OLGU SUNUMU

D.E.Ü.T.F. GÖĞÜS HASTALIKLARI A.D.

Prof Dr Atila AKKOÇLU

OLGU

- 48 yaşında erkek ,
- Matbaa işinde çalışıyor.
- Romatoloji servisinde ankilozan spondilit tanısı ile tetkik ve tedavi ediliyor
- Öksürük, bazen kahverengi renkte balgam çıkarma,
- Göğüs Hastalıkları konsültasyonu isteniyor.

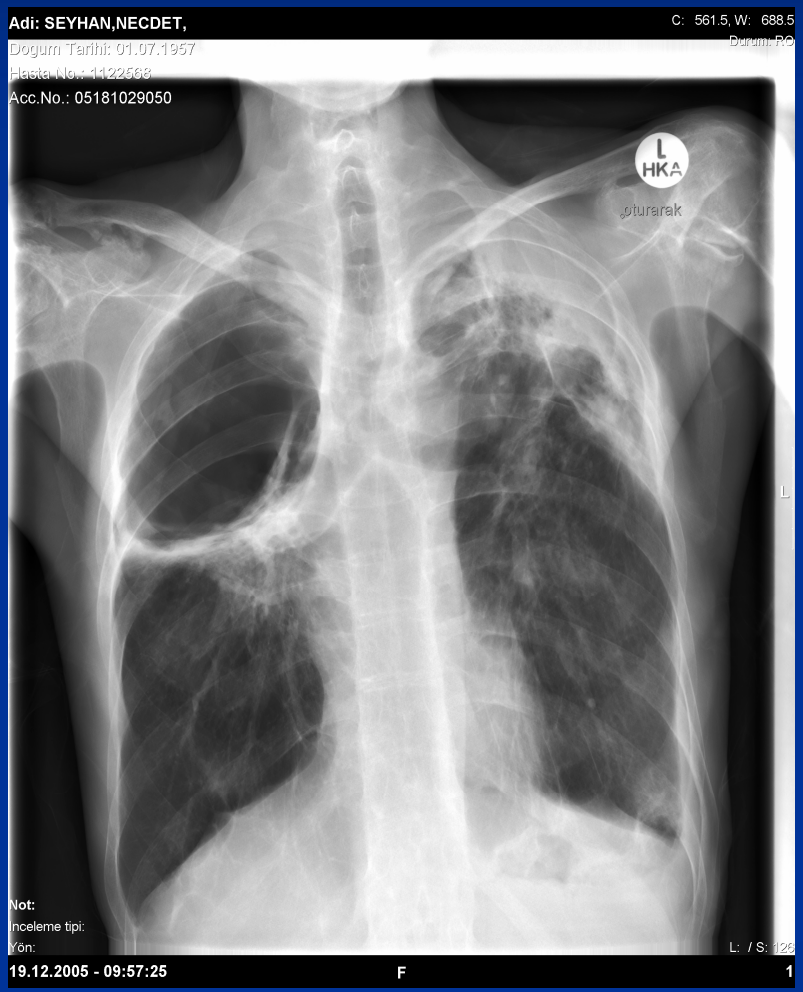
ÖYKÜ

- 30 yıldır ankilozan spondilit tanısı var,
- NSAİ ilaç dışında ilaç kullanım öyküsü yok,
- 25 yıl önce bilateral total kalça protezi operasyonu geçirmiş,
- 1,5 yıl önce 3 kez üveit atağı ve
- 10 yıl önce akciğer tüberkülozu tanısı ile 1 yıl süreli anti-Tbc tedavi görmüş,
- Sigara: 20 paket/yıl

FİZİK MUAYENE

- ✓ Kaşektik görünümde,
- ✓ Kifoskolyozu mevcut,
- ✓ Sağ akciğerde üst ve orta zonlarda solunum sesleri şiddeti azalmış, seyrek raller duyuluyor.

