

En Zor Olgum

Doç Dr Nefise Öztoprak

Antalya Eğitim ve Araştırma Hastanesi
Enfeksiyon Hastalıkları ve Klinik
Mikrobiyoloji Kliniği

Her Şey Bir Sonbahar Günü Başlıyor...



- **25 yaşında erkek hasta**
- **3 yaşından beri tekrar eden oral kandidiyazis ve tinea versicolor** dışında bir şikayeti yok
- **3 Ekim 2013'te** 15-20 gündür devam eden **baş ağrısı, kusma, donuk bakış** şikayetleri ve orofaringeal kandidiyazis bulgusu ile **Nöroloji kliniğine** yatırılıyor
- 1 haftadır tonsillit nedeniyle AMC tb kullanımı var

- **11/10/2013 (Enfeksiyon HKM Kliniğine Devir)**
- **EEG:** Sol temporal ve arka kafa bölgelerinde izlenen teta yavaşlaması ve keskin karakterli yavaş dalgalar
- **Kranial MRG:** Granülomatöz meningoensefalit ile uyumlu bulgular (+)
- **BOS:** 150 lenfosit/mm³, protein 116mg/dl,
glukoz 31/100 mg/dl
BOS *Brucella* TA negatif,
BOS VDRL,RPR negatif
BOS AARB negatif
- **Seftriakson, Vankomisin ve Anti-tbc (4'lü Tedavi)**

14/10/13

- **BOS kültürü: *Candida albicans***
- **BOS TBC PCR: negatif**
- **Tedaviye Flukonazol 1x800 mg İV eklendi**
- **EKO'da vejetasyon izlenmedi**

Fungal SSS Enfeksiyonları

Table II. Common fungi and spectra of CNS infections caused by them.

Genus	Incidence	Predilection for CNS	Setting	Clinicopathological manifestations of CNS disease		
				Meningitis	Abscess	Infarct
<i>Candida</i>	Common	+	Neurosurgery Neutropenia Systemic candidiasis IV drug use	+++	++	+
<i>Aspergillus</i>	Occasional	++	Neutropenia Invasive sinusitis HIV infection IV drug abuse	+	+++	++++
<i>Zygomycetes*</i>	Occasional	++	Diabetes Neutropenia	+	+	++++
<i>Histoplasma</i>	Occasional	+	HIV infection Steroid use	+	+	+
<i>Blastomyces</i>	Occasional	+	Normal host	+	+	—
<i>Cryptococcus</i>	Common	++++	HIV infection Steroid use Normal host†	++++	+	+
<i>Coccidioides</i>	Common	+++	Normal host HIV infection	++++	+	+

Table III. Clinical and radiographic presentations of neurocandidiasis.

Clinical and radiographic features

Cerebral microabscesses

Diffuse encephalopathy

Cerebral CT scan and lumbar puncture not diagnostic

Diagnosis is usually postmortem

Meningitis

Subacute onset with fever and headache

Cerebral CT scan could show hydrocephalus

Culture of CSF often gives the diagnosis

Cerebral macroabscesses

Less frequent

Focal neurological signs and seizures

Diagnosis based on neuroimaging studies and biopsy

Vascular complications

Cerebral infarction

Mycotic aneurysms

Subarachnoid haemorrhage

Up to Date- Tedavi Önerileri

Treatment of *Candida* infections of the central nervous system in adults

Primary

A lipid formulation of amphotericin B 3 to 5 mg/kg IV daily with or without flucytosine 25 mg/kg orally four times daily for several weeks, followed by fluconazole 400 to 800 mg (6 to 12 mg/kg) orally* daily

Alternative

Fluconazole 400 to 800 mg (6 to 12 mg/kg) orally* daily for patients unable to tolerate a lipid formulation of amphotericin B

Comments

Treat until all signs and symptoms, cerebrospinal fluid abnormalities, and radiographic abnormalities have resolved. Removal of intraventricular devices is recommended.

Fungal Infections of the CNS

Treatment Strategies for the Immunocompromised Patient

Katharine E. Black and Lindsey R. Baden

Table I. Overview of fungal infections of the CNS^a

Pathogen	Epidemiological features	Typical characteristics	Treatment
<i>Candida</i>	AIDS, haematological malignancy, organ transplant	Subacute meningitis. CSF shows low glucose, protein-positive, culture-positive, possibly mannan-positive	IV amphotericin B ^b ± oral flucytosine ^c × 2–4wk; then oral fluconazole 800 mg/day ^d
	Candidiasis from other sources	Micro-abscesses typically with sterile CSF, <3mm ring-enhancing lesions on brain MRI	IV amphotericin B ^b ± oral flucytosine ^c × 2–4wk; then oral fluconazole 800 mg/day ^d Possibly posaconazole
<i>Cryptococcus</i>	HIV/AIDS	Meningoencephalitis. CSF normal, elevated ICP, serum positive for cryptococcal antigen	IV amphotericin B ^b ± oral flucytosine ^c × 2wk, then oral fluconazole 400 mg/day × 8wk Typically lifelong oral fluconazole 200 mg/day
	Non-HIV: lymphoma, high-dose corticosteroids	Meningoencephalitis. CSF lymphocyte leucocytosis and positive for cryptococcal antigen, serum may or may not be positive for cryptococcal antigen	IV amphotericin B ^b 0.7–1 mg/kg/day + oral flucytosine ^c to clear CSF (usually 2–4wk) Typically oral fluconazole 400 mg/day × 8–10wk; 200 mg/day for 6–12mo

Drug	Pharmacokinetics	CSF concentrations
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Azoles

