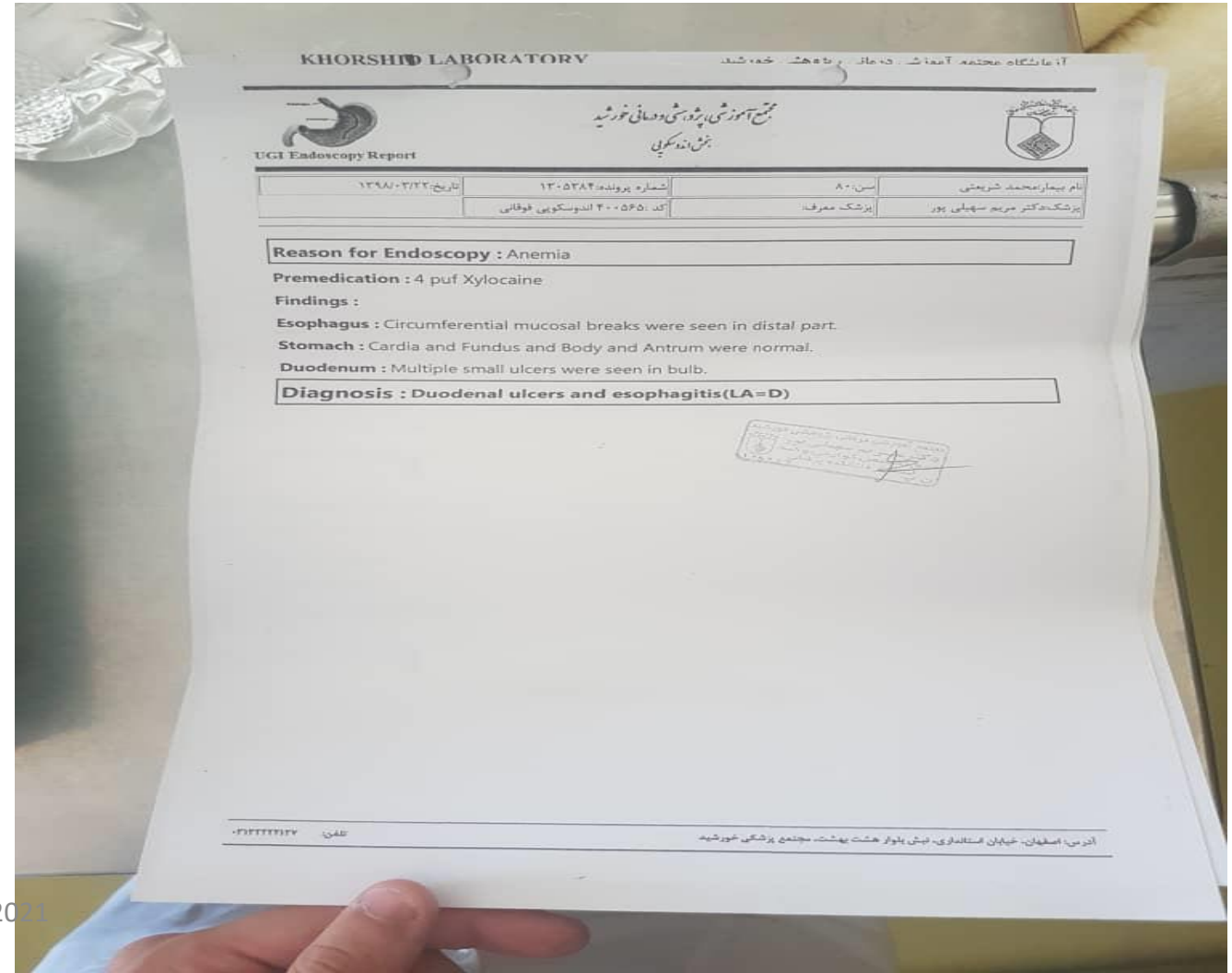
-Heavy smoker +

-2 months ago he hospitalized because of anemia(Hb: 5.3 g/dl)

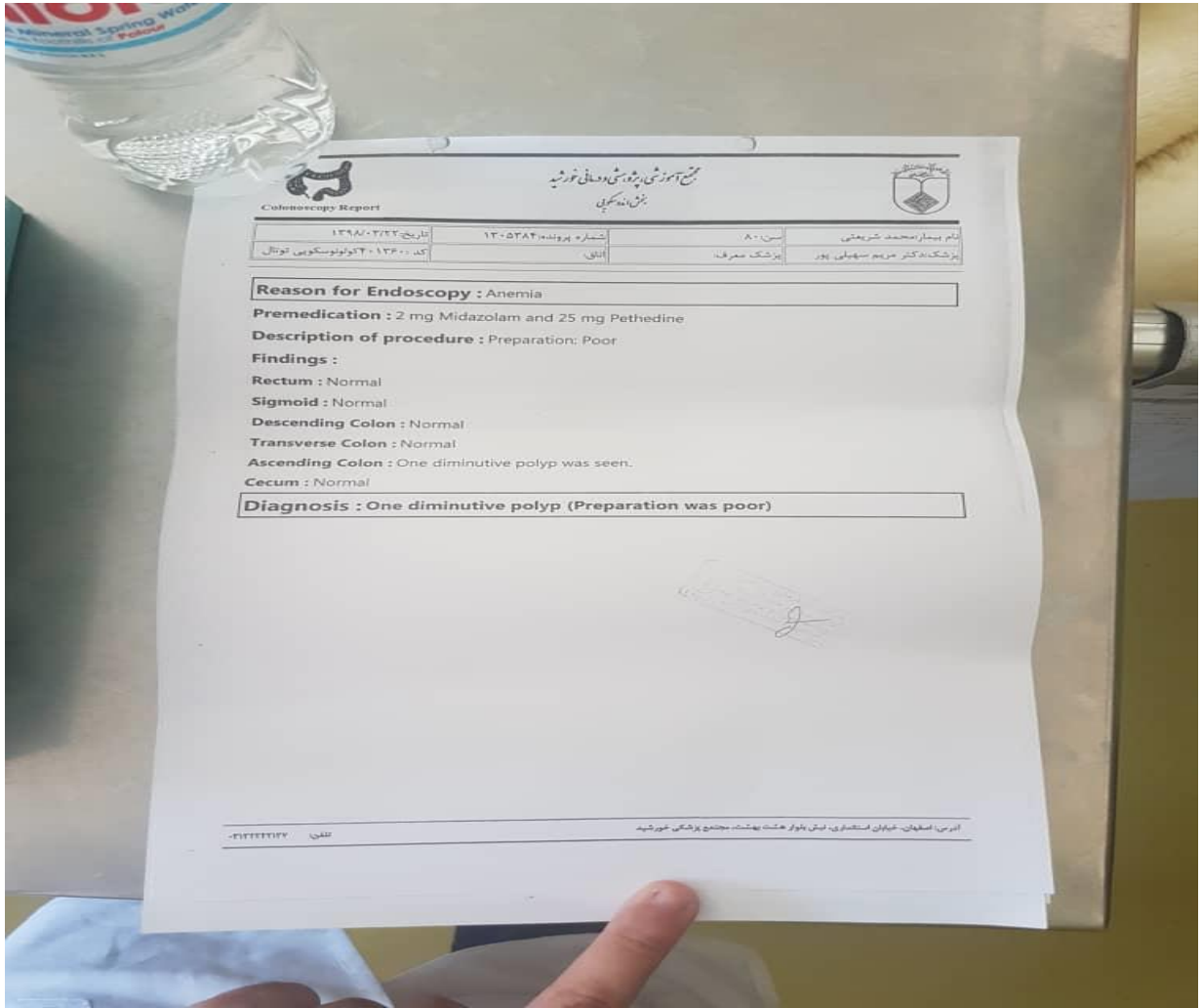
-His Cr was 0.8-1.2 mg/dl

-GI endoscopy and colonoscopy was done for him

Endoscopy: duodenal ulcers and esophagitis



Colonoscopy: one polyp



مجتمع آموزشی پژوهشی دهسانی خورشید

بخش داخلی گوارش

Colonoscopy Report

نام بیمار:محمد شریعتی	سن: ۸۰	شماره پرونده: ۱۳۰۵۳۸۴	تاریخ: ۱۳۹۸/۰۳/۲۲
پزشک:دکتر مریم سپهرلی پور	پزشک معرف:	اتاق:	کد: ۲۰۱۳۶۰ کولونوسکوپی توتال

Reason for Endoscopy : Anemia

Premedication : 2 mg Midazolam and 25 mg Pethedine

Description of procedure : Preparation: Poor

Findings :

Rectum : Normal

Sigmoid : Normal

Descending Colon : Normal

Transverse Colon : Normal

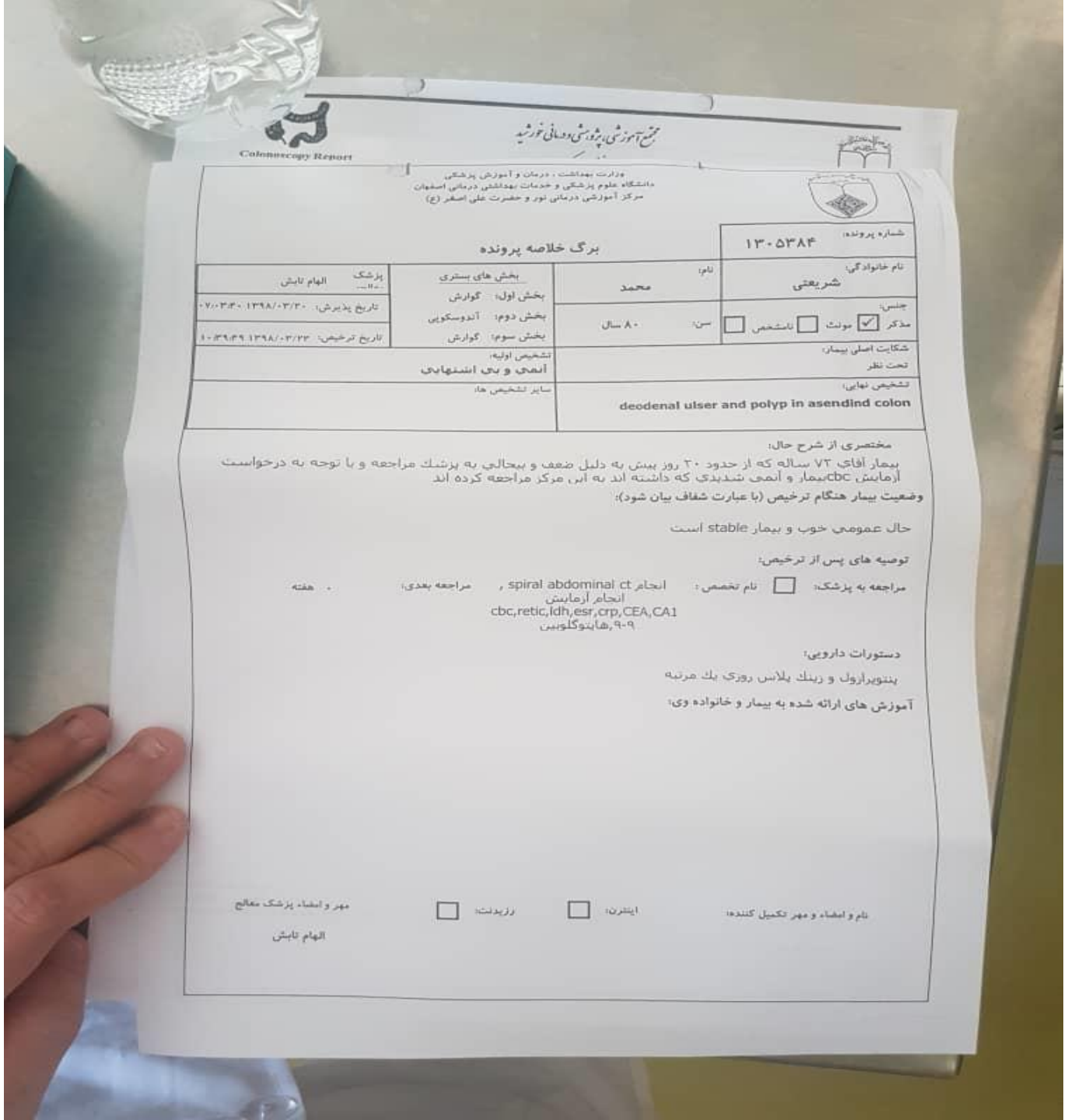
Ascending Colon : One diminutive polyp was seen.