PA akciğer grafisi



- Sağ akc üst zonda kalın cidarlı kavite,içinde bant tarzında uzantılar,
- Sol üst zonda plevral kalınlaşma ve sekel bulguların eşlik ettiği non-homojen dansite
- Hemidiafragmalar düzleşmiş ve hiperaerasyon

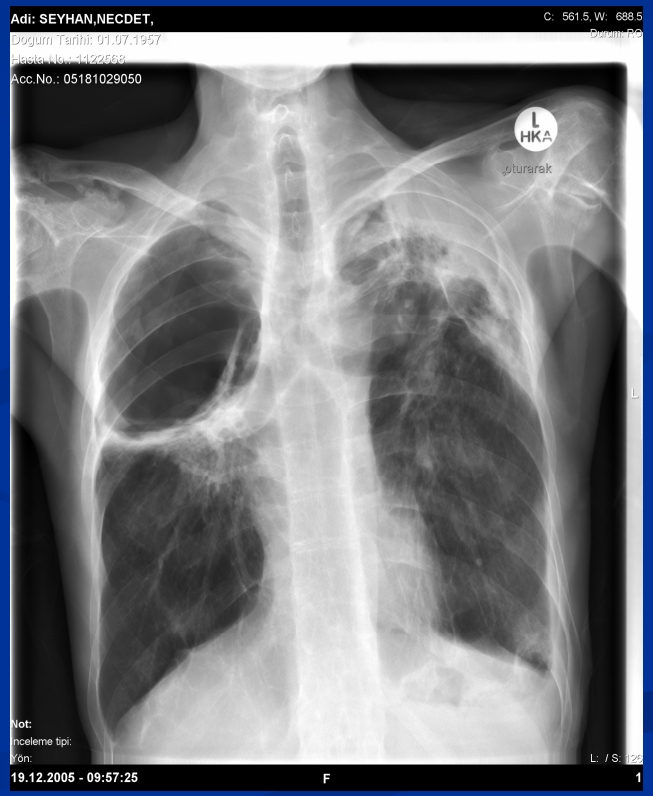
KİSTİK- KAVİTER HASTALIKLAR

- Abse
- Septik emboli
- Pnömotosel
- İnfeksiyonlar

Staf.Aureus, Psödomonas, Tbc, Mantar, anaerob , PCP

ÖN TANI

- Tüberküloz (Aktivitesi ?)
- Hava kisti+Pl. kalınlaşma
- Ank.Spondilit Akciğeri
- Geçirilmiş İnf.'a bağlı sekel değişiklikler (+Tm?)



İleri İnceleme İstermisiniz ?