Fluconazole (Diflucan®, Pfizer, Inc.) Generic	11–13% protein bound 80% unchanged drug excreted in urine, 11% metabolites in urine	CSF 50–90% of serum concentrations
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Itraconazole ^a (Sporanox®, Janssen-Cilag)	99.8% protein bound Metabolised by CYP3A4; renal excretion 40%, faecal excretion 3–18%	Negligible; some meningeal penetration
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Voriconazole (Vfend®, Pfizer, Inc.)	58% protein bound Predominantly hepatic elimination (<2% renal); metabolised by CYP3A4, CYP2C9, CYP2C19	CSF concentrations 42–67% of serum concentrations (data from one patient)
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Posaconazole (Noxafil®, Schering Plough)	98–99% protein bound, Inhibitor of CYP3A4. Undergoes glucuronidation hepatic metabolism Excretion 14% renal and 77% faecal Food increases oral absorption	Data not available
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Drug	Pharmacokinetics	CSF concentrations
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Polyenes

Amphotericin B deoxycholate (conventional) [Fungizone®, Bristol Meyers Squibb]	>90% protein binding 40% renally excreted; not dialysable	CSF concentration seldom over 2.5% of serum concentration
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Liposomal amphotericin B (AmBisome®, Astellas Pharma, Inc./ Gilead Sciences, Inc.)	Up to 30% renal excretion Elimination half-life range 7–153h ^b	Data not available
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Amphotericin B lipid complex (ABLC) [Abelcet®, Enzon Pharmaceuticals, Inc.]	Approximately 1% renal excretion Elimination half-life approximately 170h ^b	Data not available
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Amphotericin B cholesteryl sulfate complex (Amphotec®)	Not dialysable Elimination half-life 28–29h	Data not available
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CASE REPORT

Simultaneous cryptococcal and tuberculous meningitis in a patient with systemic lupus erythematosus

Bilgul Mete^{a,*}, Nese Saltoglu^a, Ersin Vanli^a, Cigdem Ozkara^b,
Ferhat Arslan^a, Ali Mert^a, Resat Ozaras^a, Fehmi Tabak^a, Recep Ozturk^a

Simultaneous central nervous system (CNS) infection with *Cryptococcus* and tuberculosis (TB) is very rare. Despite improved therapeutic options, treatment of CNS cryptococcosis is still difficult and needs invasive treatment modalities, such as intrathecal or intraventricular amphotericin B, in refractory cases. We describe a patient with systemic lupus erythematosus diagnosed with simultaneous cryptococcal and TB meningitis who had a poor response to intravenous liposomal amphotericin B and fluconazole, but was successfully treated with intraventricular amphotericin B, in addition to anti-TB therapy.

Lipozomal Amp B intratekal yoldan 1mg/gün

72 saatte bir- üç doz

23/10/13 (TT 12, Fluk 9. günü)

- **BOS: 200 lenfosit/mm³ , 180 eritrosit /mm³
protein 73mg/dl , glukoz 33/150 mg/dl**
- **BOS AARB negatif**
- **BOS kültürü steril**

- **Lipozomal Amfoterisin B 5 mg/kg/gün (500 mg)
eklendi**

- **Beyin MRG:** 09.10.2013 tarihli MR tetkikine göre tentorial kalınlaşma ve sinyal artışında **minimal regresyon**;
postkontrast serilerde subependimal milimetrik **nodüler** sinyal intensite artışı
3. ventrikül sol lateral kesiminde subependimal nodüler sinyal intensite artışında **totale yakın regresyon**

25/10/13

Konse

- İmmunoloji- Nöroloji- Radyoloji-KBB Klinikleri
 - Mukokutanöz Kandidiazis ??
 - Alerji açısından PPD yapılması
 - Quantiferon testi
 - Kandidin deri testi
 - Lenfosit alt gruplarının çalışılması
 - Kranial sinir tutulumu açısından işitme testi yapılması
 - **Anti-Tbc ve anti-fungal tedavinin devamına;
anti-bakteriyel tedavinin (14.gün) kesilmesine
karar verildi**

- **PPD 10 mm**
- **Quantiferon negatif**
- **İmmunglobulinler (IgM-G-E-A) normal**
- **Lenfosit alt grupları**
CD^{3,4,8,19, 16-56} normal
- **Kandidin deri testi negatif**
- **İşitme Testi: Bilateral SIN tipi hafif işitme kaybı**

31/10/2013

(TT 18, Fluk 15, Amp-B 8.gün)

- **BOS** 80 lenfosit/mm³ , 2x10 eritrosit/mm³,
protein 73mg/dl, glukoz 36 /128 mg/dl
- BOS kültürü: steril

4/11/2013
(T 22,Fluk 19, AmpB 12. gün)

- Kreatinin değerlerinde yükselme başladı
- Nefroloji kliniğinin önerisiyle
Ürikoliz 1/2tb gün aşırı başlandı

12/11/2013

(TT- Anti TB 30, Fluk 27, AmpB 20. gün)

- **Beyin MRG**

III. ve her iki lateral ventrikül ileri derecede geniş

Özellikle bifrontal bölgede periventriküler beyaz cevherde hipodens BOS rezorbsiyonu ile uyumlu görünümüler izlenmekte

22/10 tarihli Beyin MR a göre önceki mevcut lezyonlarda **minimal gerileme** mevcut

- BOS: **120 lenfosit/mm³** 100 eritrosit /mm³, BOS **protein 87 mg/dl** , BOS glukoz 35/92 mg/dl
- BOS kültürü steril
- Nefrotoksisite ve yanıtsızlık nedeniyle Lipozomal Amfoterisin-B kesildi
- TBC kültürü negatif
- **Anti-tbc tedavi kesildi**
- Flukonazol dozu **2x600 mg/güne** çıkarıldı

29/11/2013

(TT 46.günü- YD Flukonazol 16. günü)

- **BOS 50 lenfosit/mm³ , protein 101mg/dl, glukoz 45/123 mg/dl**
- **BOS kültürü steril**
- **Hastanın takiplerinde genel durumu iyi vitalleri stabil, renal fonksiyonları normal**
- **Flukonazol kesildi, vorikonazol 2x400mg başlandı**