Cecum : Normal

Diagnosis : One diminutive polyp (Preparation was poor)

آدرس: اصفهان- خیابان فلسطین، نبش بلوار هشت بهشت، مجتمع پزشکی خورشید

تلفن: ۰۳۱۳۲۲۲۲۳۲



مجتمع آموزشی، پژوهشی و درمانی خورشید

Colonoscopy Report

وزارت بهداشت، درمان و آموزش پزشکی
دانشگاه علوم پزشکی و خدمات بهداشتی درمانی اصفهان
مرکز آموزشی درمانی نور و حضرت علی اصغر (ع)

برگ خلاصه پرونده

شماره پرونده: ۱۳۰۵۳۸۴

نام خانوادگی: شریعتی

نام: محمد

جنس: مذکر ☑ مونث ☐ نامشخص ☐

سن: ۸۰ سال

شکایت اصلی بیمار: تحت نظر

تشخیص نهایی: deodenal ulser and polyp in asendind colon

بخش های بستری
بخش اول: گوارش
بخش دوم: آندوسکوپی
بخش سوم: گوارش

پزشک: الهام تابش

تاریخ پذیرش: ۱۳۹۸/۰۳/۲۰ ۰۷:۰۳:۴۰

تاریخ ترخیص: ۱۳۹۸/۰۳/۲۳ ۱۰:۳۹:۴۹

تشخیص اولیه: آنمی و بی اشتهایی

سایر تشخیص ها:

مختصری از شرح حال:
بیمار آقای ۷۲ ساله که از حدود ۲۰ روز پیش به دلیل ضعف و بیحالی به پزشک مراجعه و با توجه به درخواست آزمایش cbcبیمار و آنمی شدیدی که داشته اند به این مرکز مراجعه کرده اند

وضعیت بیمار هنگام ترخیص (با عبارت شفاف بیان شود):

حال عمومی خوب و بیمار stable است

توصیه های پس از ترخیص:

مراجعه به پزشک: ☐ نام تخصص: انجام spiral abdominal ct , مراجعه بعدی: هفته

انجام آزمایش cbc,retic,ldh,esr,crp,CEA,CA1 ,۹-۹هایتوگلوبین

دستورات دارویی:

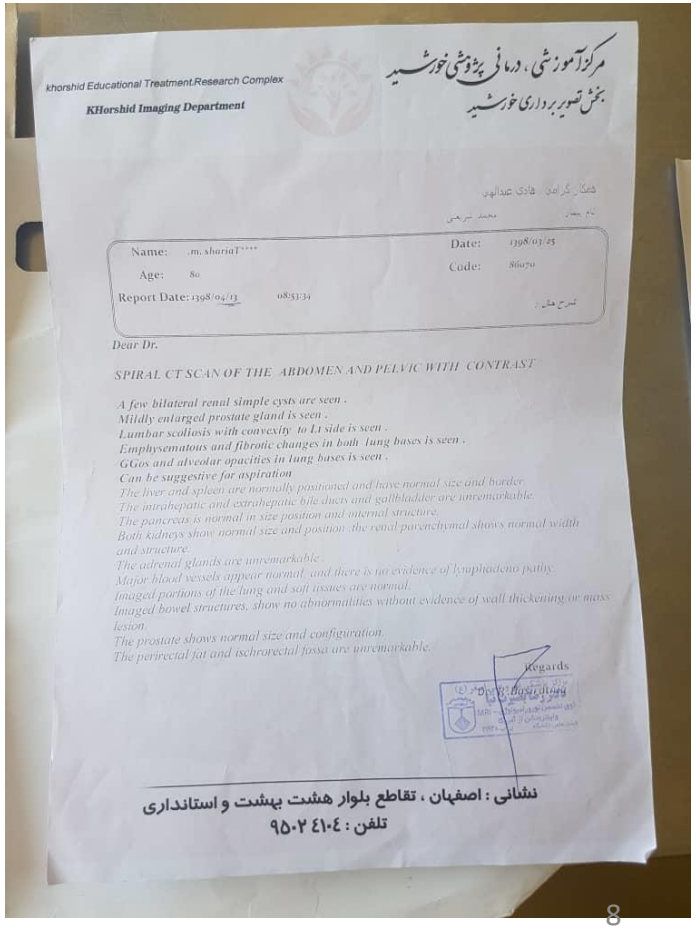
پنتوپرازول و زینک پلاس روزی یک مرتبه

آموزش های ارائه شده به بیمار و خانواده وی:

نام و امضاء و مهر تکمیل کننده: اینترن: ☐ رزیدنت: ☐ مهر و امضاء پزشک معالج

الهام تابش

Spiral CT scan of the lung and abdominopelvic with contrast :***emphysematous and fibrotic changes in both lung bases is seen and alveolar opacities in lung base is seen***



مرکز آموزشی، درمانی پژوهشی خورشید
بخش تصویر برداری خورشید

khorshid Educational Treatment,Research Complex
KHorshid Imaging Department

Name: m. shariaT****
Age: 80
Report Date: 1398/04/13 08:53:34
Date: 1398/03/25
Code: 86070

Dear Dr.

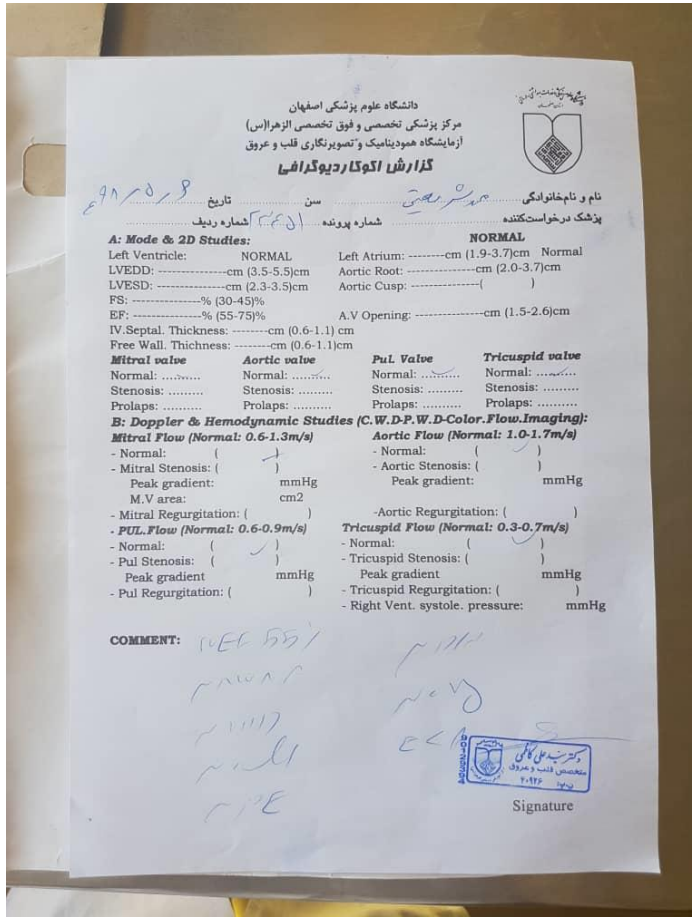
SPIRAL CT SCAN OF THE ABDOMEN AND PELVIC WITH CONTRAST

A few bilateral renal simple cysts are seen .
Mildly enlarged prostate gland is seen .
Lumbar scoliosis with convexity to L1 side is seen .
Emphysematous and fibrotic changes in both lung bases is seen .
GGos and alveolar opacities in lung bases is seen .
Can be suggestive for aspiration
The liver and spleen are normally positioned and have normal size and border.
The intrahepatic and extrahepatic bile ducts and gallbladder are unremarkable.
The pancreas is normal in size position and internal structure.
Both kidneys show normal size and position ,the renal parenchymal shows normal width and structure.
The adrenal glands are unremarkable .
Major blood vessels appear normal, and there is no evidence of lymphadeno pathy.
Imaged portions of the lung and soft tissues are normal.
Imaged bowel structures, show no abnormalities without evidence of wall thickening or mass lesion.
The prostate shows normal size and configuration.
The perirectal fat and ischiorectal fossa are unremarkable.

Regards

نشانی : اصفهان ، تقاطع بلوار هشت بهشت و استانداری
تلفن : ۹۵۰۲ ٤١٠٤

Ef :55%



دانشگاه علوم پزشکی اصفهان
مرکز پزشکی تخصصی و فوق تخصصی الزهرا(س)
آزمایشگاه همودینامیک و تصویرنگاری قلب و عروق

گزارش اکوکاردیوگرافی

نام و نام‌خانوادگی ..... سن ..... تاریخ .....
پزشک درخواست‌کننده ..... شماره پرونده ..... شماره ردیف .....