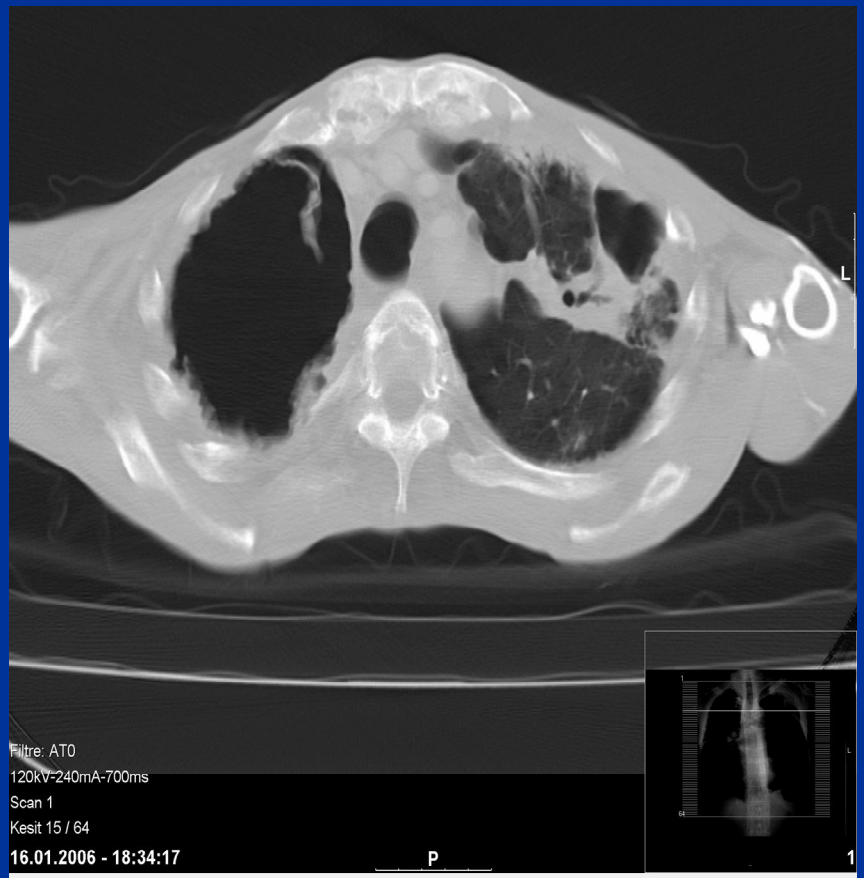
- Evet
- Hayır

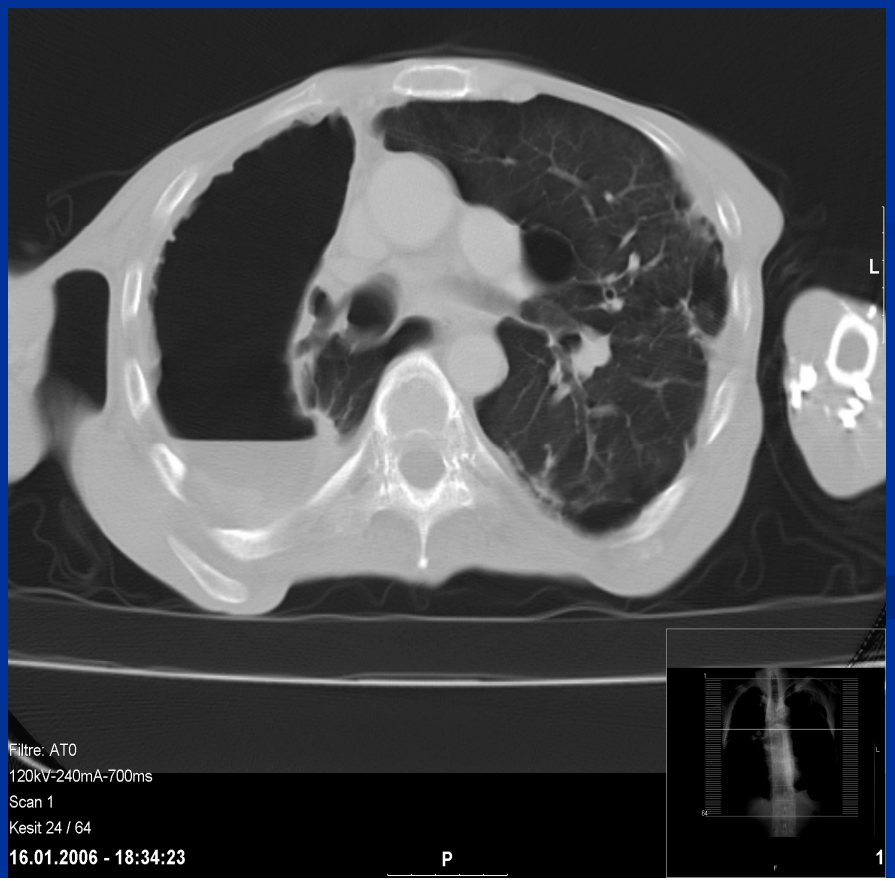
Evet,
Hangi tetkiki istersiniz ?

- Toraks BT (HRCT)
- Balgam tetkiki (ARB ve diğer, sitoloji..)
- FOB (BAL+ TBB..)
- Hepsi

TORAKS BT

Sağ lobun hemen tamamını kaplayan, içinde lif şeklinde uzantılar olan alt duvarı düzensiz ve kalın,sıvı seviyesi gösteren kavite, sol üst lob apikal kesimde plevral kalınlaşma ve sekel fibrotik parankimal değişiklikler, yaygın amfizematö değişiklikler