6/12/2013 (TT 54, Vori 8. günü)

- Göz dibinde PAPİL ÖDEM saptandı
- Hastaya Mannitol %20 lik 100 ml 4x1 başlandı (4 gün)
- Beyin MR belirgin farklılık yok
- Damar yolu problemi nedeniyle Vorikonazol tb. geçildi

10/12/2013 (TT 58, Vori 12. günü)

- BOS **70 lenfosit/mm³**, protein **74mg/dl**, glukoz 45/93
- BOS kültür steril
- BEYİN MRG: eski tetkiklerine göre **minimal gerileme**

13/12 /2013 (TT 61, Vori 15. gün)

- **VORİKONAZOL 2x400mg tb ile taburcu edildi.....**

25/12/13 (TT 73. günü, Vorikonazol 27. günü)

- Beyin MRG: hidrosefalide ilerleme yok
- BOS 45 lenfosit/mm³ protein 70mg/dl

08/01/14

(TT 90.günü Vorikonazol 40.günü)

- Eskiye göre ödemde azalma, sağda belirgin olmak üzere papillalarda nazal sınırlarda siliklik
- BOS **70 lenfosit/mm³, protein 79mg/dl, glukoz N**
- BOS kültürü: ***C.albicans* !!!**

12.01.2014

(TT 99; Vorikonazol 49. günü)

- **Vorikonazol STOP**
- **Amp B 1x300 mg IV + iT 1mg (haftada 2) başlandı**

***Candida* Meningitis Post Gliadel Wafer Placement Successfully Treated with Intrathecal and Intravenous Amphotericin B**

Jorie A Glick, Robert S Graham, and Stacy A Voils

CASE SUMMARY: A 33-year-old white female with a history of recurrent oligodendroglioma was admitted to the neuroscience intensive care unit with acute mental status changes. Computed tomography of the head demonstrated a cystic dilation of the right frontoparietal tumor resection cavity with Gliadel wafers in place and the presence of a large fluid collection. The cavity was debried surgically and a ventriculostomy catheter was left in place. Cerebrospinal fluid (CSF) cultures were positive for *Candida albicans* and methicillin-resistant coagulase-negative *Staphylococcus* spp. Antiinfective therapy with intrathecal and intravenous amphotericin B as well as flucytosine and vancomycin was started. The patient had subsequent improvement in clinical manifestations, resolution of CSF leukocytosis, and mycologic cure.

CONCLUSIONS: This case demonstrates successful treatment of *Candida* meningitis post Gliadel wafer placement with the combination of intrathecal and intravenous amphotericin B. This treatment modality may provide an effective therapeutic option for other patients with *Candida* meningitis, especially those unresponsive to intravenous therapy.

Candida Meningitis Post Gliadel Wafer Placement Successfully Treated with Intrathecal and Intravenous Amphotericin B

Jorie A Glick, Robert S Graham, and Stacy A Voils

Hospital Day	Culture	Gram Stain	Preliminary Report	Final Report	Antiinfective Regimen
1	CSF	No microorganisms	Coagulase-negative <i>Staphylococcus</i> spp., <i>Candida albicans</i>	Coagulase-negative <i>Staphylococcus</i> spp., <i>C. albicans</i>	None
3	CSF	Few yeast	<i>C. albicans</i>	<i>C. albicans</i>	Vancomycin, fluconazole
4	CSF	Rare yeast	<i>C. albicans</i>	<i>C. albicans</i>	Vancomycin, intravenous amphotericin B, flucytosine
	Head tissue	Rare gram-positive cocci in pairs	<i>C. albicans</i>	<i>C. albicans</i>	
	Deep head wound (surgical cavity)	No microorganisms	Few mixed aerobic bacteria	Few mixed aerobic bacteria, <i>C. albicans</i>	
6	CSF	No microorganisms, few PMNs, rare RBCs	No growth	No growth	Vancomycin, intravenous amphotericin B, intrathecal amphotericin B, flucytosine
7	CSF	No microorganisms	No growth	<i>Propionibacterium</i> (broth only)	Vancomycin, intravenous amphotericin B, intrathecal amphotericin B, flucytosine
8 ^a	CSF	Few yeast	No growth	No growth	Vancomycin, intravenous amphotericin B, intrathecal amphotericin B, flucytosine

17.01.2014 (TT 104.; İV-İT AMP B 5. günü)

- Özellikle sabaha karşı olan kusma şikayetleri başladı, metpamid ile rahatladı
- Nörolojik muayene: N, beyin ödemi tespit edilmedi. Kusmalar **hidrosefalide artışa** bağlandı
- BOS: **55 lenfosit/mm³, protein 77 mg/dl**
- BOS kültürü: ***C.albicans* !!!**

- **Beyin MR:** Hidrosefalide progresyon ve interstisyel ödemde artış. Pons sol anterior lateral kesiminde yeni gelişen fokal pia-araknoidal sinyal intensite artışı, **akuaduktusta stenoz**, distal akuaduktus serebri ve suprasellar sistern düzeyinde görünüm özelliklerinde stabilizasyon saptanan **nodüler oluşumlar...**

20.01.14

(TT 107, İV-İT AmpB 8. günü)

- Ajitasyon ve uyku bozukluğu (+)
- Psikiyatri Seraquel 25 mg 1x1 başladı

• **Servikal, Torakal ve Lumbal MR:**

4.ventrikül çıkış düzeyinden C3 vertebra seviyesine kadar posteriorda meninkste geniş plak tarzında ve C6 vertebra düzeyinde ise fokal milimetrik nodüller

24.01.2014 (TT 111.; İV-İT Amp B 12. günü)

- **BOS: 180 lenfosit/mm³, protein 81 mg/dl**
- **Yürüme bozukluğu ve bilinçte küntleşme !!**