A: Mode & 2D Studies: **NORMAL**

Left Ventricle: NORMAL
LVEDD: ----------cm (3.5-5.5)cm
LVESD: ----------cm (2.3-3.5)cm
FS: ----------% (30-45)%
EF: ----------% (55-75)%
IV.Septal. Thickness: --------cm (0.6-1.1) cm
Free Wall. Thichness: --------cm (0.6-1.1)cm

Left Atrium: --------cm (1.9-3.7)cm Normal
Aortic Root: ----------cm (2.0-3.7)cm
Aortic Cusp: ----------( )
A.V Opening: ----------cm (1.5-2.6)cm

Mitral valve	***Aortic valve***	***Pul. Valve***	***Tricuspid valve***
Normal:	Normal:	Normal:	Normal: .....
Stenosis:	Stenosis:	Stenosis:	Stenosis: .....
Prolaps:	Prolaps:	Prolaps:	Prolaps: .....

B: Doppler & Hemodynamic Studies (C.W.D-P.W.D-Color.Flow.Imaging):

Mitral Flow (Normal: 0.6-1.3m/s)
- Normal: ( )
- Mitral Stenosis: ( )
  Peak gradient: mmHg
  M.V area: cm2
- Mitral Regurgitation: ( )

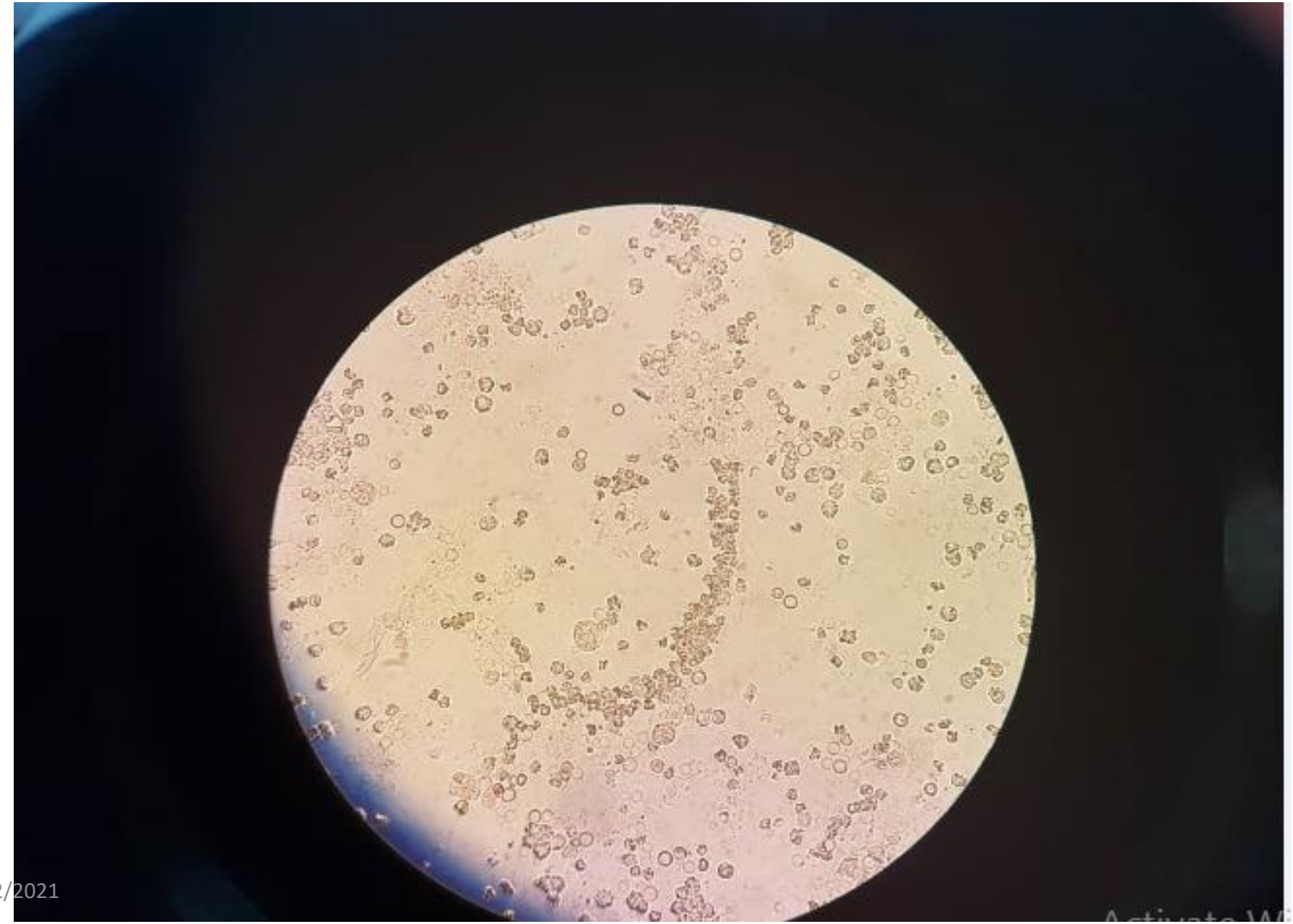
Aortic Flow (Normal: 1.0-1.7m/s)
- Normal: ( )
- Aortic Stenosis: ( )
  Peak gradient: mmHg
- Aortic Regurgitation: ( )

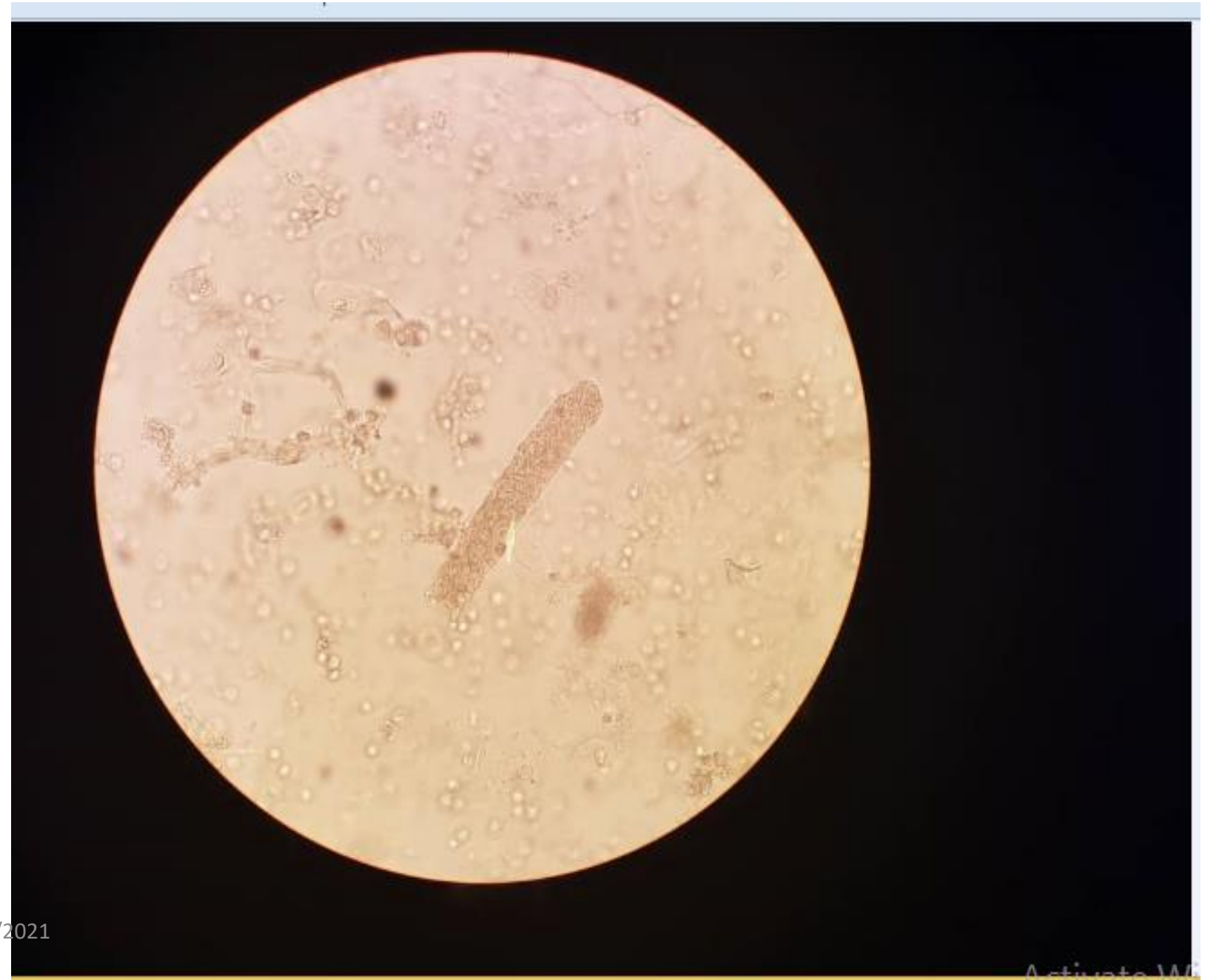
. PUL.Flow (Normal: 0.6-0.9m/s)
- Normal: ( )
- Pul Stenosis: ( )
  Peak gradient mmHg
- Pul Regurgitation: ( )