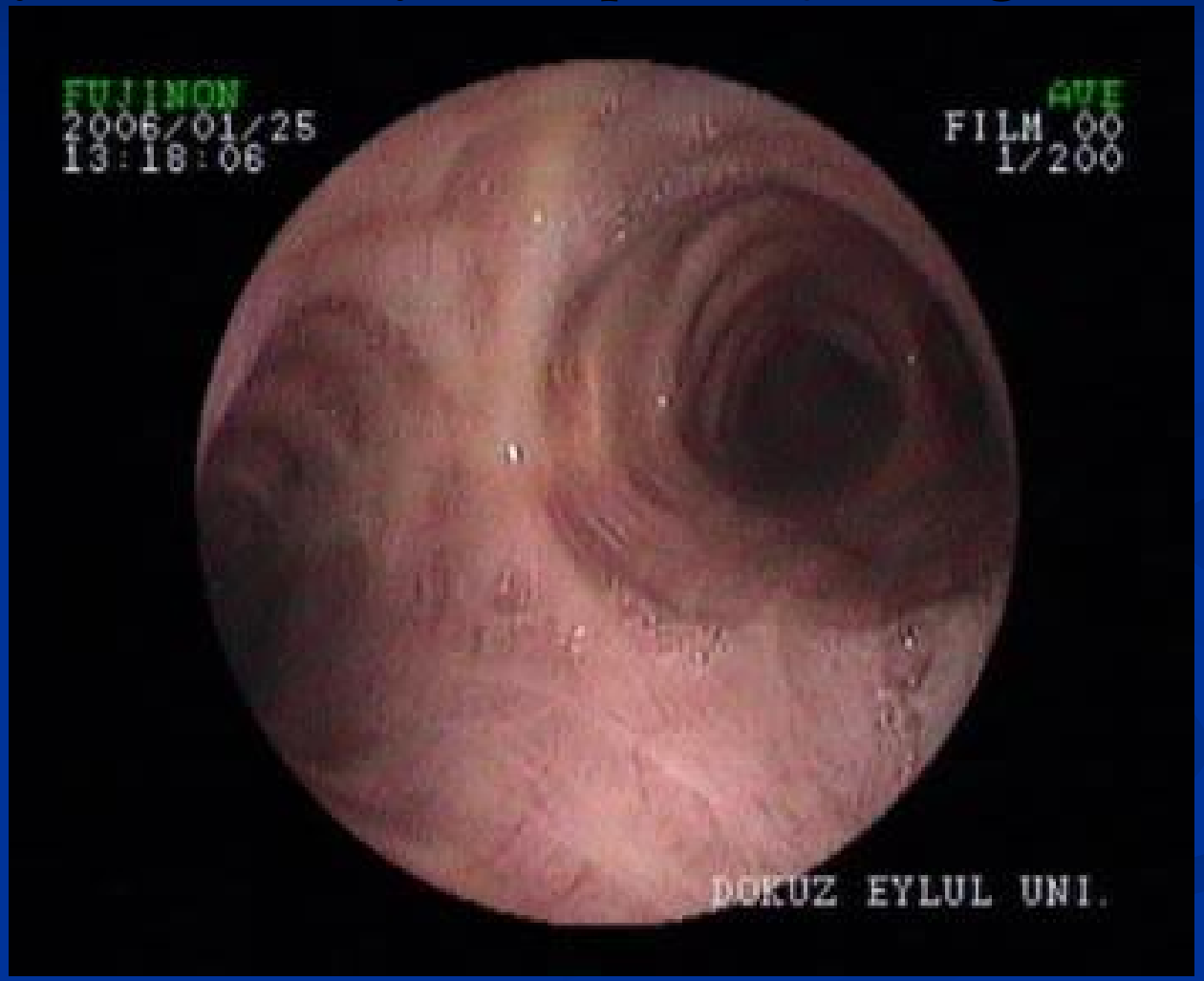


BALGAM İNCELEMESİ

- Balgam ARB: 3 kez negatif
- Balgam sitolojisi: 2 kez şiddetli akut inflamasyon bulguları
- Balgam mikolojik bakı-kültür: Mantar elemanı görülmedi, kültürde ***Aspergillus fumigatus*** üredi

FOB

Sağ akciğer üst lobda direkt anterior bronşa açılmış kavite ve kavite içinde yüzeyi düzensiz görünümde beyaz kitle ve yer yer nodüler lezyonlar , patlamış mısır görünümleri