II. Konsey

- **İmmünoloji, Nöroloji, Beyin Cerrahi, KBB, Radyoloji**
- Hidrosefalide artış olduğu ve yürüme bozukluğunun buna bağlı olabileceği
- Hidrosefali için **EVD ve Ventriküloperitoneal şant takılması** ancak operasyon öncesinde BOS kültür sterilliğinin sağlanması
- Mukokutanöz kandidiyazis yüksek olasılık nedeniyle **haftada 3 gün 5×10^6 Ü G-CSF verilmesi;**
- Mevcut tedaviye **Flukonazol 2x600 mg** eklenmesine karar verildi

Therapy should be continued for at least 4 weeks after full resolution of all signs and symptoms of the disease. In patients with meningitis, follow-up CSF studies should be conducted to check for normalisation of pleocytosis. Micro-abscesses can be followed-up until resolution using MRI. The Infectious Diseases Society of America (IDSA) recommends that neutropenic patients who develop candidaemia receive a cytokine such as granulocyte colony-stimulating factor or granulocyte-monocyte colony-stimulating factor to enhance neutrophil recovery.

28.01.14

(TT 115; İM-İT AmpB 16; Fluk 2, G-CSF 2. günü)

- **Ağız içinde beyaz plaklar**
- Yaymada maya hücreleri (+)
- **Orofarengeal kandidiyazis**
- Mevcut tedavisine **Caspofungin** eklendi

Favorable Outcome of Neonatal Cerebrospinal Fluid Shunt-Associated *Candida* Meningitis with Caspofungin

Jop Jans, Roger J. M. Brüggemann, V. Christmann, Paul E. Verweij and Adilia Warris
Antimicrob. Agents Chemother. 2013, 57(5):2391. DOI:
10.1128/AAC.02085-12.
Published Ahead of Print 25 February 2013.

Invasive *Candida* infections associated with medical devices are very difficult to cure without device removal. We present a case of neonatal cerebrospinal fluid shunt-associated *Candida* meningitis, in which removal of the device was precluded, that was successfully treated with caspofungin. Pharmacokinetic assessment of caspofungin concentrations in cerebrospinal fluid showed that exposure was adequate in the presence of a high systemic exposure. In complex cases of neonatal *Candida* infections involving medical devices, the addition of caspofungin might be beneficial.

Successful Treatment of Azole-resistant Chronic Mucocutaneous Candidosis with Caspofungin

Melany Jayasinghe, Sibylle Schmidt, Birgit Walker, Martin Röcken and Martin Schaller

Department of Dermatology, University of Tübingen, Liebermeisterstrasse 25, DE-72076 Tübingen, Germany.

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DOI: 10.2340/00015555-0165

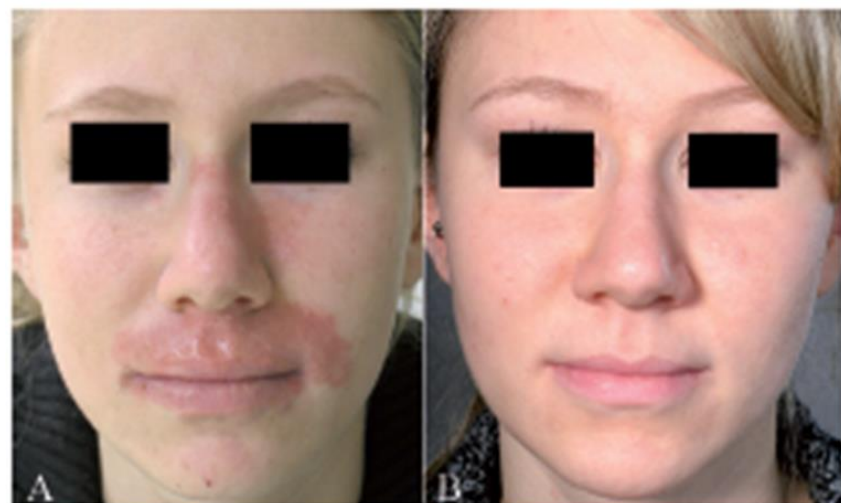


Fig. 1. (A) Perioral/paranasal erythematous and erosive lesions of the face before therapy. (B) Normal appearance of the face during caspofungin therapy.



Fig. 2. (A) Fingernails showing brown discoloration, swelling and dystrophy. Periungual erythema. (B) Normal appearance of the distal nail plate after 6 months of caspofungin treatment.

07.02.14

(TT 125; İV-İT AmpB 26; Fluk 12, Caspo 11. günü)

- Hidrosefali için EVD takıldı
- **BOS-EVD: 10 lenfosit/mm³ ve 90 eritrosit/mm³
protein 25 mg/dl glukoz N**
- Hastanın burun kanaması ve sol kulakta çınlama nedeniyle Betaserc tb 2x1 ve İliadin sprej 3x2 önerildi

12/02/14

(TT 130, AmpB 31, Fluk 17, Casp 16, G-CSF 17. gün)

- **BOS-EVD** 25 lenfosit/mm³ ve bol eritrosit protein 39 mg/dl; glukoz 58/103 mg/dl
- **BOS-LP** 100 lenfosit/mm³ ve bol eritrosit protein 109 mg/dl; glukoz 38/103 mg/dl

21/02/14

- BOS: 5 lenfosit/mm³ Protein 39 mg/dl

ilk kez biraz rahat bir uyku.....