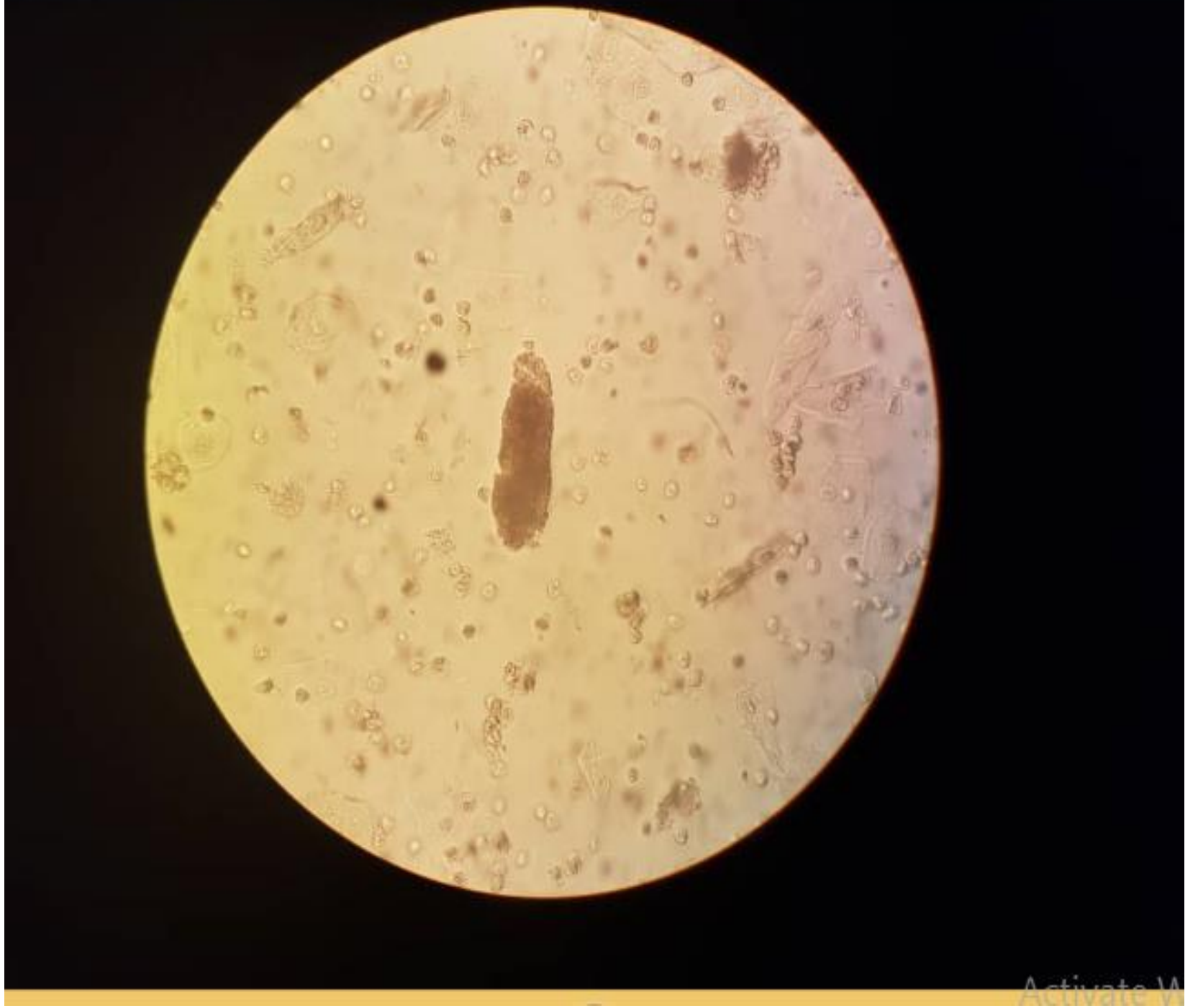
Tricuspid Flow (Normal: 0.3-0.7m/s)
- Normal: ( )
- Tricuspid Stenosis: ( )
  Peak gradient mmHg
- Tricuspid Regurgitation: ( )
- Right Vent. systole. pressure: mmHg

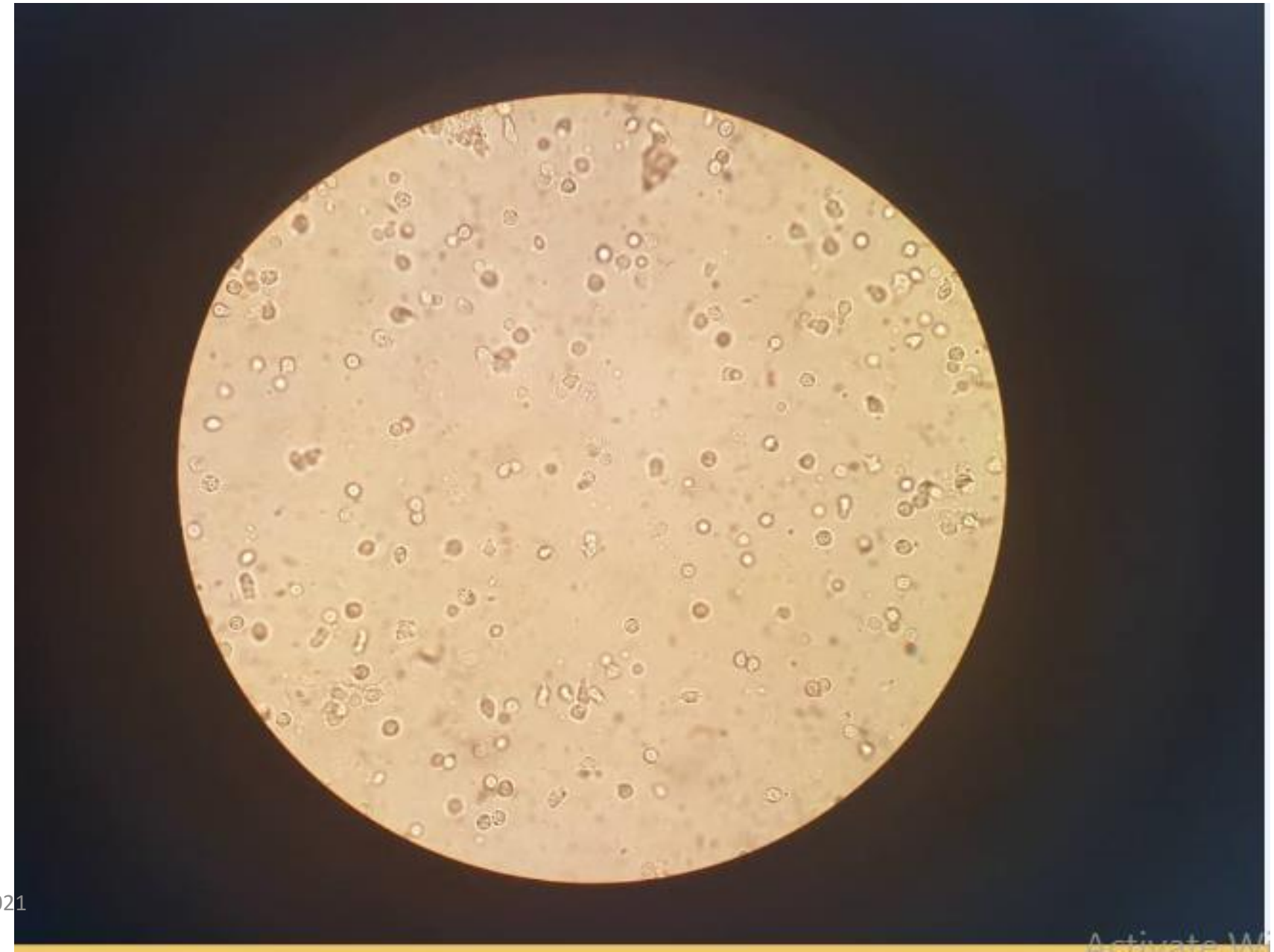
COMMENT:

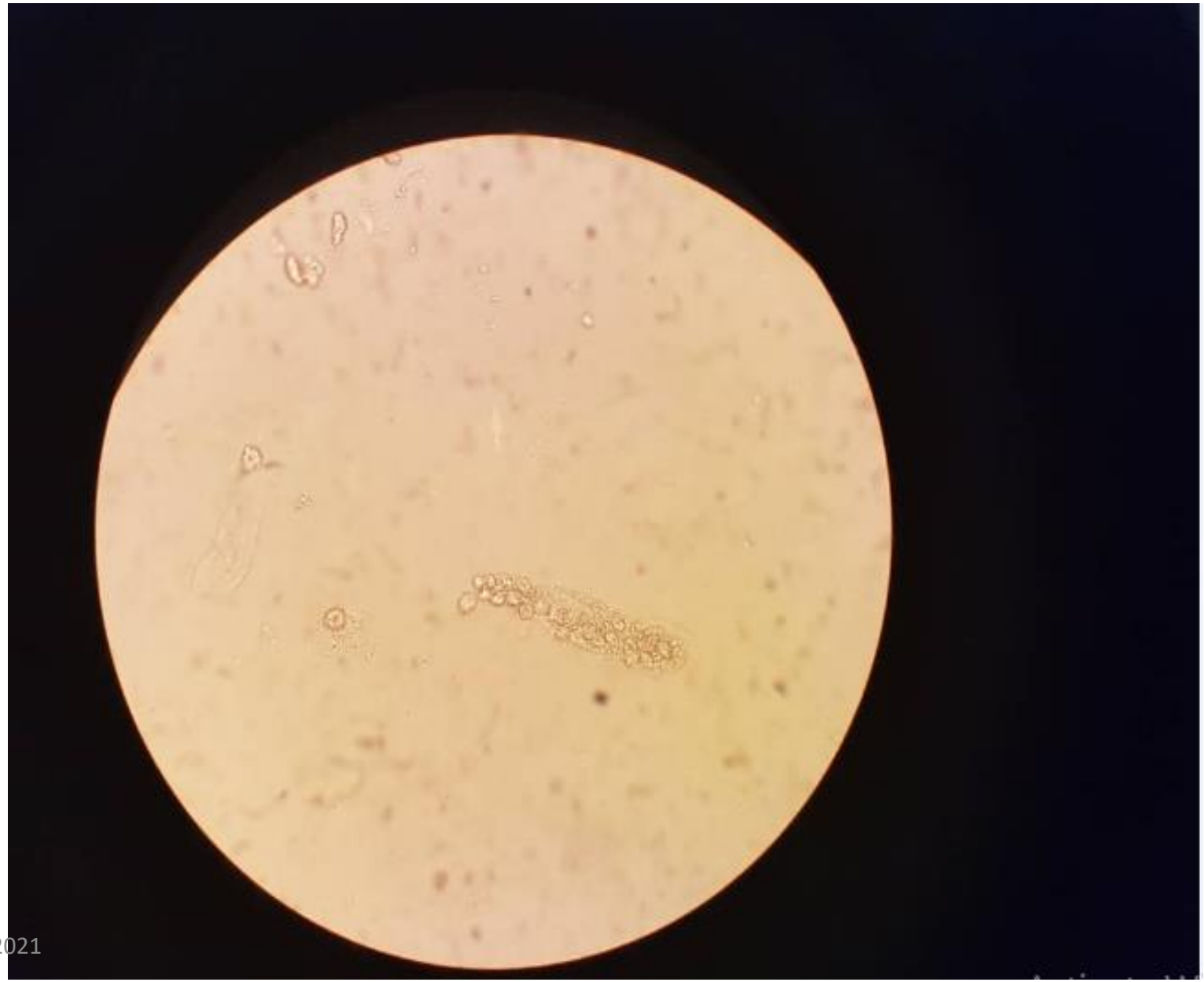
Signature







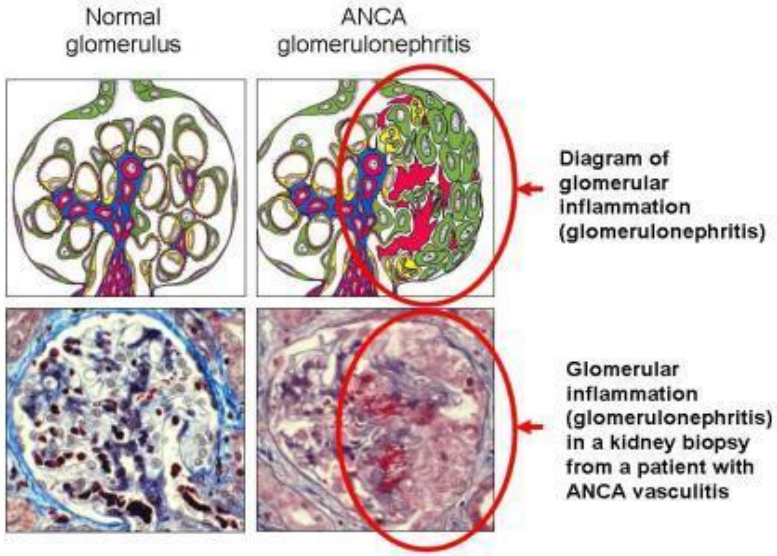


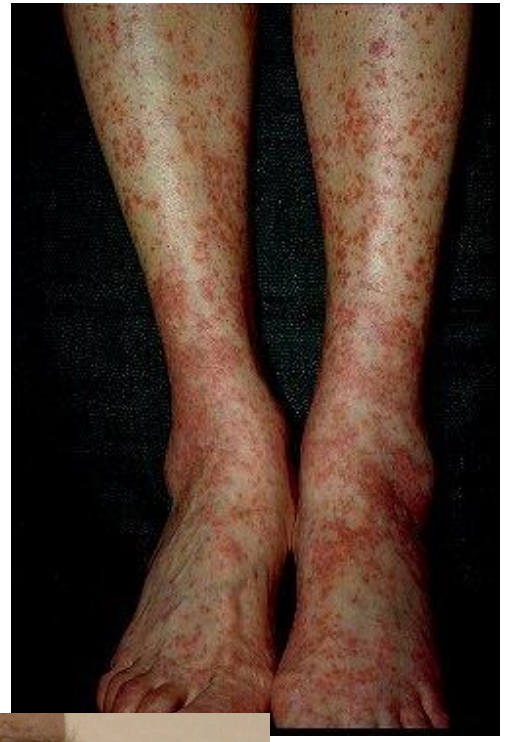


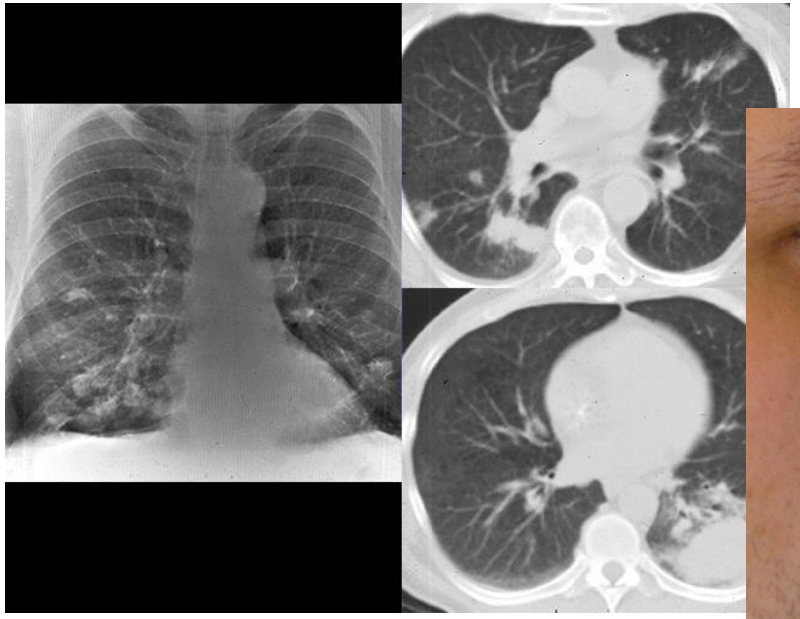
Serologic exam

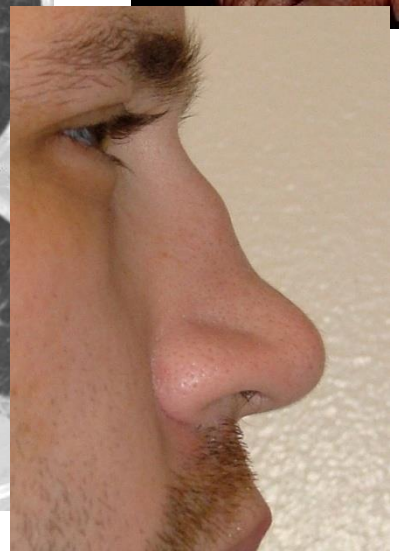
- mpo-ANCA :180 negative<5
- Anti GBM:172 negative<12

Overview of and approach to the vasculitides in adults


Normal glomerulus
ANCA glomerulonephritis
Diagram of glomerular inflammation (glomerulonephritis)
Glomerular inflammation (glomerulonephritis) in a kidney biopsy from a patient with ANCA vasculitis



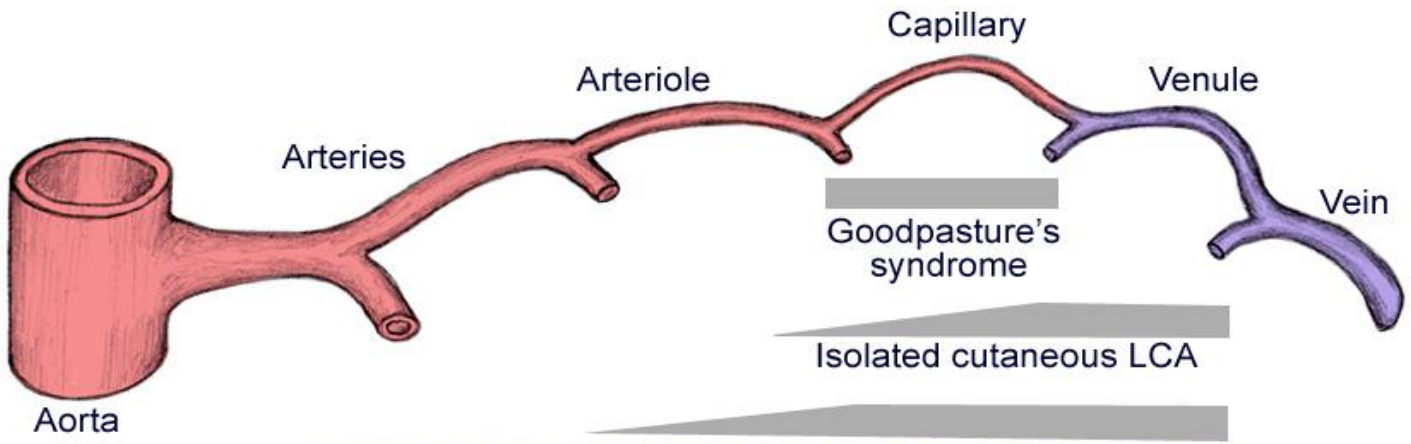




Small-Vessel Vasculitis
(e.g., microscopic polyangiitis, Wegener's granulomatosis)

Medium-Sized-Vessel Vasculitis
(e.g., polyarteritis nodosa, Kawasaki's disease)

Large-Vessel Vasculitis
(e.g., giant-cell arteritis, Takayasu's arteritis)



Henoch-Schonlein purpura and cryoglobulinemic vasculitis

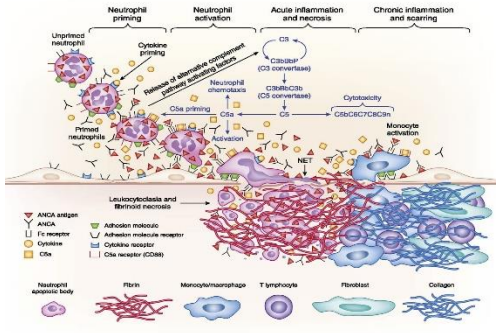
Microscopic polyangiitis, Wegener's granulomatosis, and Churg-Strauss syndrome

Overview of and approach to the vasculitides in adults

- The vasculitides are defined by the presence of inflammatory leukocytes in vessel walls with reactive damage to mural structures.

- Both loss of vessel integrity leading to bleeding, and compromise of the lumen may result in downstream tissue ischemia and necrosis

Small-vessel vasculitis-ANCA-associated vasculitis



- Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a necrotizing vasculitis that does not substantially involve the deposition of immune complexes.

- AAV predominantly affects small vessels and is associated with ANCA specific for myeloperoxidase (MPO ANCA) or proteinase 3 (PR3-ANCA)

ANCA-negative AAV

- Cases of ANCA-negative AAV do occur, especially in eosinophilic granulomatosis with polyangiitis (EGPA) but also to some extent in granulomatosis with polyangiitis (GPA).

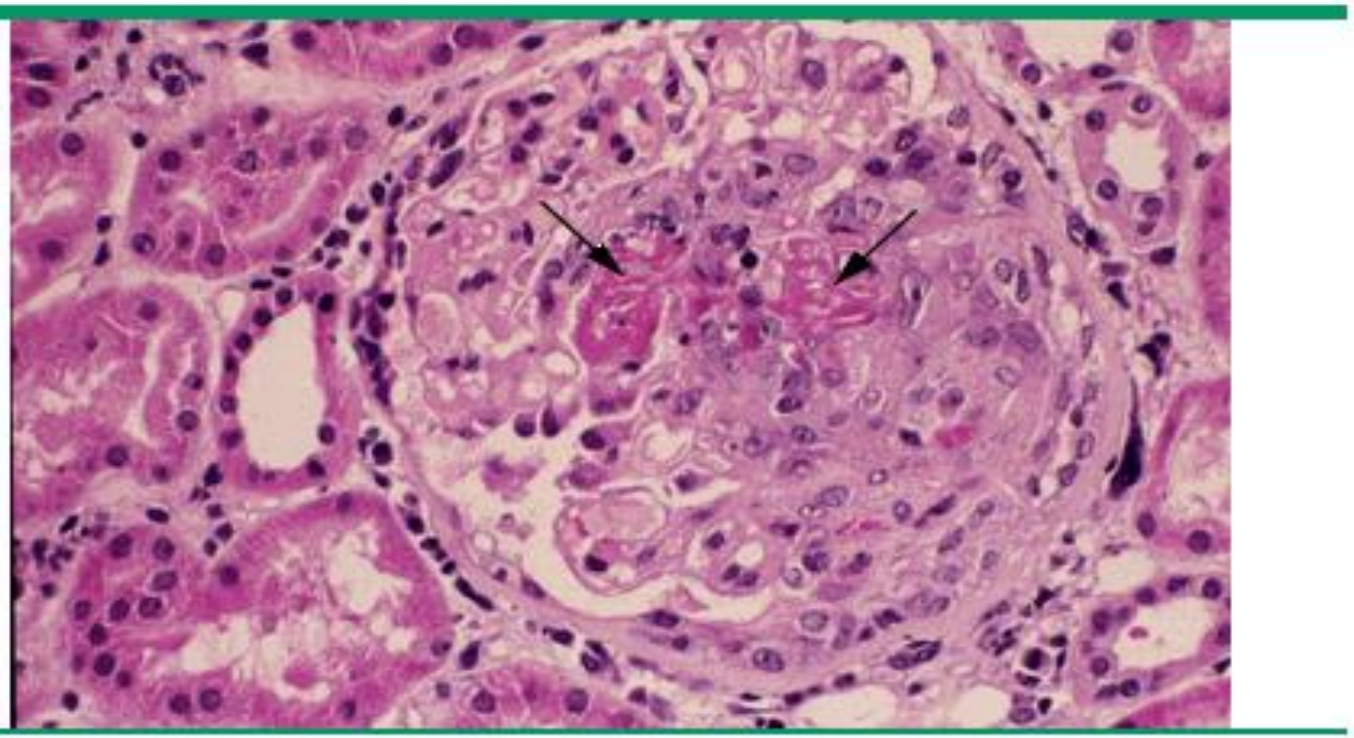
- ANCA-negative AAV describes cases in which the patient otherwise fulfills the definition for AAV but has negative results on serologic testing for ANCA
- The major clinicopathologic variants of AAV include microscopic polyangiitis (MPA), GPA, and EGPA; additionally, AAV can occur in only a single organ, especially a subset referred to as renal-limited AAV.

Microscopic polyangiitis

- MPA is a necrotizing vasculitis that primarily affects capillaries, venules, or arterioles, most commonly manifesting as necrotizing glomerulonephritis and/or pulmonary capillaritis.

- Involvement of medium- and small- sized arteries may also be present.
- Granulomatous inflammation is usually absent.
- ANCA is present in >90 percent of patients with MPA

Necrotizing glomerulonephritis



Light micrograph showing fresh segmental necrotizing lesions with bright red fibrin deposition (arrows). A necrotizing glomerulonephritis can be seen in a variety of inflammatory disorders including vasculitis and lupus nephritis. The latter has prominent immune complex deposition which is generally absent in vasculitis.

Courtesy of Helmut Rennke, MD.

Granulomatosis with polyangiitis (Wegener's)

- GPA is a necrotizing vasculitis predominantly involving small- to medium-sized vessels (eg, capillaries, venules, arterioles, arteries, and veins).
- It typically produces granulomatous inflammation of the upper and lower respiratory tracts as well as necrotizing, pauci-immune glomerulonephritis.

- ANCA is present in >80 percent of patients with GPA.

Granulomatosis with polyangiitis (Wegener's)

- While MPA and GPA continue be regarded as distinct entities within AAV, they have markedly overlapping manifestations and it can be sometimes extremely difficult to differentiate between these two diseases within a patient.
- Furthermore, there is a growing recognition that ANCA type (anti-MPO or anti-PR3) has more prognostic and clinical meaning rather than the disease type (MPA or GPA), leading some experts to refer

to MPO-AAV or PR3-AAV, and many clinical trials in AAV now stratify enrollment by ANCA type (MPO or PR3) and report results for each

- subgroup.

Eosinophilic granulomatosis with polyangiitis (Churg-Strauss)

- EGPA is an eosinophilic-rich necrotizing vasculitis predominantly affecting small- to medium-sized vessels.
- Patients often have chronic rhinosinusitis, asthma, and prominent peripheral blood eosinophilia.
- ANCA is present in approximately 40 percent of patients with EGPA, usually anti-MPO ANCA.
- The presence of ANCA is more frequent in patients with glomerulonephritis.

Immune complex small-vessel vasculitis

- Immune complex small-vessel vasculitis refers to vasculitis with moderate to marked vessel wall deposits of immunoglobulin and/or complement, predominantly affecting small vessels. Glomerulonephritis is often present.
- Medium-sized arterial involvement is much less common in immune complex vasculitis compared with AVV.

Anti-glomerular basement membrane disease

- Anti-glomerular basement membrane (GBM) disease is a vasculitis affecting glomerular capillaries, pulmonary capillaries, or both, with

basement membrane deposition of anti-basement membrane autoantibodies.

- Lung involvement typically causes pulmonary hemorrhage, and renal involvement causes glomerulonephritis with necrosis and crescents

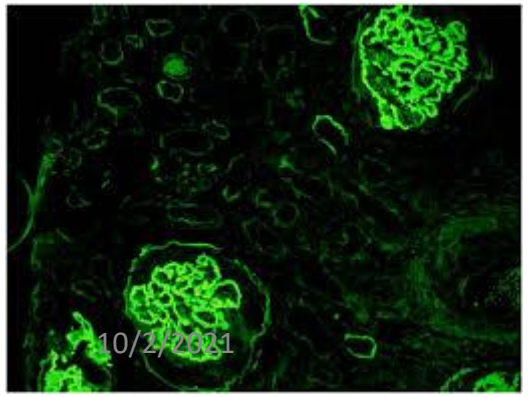


Table 1. CHCC 2012 categories of ANCA-associated vasculitis (modified from reference (1))

CHCC 2012 Name	CHCC 2012 Definition
ANCA-associated vasculitis	Necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels (*i.e.*, capillaries, venules, arterioles, and small arteries), associated with myeloperoxidase (MPO) ANCA or proteinase 3 (PR3) ANCA. Not all patients have ANCA. Add a prefix indicating ANCA reactivity, *e.g.*, MPO-ANCA, PR3-ANCA, ANCA-negative.
Microscopic polyangiitis	Necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels (*i.e.*, capillaries, venules, or arterioles). Necrotizing arteritis involving small and medium arteries may be present. Necrotizing GN is very common. Pulmonary capillaritis often occurs. Granulomatous inflammation is absent.
Granulomatosis with polyangiitis (Wegener)	Necrotizing granulomatous inflammation usually involving the upper and lower respiratory tract, and necrotizing vasculitis affecting predominantly small-to-medium vessels (*e.g.*, capillaries, venules, arterioles, arteries, and veins). Necrotizing GN is common.
Eosinophilic granulomatosis with polyangiitis (Churg–Strauss)	Eosinophil-rich and necrotizing granulomatous inflammation often involving the respiratory tract, and necrotizing vasculitis predominantly affecting small-to-medium vessels, and associated with asthma and eosinophilia. ANCA is more frequent when GN is present.

CHCC 2012, 2012 International Chapel Hill Consensus Conference on the Nomenclature of Vasculitides.

CLINICAL FEATURES SUGGESTIVE OF SYSTEMIC VASCULITIS

- In general, the presence of vasculitis should be considered in patients who present with systemic or constitutional symptoms in combination with
- evidence of single and/or multiorgan dysfunction,
- The diagnosis of vasculitis is often delayed because the clinical manifestations can be mimicked by a number of other diseases.

Laboratory tests

- ANCA – Although not fully diagnostic on its own, the presence of ANCA directed against either protease 3 (PR3) or myeloperoxidase (MPO) is extremely specific(often >95 percent) for a diagnosis of AAV in patients with some reasonable pre-test suspicion.

Initial immunosuppressive therapy in granulomatosis with polyangiitis and microscopic polyangiitis

- Immunosuppressive therapy is warranted in almost all patients with active GPA or MPA

- Induction of complete remission is the goal and expectation of treatment with immunosuppressive therapy in GPA or MPA and is defined as the absence of active disease (ie, the absence of any clinical manifestations that are deemed secondary to ongoing active vasculitis)

Initial immunosuppressive therapy

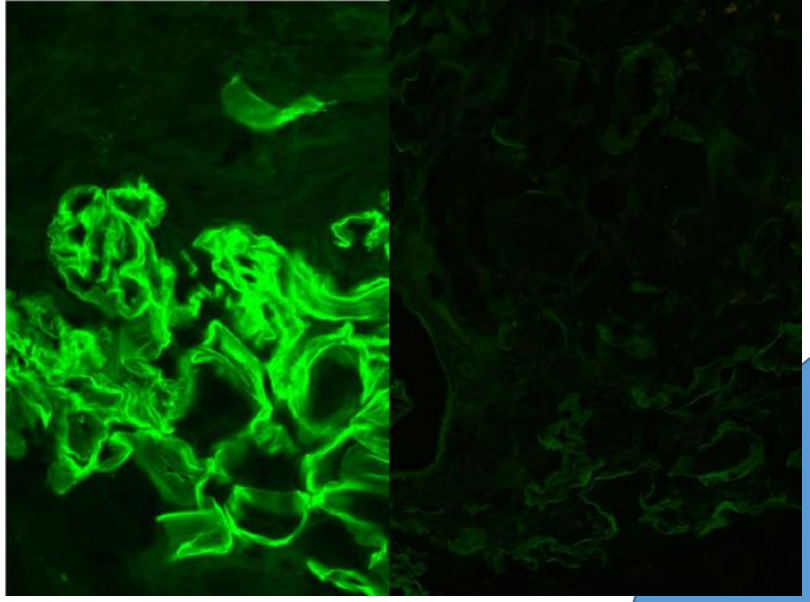
- Initial immunosuppressive therapy in GPA and MPA typically consists of glucocorticoids combined with either cyclophosphamide or rituximab.
- Selected patients with severe disease may benefit from the addition of plasma exchange
- The use of aggressive initial immunosuppression is justified because the mortality rate in untreated generalized GPA is as high as 90 percent at two years, usually due to respiratory or renal failure

plasma exchange in addition to glucocorticoids and either cyclophosphamide or rituximab

- Patients who have rapidly deteriorating kidney function or severe kidney dysfunction (eg, those who have a serum creatinine above 4.0 mg/dL [354 micromol/L] or who require dialysis).

- Patients who have pulmonary hemorrhage – Some contributors to this topic would treat all patients who have pulmonary hemorrhage with plasma exchange, while others would use plasma exchange in only those patients who also have severe respiratory impairment (eg, dyspnea or hypoxia) or if the patient does not respond quickly to therapy with intravenous glucocorticoids.

- Patients who have a concomitantly positive anti-glomerular basement membrane (anti-- GBM) autoantibody.