12 Gün Sonra.....

24/02/14

- TA: 180/110 mg
- 8-10 defa fıskırır tarzda kusması
- Dahiliye: Norvasc 10 mg 1x1 başladı
- Akşam 19.00 da 37.8 °C **ateş**

25/02/14

- Sabah 06.00 da 38.9°C **ateş**

25/02/14

(TT 143,AmpB 44, Fluk 30, Caspo 29. gün)

- **BOS EVD 350** lenfosit/mm³ ;protein 61 mg/dl;
glukoz 69/98 mg/dl
- Yaymada her sahada **Gram (+) koklar** görüldü
- Mevcut tedaviye **LİNEZOLİD** 2x600mg eklendi

- **Torakal MR:** T5 ve T7 düzeylerinde meninkslerde T5 düzeyindeki daha belirgin olan kontrastlanmalar mevcut
- Hastanın eski tetkiklerinde olmayan **torakal seviyede meninks tutulumu izlendi**

- **BOS kültürü: MRSE**
- **Beyin Cerrahisi tarafından EVD çekildi**
- **EVD katater ucu kültürü: MRSE**
- EVD çekilen yerden sızıntı şeklinde BOS kaçağı oldu sık pansuman değişimi ile takip önerildi
- BOS kaçağı devam ettiği için steplerle sütur atıldı

11/03/14

(TT 157, AmpB 58, Fluk 44, Casp 43, Lin 14, G-CSF 44. gün)

- **BOS:** 40 lenfosit/mm³, protein 42mg/dl
- Linezolid tedavisi 14 günde kesildi

1 hafta Sonra....

- BOS:150 lenfosit/mm³ protein: 120 mg/dl
- BOS kültür şişesinde sinyal !!
(yaymada **Gram pozitif kok** görüldü)
- LINEZOLİD 2x600mg tekrar başlandı
- BOS kültürü: **MRSE**

10.04.2014

**(TT 181, AmpB 95, Flu 82, Caspo 77, Lin 30,
G-CSF 81. gün)**

- **BOS:** 40 lenfosit/mm³, protein 78 mg/dl
- **Linezolid 4 haftaya tamamlandı ve kesildi**

17.04.2014 (Yatışının ~ 6. ayı)

(TT188, Amp B 102, Fluk 90, Casp 84, G-CSF 90. gün)

- **G-CSF, Caspofungin, İV ve İT AMP-B STOP**
- **Flukonazol 2x600 mg tb ile taburcu....**

2 hafta Sonra...

30.04.2014 (TT 201, Fluk 103. günü)

- **38.1 °C ateş**
- **BOS 330 lenfosit/mm³, protein 93 mg/dl**
- **BOS kültürü: MRSE**
- **Linezolid 2x600 mg tb başlandı**

09.05.2014 (TT 210, Fluk 112, Lin 9. günü)

- BOS 40 lenfosit/mm³, protein: 109 mg/dl,
- BOS kültürü: üreme yok

15.05.2014 (TT 216, Flu 118, Lin15. günü)

- BOS 15 lenfosit/mm³, protein: 95 mg/dl
- BOS kültürü üreme yok
- Flukonazol tedavisi **1x600 tb mg/gün**

Başvurusunun 9. Ayı

12.06.2014 (TT 247, Fluk 143, Lin 46. günü)

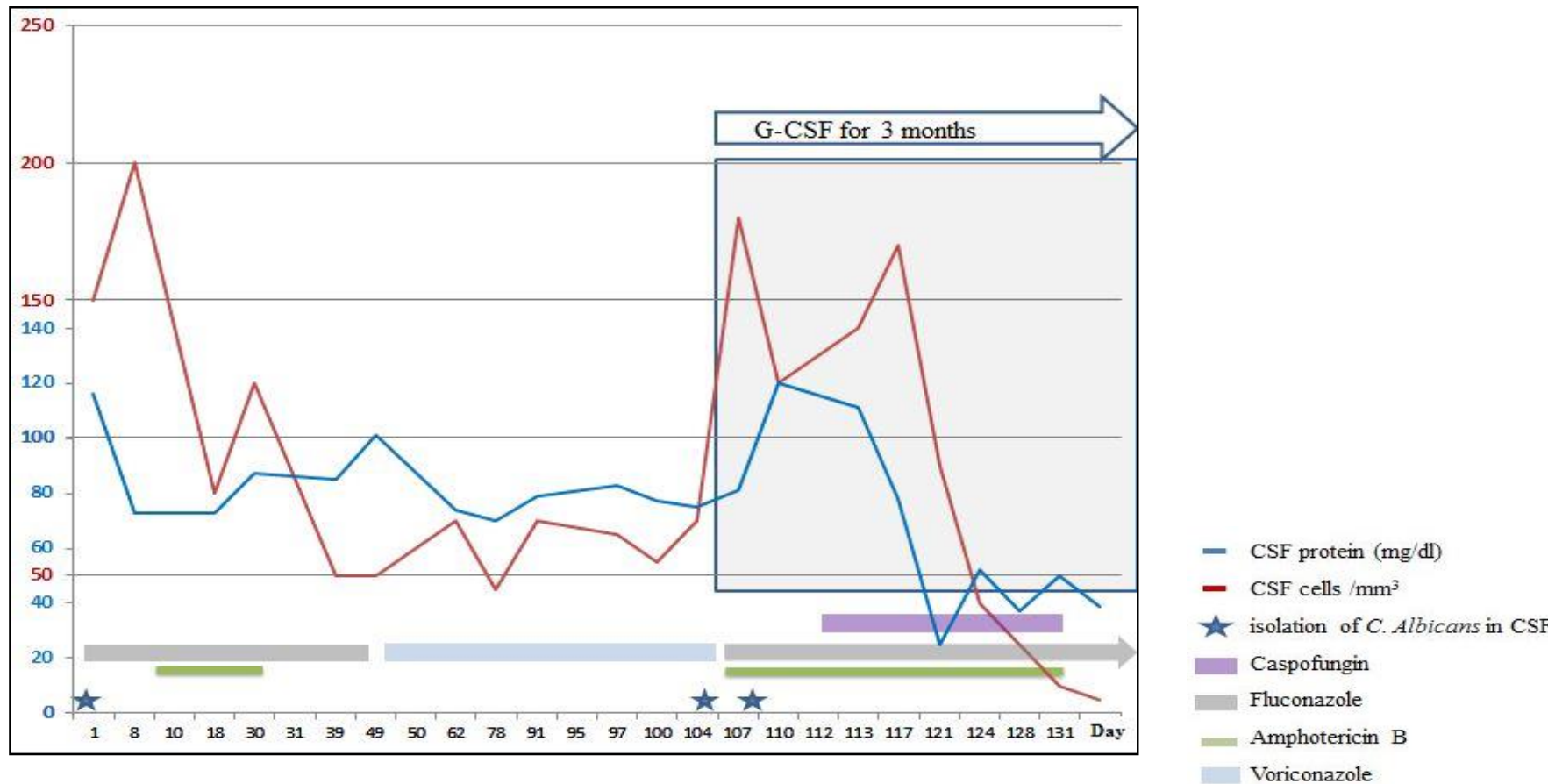
- **BOS : 5 lenfosit/mm³ protein: 69 mg/dl**
- **BOS kültürü: üreme yok**