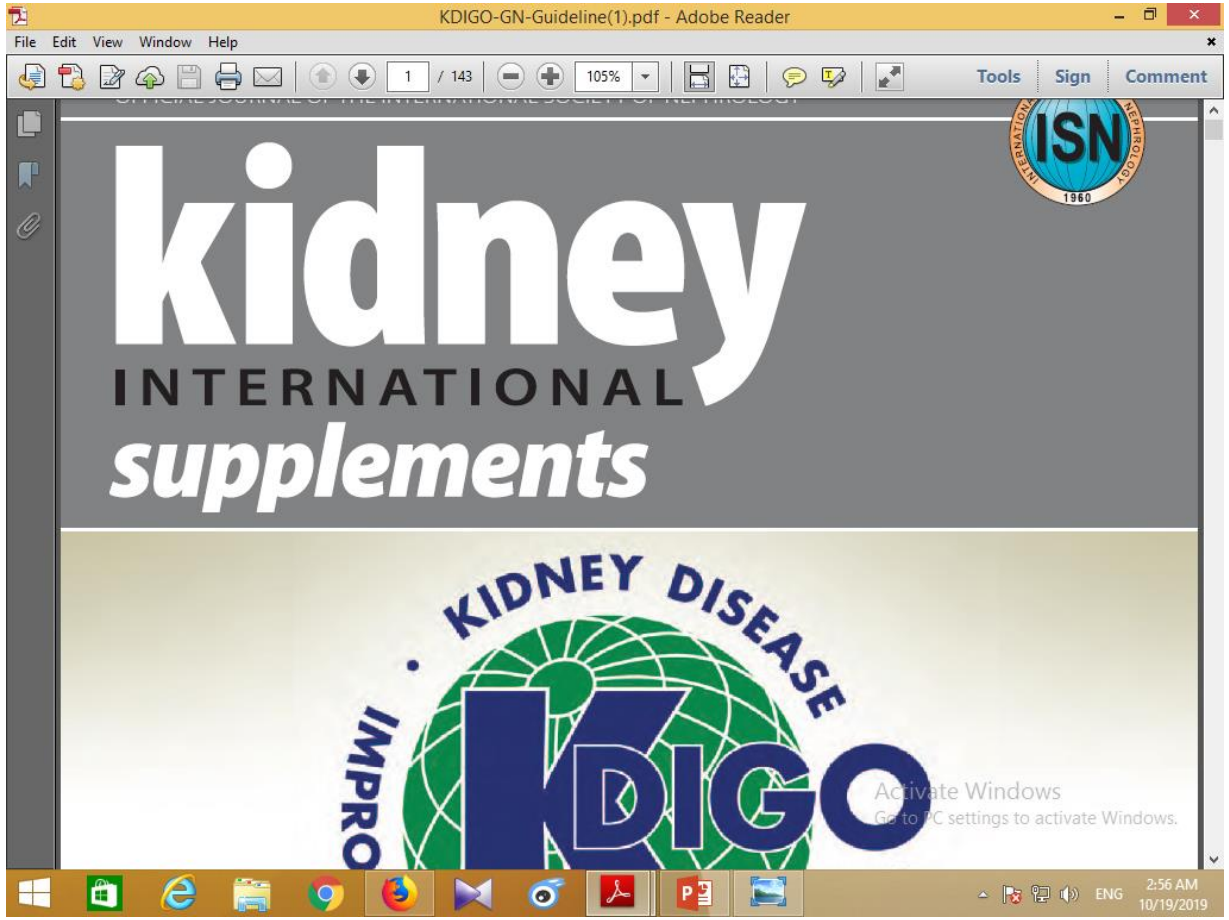
Patients double-seropositive for ANCA and anti-GBM

- Co-presentation with both ANCA and anti-GBM antibodies is thought to be relatively rare.

Patients with ANCA Vasculitis: Anti-GBM GN Overlap Syndrome

- The recommendation for plasmapheresis, in addition to corticosteroids and cyclophosphamide for patients with both Kidney International Supplements.

-Patients with ANCA/anti-GBM overlap have a worse outcome than patients with ANCA vasculitis alone, or anti-GBM alone.


KDIGO-GN-Guideline(1).pdf - Adobe Reader
File Edit View Window Help
Tools Sign Comment
kidney
INTERNATIONAL
supplements
ISN
1960
KIDNEY DISEASE
IMPRO
KDIGO
Activate Windows
Go to PC settings to activate Windows.
ENG
2:56 AM
10/19/2019

- Anti-glomerular basement membrane (GBM) disease and the anti-neutrophil cytoplasm antibody (ANCA)-associated vasculitides (AAV) are rare conditions, with estimated incidences in Europe of 1 and 20 per million population per year, respectively.

- It is clear that the 2 antibody populations associated with these diseases are antigenically distinct,[9] and that this phenomenon is not due to cross-reactivity, although the mechanisms of the association are not fully understood.

Clinical presentation and serology

Patients double-seropositive for ANCA and anti-GBM antibodies have varied renal survival, frequency of relapse, and outcomes compared to single-seropositive patients

see commentary on page 544

OPEN

Stephen P. McAdoo[1], Anisha Tanna[1], Zdenka Hrušková[2], Lisa Holm[3], Maria Weiner[4], Nishkantha Arulkumaran[1], Amy Kang[1], Veronika Satrapová[2], Jeremy Levy[1], Sophie Ohlsson[3], Vladimir Tesar[2], Mårten Segelmark[4] and Charles D. Pusey[1]

[1]*Renal and Vascular Inflammation Section, Department of Medicine, Imperial College London, London, UK;* [2]*Department of Nephrology, General University Hospital, Prague and First Faculty of Medicine, Charles University, Prague, Czech Republic;* [3]*Department of Nephrology and Transplantation, Skånes University Hospital, Lund, Sweden; and* [4]*Department of Nephrology and Department of Medical and Health Sciences, Linköping University, Linköping, Sweden*

Co-presentation with both ANCA and anti-GBM antibodies is thought to be relatively rare. Current studies of such 'double-positive' cases report small numbers and variable outcomes. To study this further we retrospectively analyzed clinical features and long-term outcomes of a large cohort of 568 contemporary patients with ANCA-associated vasculitis, 41 patients with anti-GBM disease, and 37 double-positive patients with ANCA and anti-GBM disease from four European centers. Double-positive patients shared characteristics of ANCA-associated vasculitis (AAV), such as older age distribution and longer symptom duration before diagnosis, and features of anti-GBM disease, such as severe renal disease and high frequency of lung hemorrhage at presentation. Despite having more evidence of chronic injury on renal biopsy compared to patients with anti-GBM disease, double-positive patients had a greater tendency to recover from being dialysis-dependent after treatment and had intermediate long-

double-positivity appears common, further work is required to define the underlying mechanisms of this association and define optimum treatment strategies.

Kidney International (2017) **92,** 693–702; http://dx.doi.org/10.1016/j.kint.2017.03.014

KEYWORDS: anti-GBM disease; anti–neutrophil cytoplasm antibody; glomerulonephritis; Goodpasture syndrome; vasculitis

Anti-glomerular basement membrane (GBM) disease and the anti-neutrophil cytoplasm antibody (ANCA)-associated vasculitides (AAV) are rare conditions, with estimated incidences in Europe of 1 and 20 per million population per year, respectively.[1,2] The concurrence of both ANCA and anti-GBM antibodies in individual patients, however, is well-recognized, and occurs at a much higher frequency than would be expected by chance alone.

Table 1 | Case identification, demographics, clinical features, and serology

				P value			
	AAV	Anti-GBM	Double positive	AAV versus DP versus GBM	AAV versus DP	GBM versus DP	AAV versus GBM
Cases, *n*	568	41	37	–	–	–	–
• United Kingdom	171	19	20				
• Sweden	100	13	8				
• Czech Republic	297	9	9				
Cases, %	87.9%	6.3%	5.7%				
Demographics							
Age, yr (range)	62.3 (11–95)	58.3 (13–91)	63.6 (17–88)	0.17	0.99	0.31	0.21
Gender							
• Male	54%	46%	38%	0.11	0.06	0.49	0.34
• Female	46%	54%	62%				
Clinical Features							
Duration of symptoms,[a] wk (range)	12 (0–56)	2 (0–20)	10 (1–26)	**<0.01**	0.99	**<0.01**	**<0.01**
Lung hemorrhage	131/568 23%	16/41 40%	14/37 38%	**0.01**	**0.04**	0.85	**0.02**
Required RRT at presentation	132/568 23%	26/41 63%	21/37 57%	**<0.01**	**<0.01**	0.55	**<0.01**
eGFR,[b] ml/min (range)	29 (5–90)	20 (5–90)	19 (6–76)	0.06	0.11	0.99	0.67
Serum creatinine,[b] µmol/l (range)	186 (39–693)	275 (62–667)	309 (71–606)	0.06	0.18	0.99	0.37
Serology							
Anti-GBM level, xULN (range)	–	5.4 (1–29.1)	14.2 (1–50.4)		–	0.06	–
Proportion seronegative for anti-GBM, %	–	4/41 11%	4/37 11%		–	1.00	–
ANCA serology, %					**<0.01**	–	–
• Anti-MPO	48%		70%				
• Anti-PR3	51%		27%				
• Anti-MPO & PR3	<1% ($n = 2$)		3%				

AAV, anti-neutrophil cytoplasm antibody–associated vasculitis; DP, double-positive; eGFR, estimated glomerular filtration rate; GBM, glomerular basement membrane; MPO, myeloperoxidase; PR3, proteinase 3; RRT, renal replacement therapy; xULN, multiples of upper limit of normal.
Results expressed as median ± range. Comparison between groups by Kruskall–Wallis test with Dunn's post-test to ascertain differences between individual groups (for continuous data), or by chi-square test (for categorical data).
[a]Calculated for a sample of 48 ANCA cases.
[b]Censored for patients on RRT.