Mutlu Son 😊

25.06.2014 (TT 258, Fluk 154. günü)

- **BOS 10 lenfosit/mm³ protein: 67 mg/dl**
- **BOS kültürü üreme yok**
- **Linezolid tedavisi 8 haftaya tamamlandı ve kesildi**
- **Flukonazol 1x400 mg tb'e geçildi.....**

Figure 2: CSF (cerebrospinal fluid) findings and treatment modalities of the patient

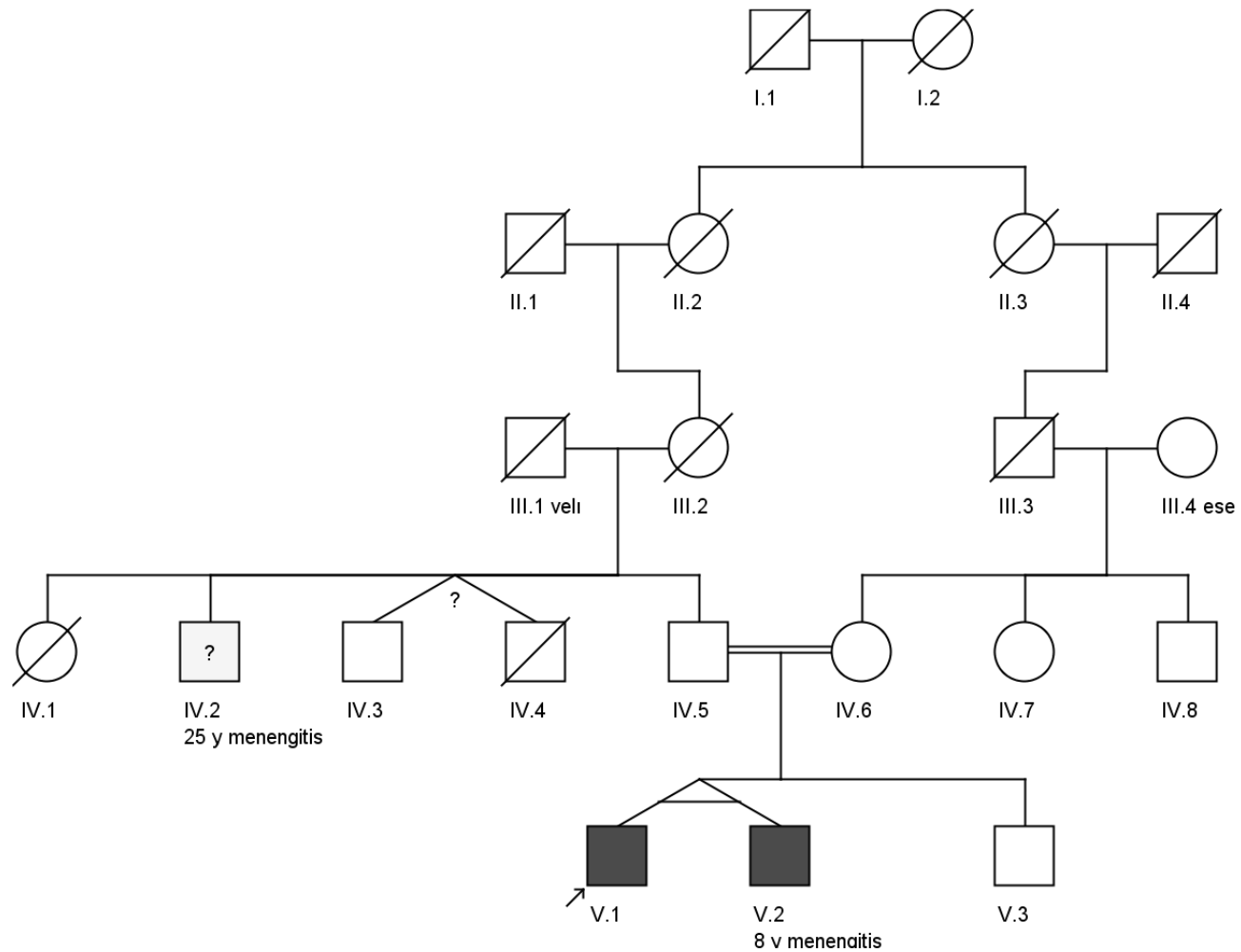


Y-axis shows both CSF protein per mg/dl and CSF cell count per mm³

X-axis shows days from the first admission

G-CSF, Granulocyte-macrophage colony-stimulating factor

Figure 1: Pedigree chart of patients



OLGUMUZDA

- **CARD9 mutasyonu (+)**
- **IL-17 ve IFN- γ eksikliği saptandı**
- **G-CSF tedavisiyle IL-17 ve IFN- γ üretiminde artış olduğu tespit edildi**

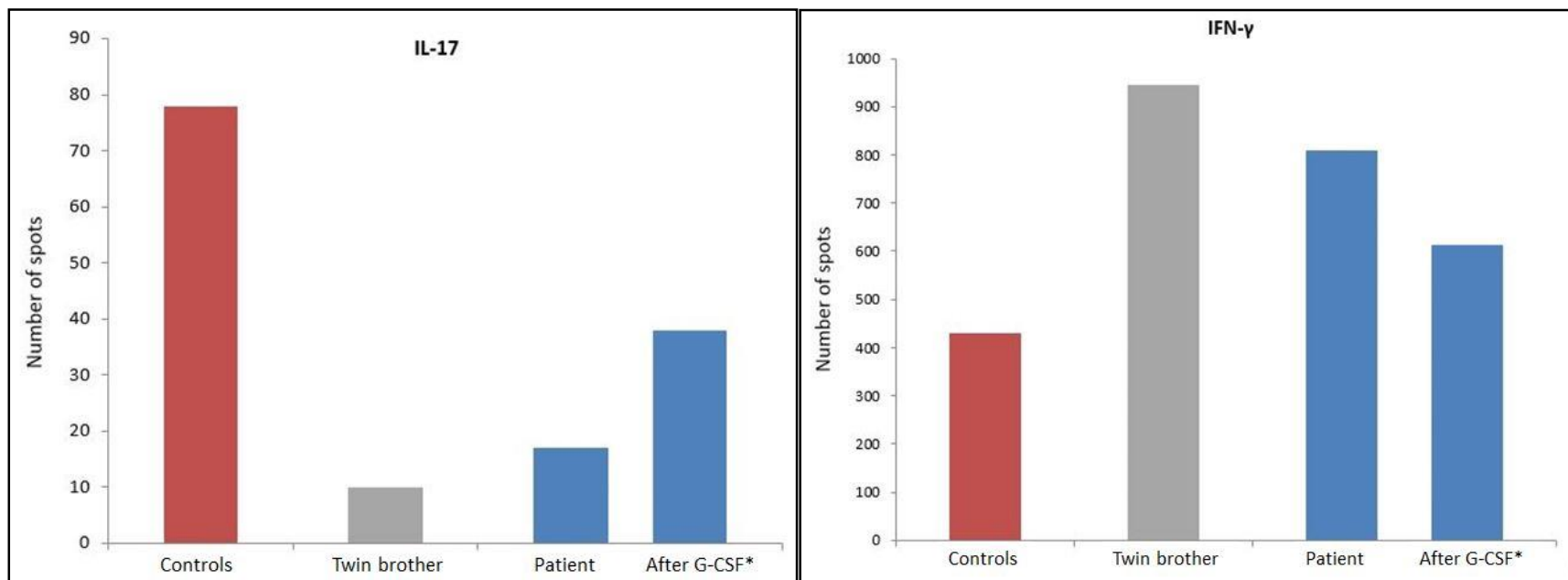


Figure 3. Enzyme-Linked ImmunoSpot (ELISPOT) test results in the patient and his twin brother; IL17 and IFN- γ levels before and after G-CSF treatment compared with healthy controls (n=2).

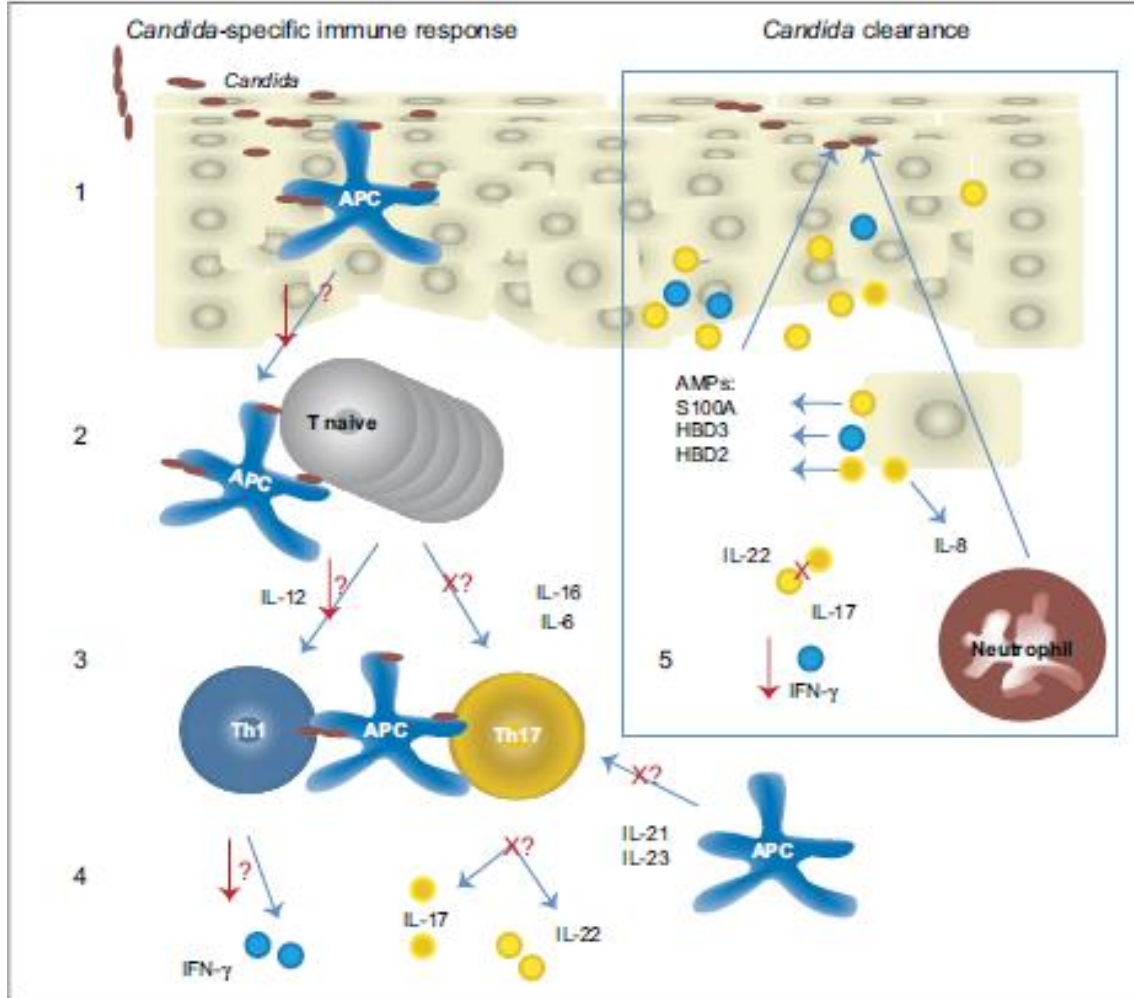
ELISPOT test was performed according to the manufacturer's instructions (GenID GmbH, Germany). Spots were counted using an automated plate reader, AID EliSpot (AID, Strassberg, Germany).