Histopathology

clinical investigation

Table 2 | Histopathology

	Anti-GBM	Double positive	*P* value
Underwent biopsy, n (%)	29 (71%)	25 (68%)	0.81
Mean age at biopsy, yr (range)	46 (13–91)	62 (46–76)	**<0.01**
Renal status at biopsy			
• Required RRT	52%	54%	1.00
• eGFR,[a] ml/min (range)	21 (5–90)	16 (8–73)	0.78
• Serum creatinine[a] µmol/l (range)	275 (62–677)	315 (71–606)	0.75
Glomerular findings			
• Crescentic glomeruli, %	64% (0–100)	64% (25–100)	0.98
• Sclerotic glomeruli, %	0% (0–80)	15% (0–100)	0.19
• Normal glomeruli, %	5% (0–100)	0% (0–67)	0.56
Tubular atrophy, % (range)	5% (0%–30%)	27% (0%–80%)	**<0.01**
Immunofluorescence pattern			0.69
• Linear IgG	79%	80%	
• Pauci-immune	3%	8%	
• Technically inadequate	17%	12%	

eGFR, estimated glomerular filtration rate; GBM, glomerular basement membrane; RRT, renal replacement therapy.
Results expressed as median ± range. Comparison between groups by Mann-Whitney test (for continuous data), or by chi-square test (for categorical data)

Treatment

- There was no detectable difference between single-positive anti-GBM and double-positive groups with regard to initial treatment administered, the majority receiving standard of care with steroids (97% vs. 100% in double-positive and anti-GBM cases, respectively; P ¼ 0.47), cyclophosphamide (100% vs. 92%; P ¼ 0.24), and plasma exchange (80% vs. 89%; P 0.33). In total, 10 patients did not undergo plasma exchange for various reasons.

Treatment

- In the double-positive group, 7 patients did not receive plasma exchange. Of these, 2 were dialysis dependent at presentation with 100% crescent formation on kidney biopsy, and in the absence of lung hemorrhage, plasma exchange was deemed futile.

- These patients received cytotoxic therapy and steroids for nonrenal manifestations

Treatment

- At 6 months, 74% of patients who were double positive were receiving ongoing immunosuppressive treatment with or without corticosteroids (71% with azathioprine, 21% with mycophenolate mofetil, and 8% with methotrexate), whereas only 14% of patients with single-positive anti-GBM disease received ongoing therapy ($P < 0.001$), of whom 80% received azathioprine and 20% received MMF.

Outcomes

Table 3| Patient and renal survival at 3 and 12 months after diagnosis

	0 Months	3 months		12 months		
Diagnosis	Independent of RRT	Patient survival	Renal survival[a]	Patient survival	Renal survival[a]	Renal recovery at 1 yea
AAV	437/568	540/568	490/540	512/568	452/512	64/131
	77%	95%	91%	90%	88%	49%
Anti-GBM	15/41	37/41	15/36	36/41	15/34	4/24
	37%	90%	42%	87%	44%	17%
Double positive	16/37	33/37	16/32	31/37	16/30	6/21
	43%	89%	50%	83%	53%	29%
P value	**<0.01**	0.13	**<0.01**	0.38	**<0.01**	**<0.01**

AAV, anti-neutrophil cytoplasm antibody–associated vasculitis; GBM, glomerular basement membrane; RRT, renal replacement therapy.
Comparison between groups by chi-square test.
[a]Censored for death.
[b]Proportion of patients requiring RRT at presentation who were alive with independent renal function at 1 year.

Outcomes

- Overall patient survival was similar in all groups at both time points
- Renal survival was favorable in the AAV group at both time points, although there was no significant difference in the proportion of patients who required dialysis in the anti-GBM and double-positive group at either time point.

Outcomes

- The proportion of patients who presented with dialysis-dependent renal failure and who recovered renal function and were alive at 1 year was significantly different between groups, varying from 17% in patients with single positive anti-GBM disease to 29% in patients who were double positive and 49% in AAV cases.

Predictors of death, ESRD, and relapse

- Unadjusted predictors of progression to ESRD included diagnosis (P < 0.01), lung hemorrhage at presentation (HR: 1.89 [1.32–2.63]; P < 0.01), and RRT at presentation (HR: 9.34 [6.53–13.33]; P < 0.01). Age was not associated with progression to ESRD (P ¼ 0.18).

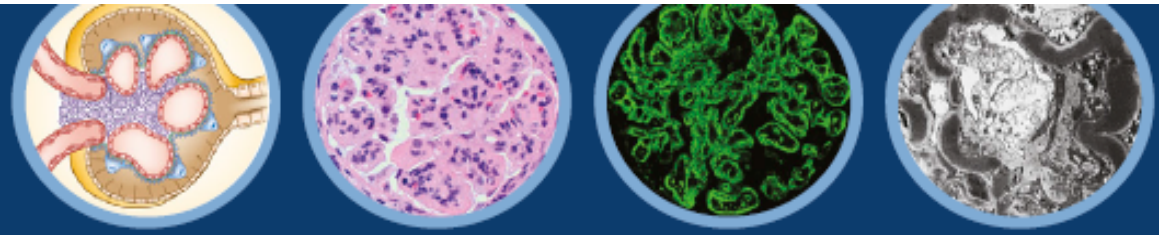
Predictors of death, ESRD, and relapse

- In multivariable analysis, RRT at presentation (HR: 7.69 [5.26–11.10]; P < 0.01) and

diagnosis (P < 0.01) increased the HR of progression to ESRD.

The risk of ESRD was increased in anti-GBM disease compared with AAV (HR: 2.66 [1.69–4.19], P < 0.01), though the risk in patients who were double positive versus those with AAV was not significantly different (HR: 0.62 [0.36– 1.06]; P ¼ 0.08), suggesting an intermediate risk of ESRD in patients who were double positive.

Glomerular Disease



ANCA Glomerulonephritis and Vasculitis

J. Charles Jennette and Patrick H. Nachman

Abstract

ANCA vasculitis has an associated autoimmune response that produces ANCAs that induce distinct pathologic lesions. Pauci-immune necrotizing and crescentic GN is a frequent component of ANCA vasculitis. ANCA vasculitis is associated with ANCA specific for myeloperoxidase (MPO-ANCA) or proteinase 3 (PR3-ANCA). A diagnosis of ANCA vasculitis should always specify the serotype as MPO-ANCA positive, PR3-ANCA positive, or ANCA-negative. To fully characterize a patient, the serotype also should be accompanied by the clinicopathologic variant if this can be determined: microscopic polyangiitis, granulomatosis with polyangiitis (Wegener), eosinophilic granulomatosis with polyangiitis (Churg–Strauss), or renal-limited vasculitis. ANCA vasculitis is most prevalent in individuals >50 years old. There are racial/ethnic and geographic influences on the prevalence, serotype frequencies, and clinicopathologic phenotypes. There is clinical, *in vitro*, and animal model evidence that ANCAs cause disease by activating neutrophils to attack small vessels. Immunomodulatory and immunosuppressive therapies are used to induce remission, maintain remission, and treat relapses. Over recent years, there have been major advances in optimizing treatment by minimizing toxic therapy and utilizing more targeted therapy.

Clin J Am Soc Nephrol 12: 1680–1691, 2017. doi: https://doi.org/10.2215/CJN.02500317

Department of Pathology and Laboratory Medicine, Department of Medicine, and Kidney Center, School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina

Correspondence: Dr. J. Charles Jennette, Kenneth M. Brinkhous

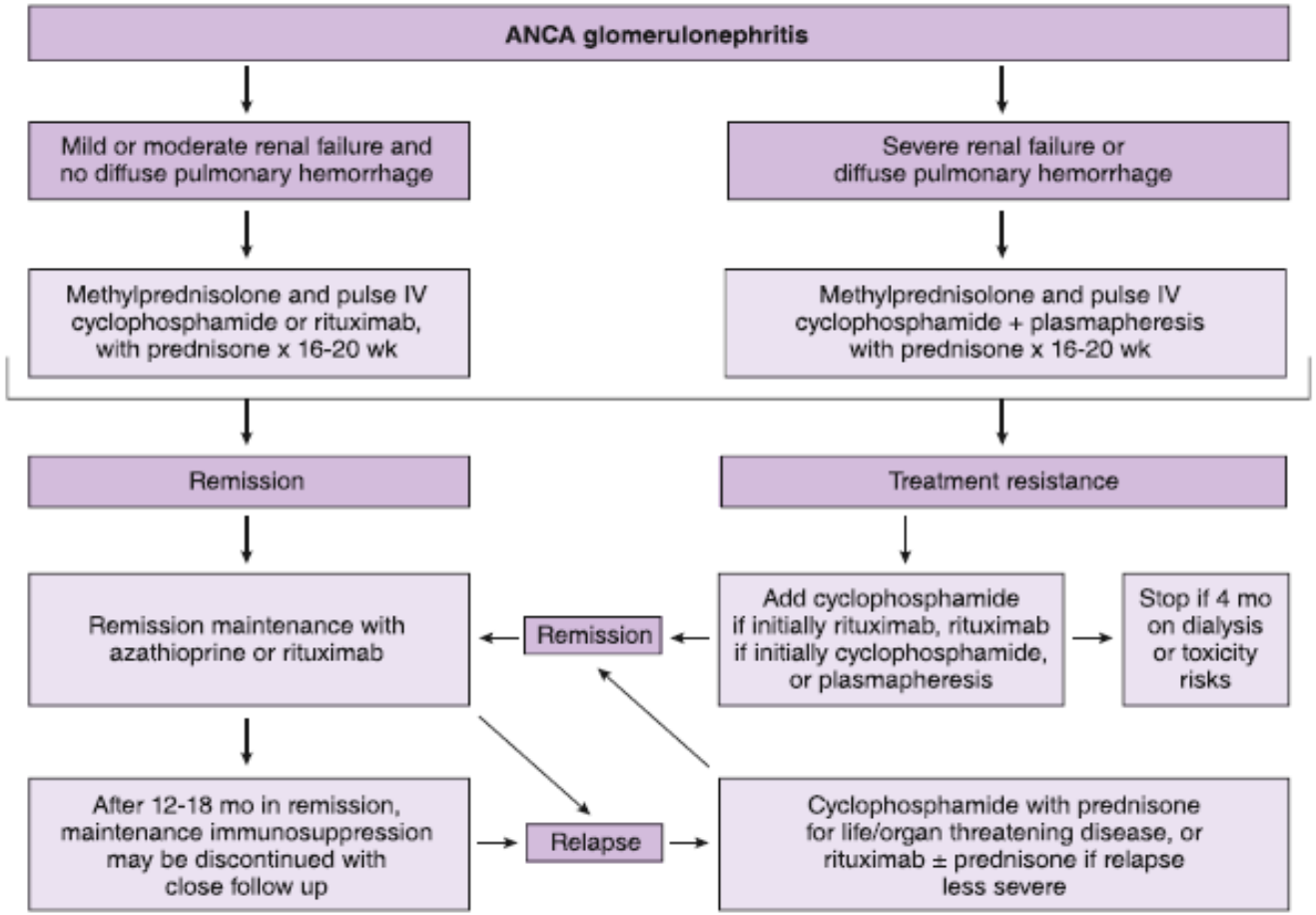


Figure 5. | ANCA vasculitis treatments algorithm in accord with current practice at the University of North Carolina Kidney Center. IV, intravenous.