* After 2-months of G-CSF treatment

Literatürde CARD9 Mutasyonu

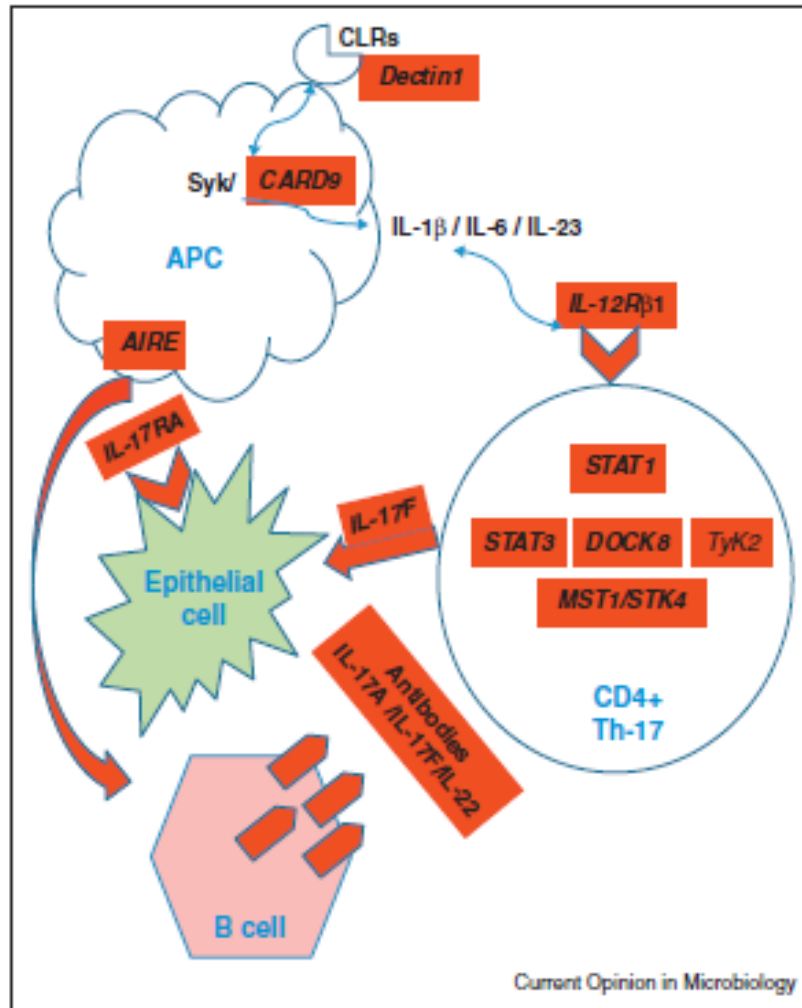
- İlk kez İranlı bir ailede tanımlanmış
(ağır ve tekrarlayıcı *Candida* meningoensefaliti)
Glocker E-O, Hennigs A, Nabavi M, et al. A homozygous CARD9 mutation in a family with susceptibility to fungal infections. *New Engl J Med*. 2009;361(18):1727-1735.
- Tekrarlayıcı *C. dublinensis* menenjitli olan bir kız
Drewniak A, Gazendam RP, Tool AT, et al. Invasive fungal infection and impaired neutrophil killing in human CARD9 deficiency. *Blood*. 2013;121(13):2385-2392.
- Tekrarlayan *C. albicans* menenjitli olan bir olgu ve GM-CSF tedavisi ile tam remisyon bildirilmiş
Gavino C, Cotter A, Lichtenstein D, et al. CARD9 Deficiency and Spontaneous Central Nervous System Candidiasis: Complete Clinical Remission With GM-CSF Therapy. *Clin Infect Dis : Off Publ Infectious Dis Soc Am*. 2014

Kronik Mukokutanöz Kandidiyazis



- Heterojen
- Persistan
- Genellikle deri, müköz membran ve tırnaklarda
- Non-invaziv kandida enfeksiyonlarıyla seyreden bir hastalık

Figure 1



Bu hastalarda

- **AIRE**
- **STAT-1**
- **Dectin-1**
- **IL-17RA**
- **IL-17F**
- **ACT1**

defekti tanımlanmış

Immune defects in mucocutaneous fungal immunity.

The image summarises currently known gene mutations and polymorphism affecting the Th-17 pathway thus predisposing to mucocutaneous fungal infections such as Chronic Mucocutaneous Candidiasis (CMC).

APC = antigen presenting cell; TLRs = Toll-like receptors; CLRs = C-type lectin receptors; IL = interleukin.

CARD9 Mutasyonu

- **CARD9 mutasyonu olan hastalarda ağır SSS enfeksiyonları meydana gelmektedir**
- **CARD9 yetmezliği non-opsonize candidalara seçici sitotoksik nötrofil yanıt oluşur**
- **SSS'de opsonin düzeyleri düşüktür**



İlginiz için

Teşekkürler.....