FOB

- Bronş lavaj ARB: negatif
- Bronş lavaj mikolojik bakı: hifler görüldü.
- Bronş lavaj mikolojik kültür:

  10 koloni/ml ***Candida albicans* üredi

  1000 koloni/ml ***Aspergillus fumigatus* üredi

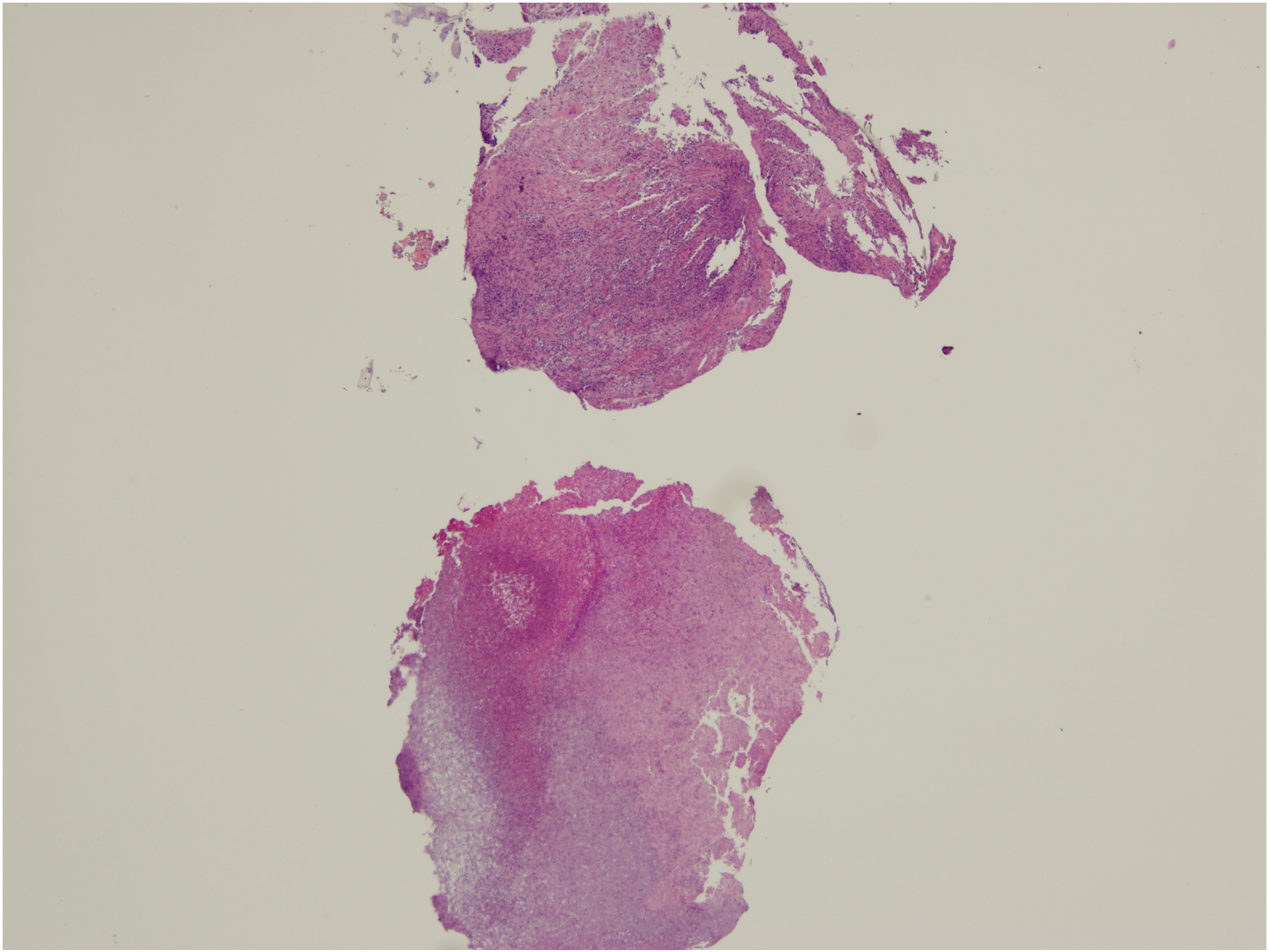
FOB

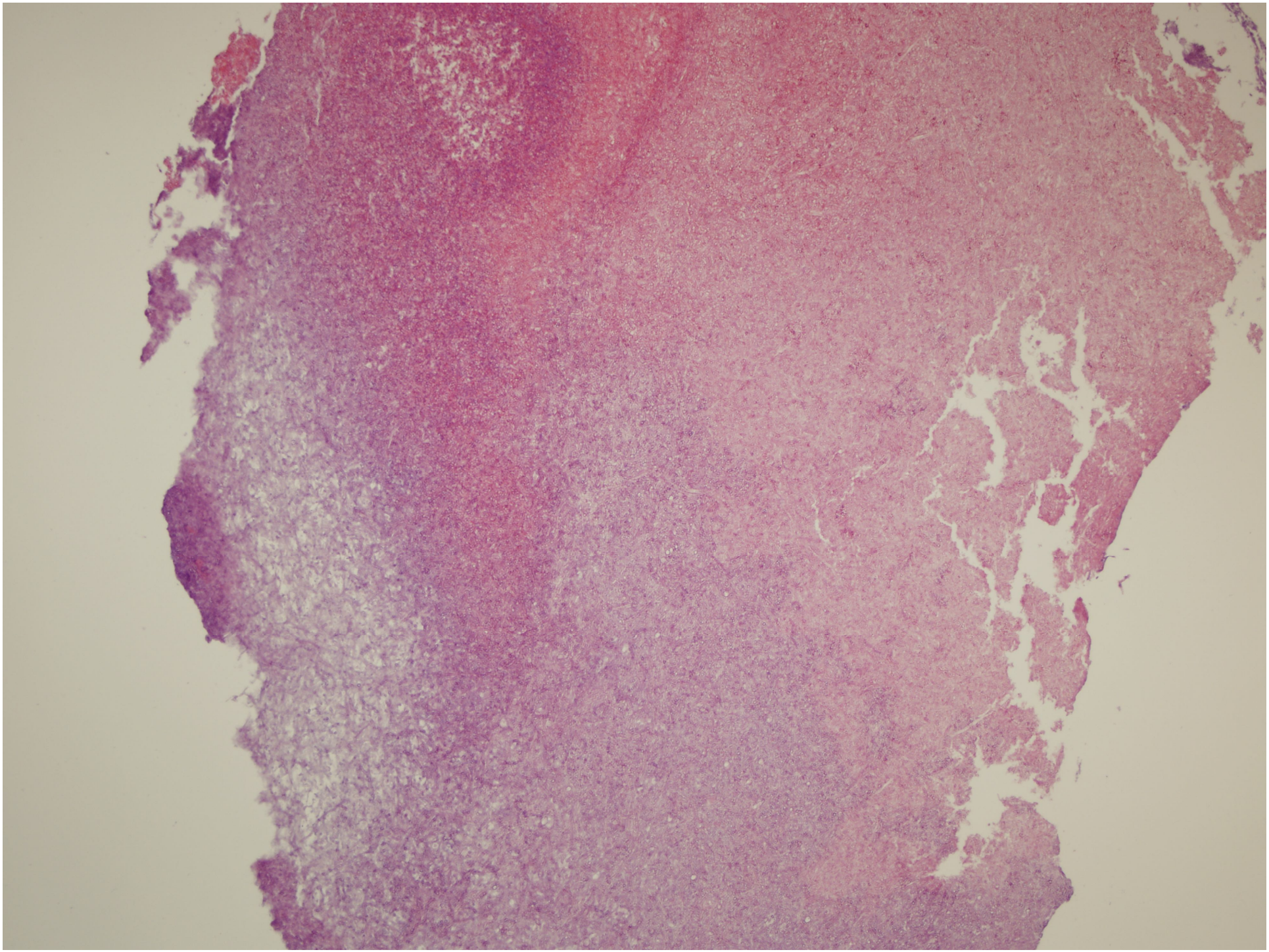
- Bronş lavaj sitolojisi: yoğun şekilde nötrofilleri içeren eksüda, arada seyrek bronş mukoza epitel hücreleri,
- Bronkoskopik biyopsi:

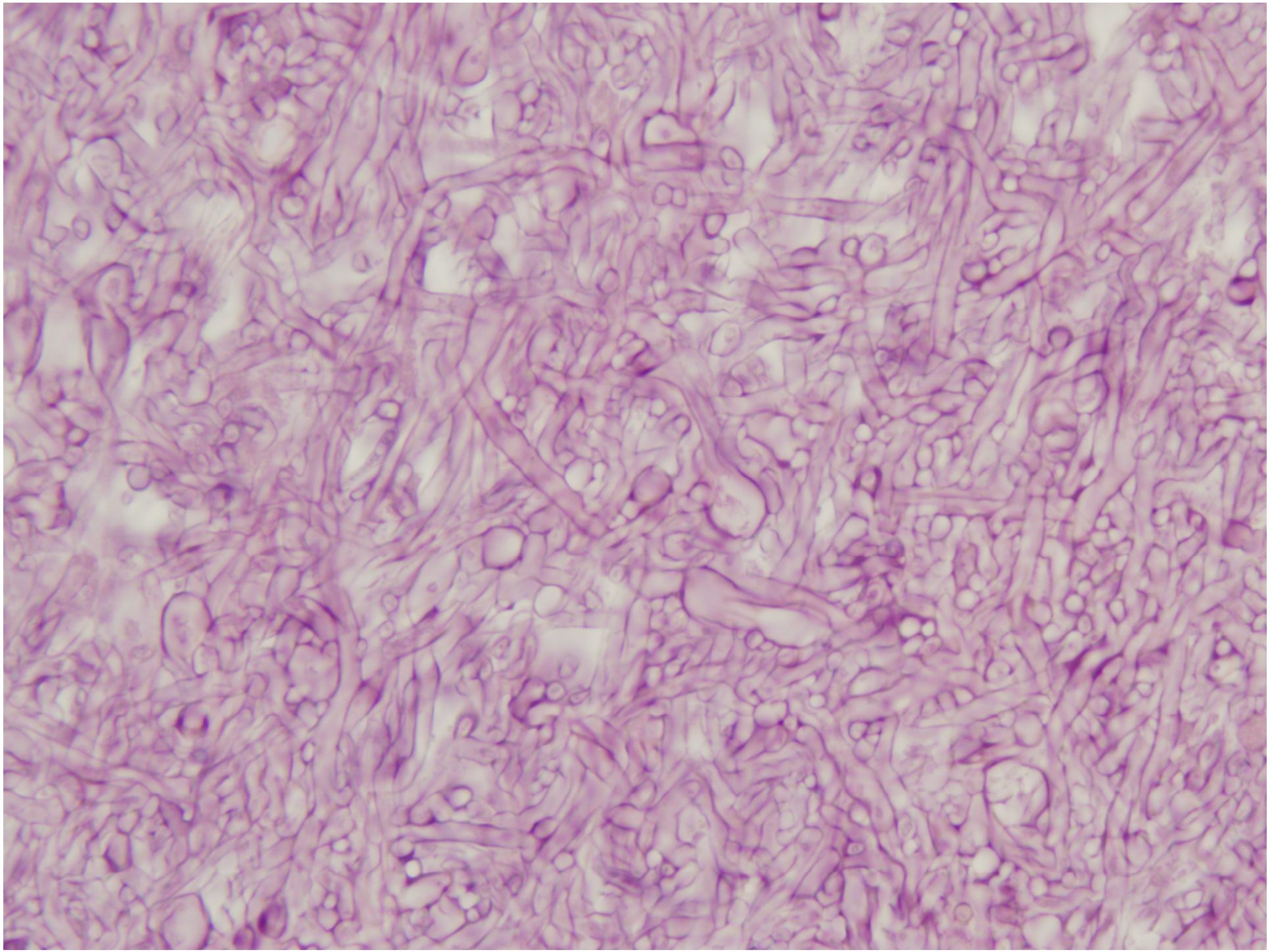
✓ Hiyalin septalı hiflerden oluşan miçelyum

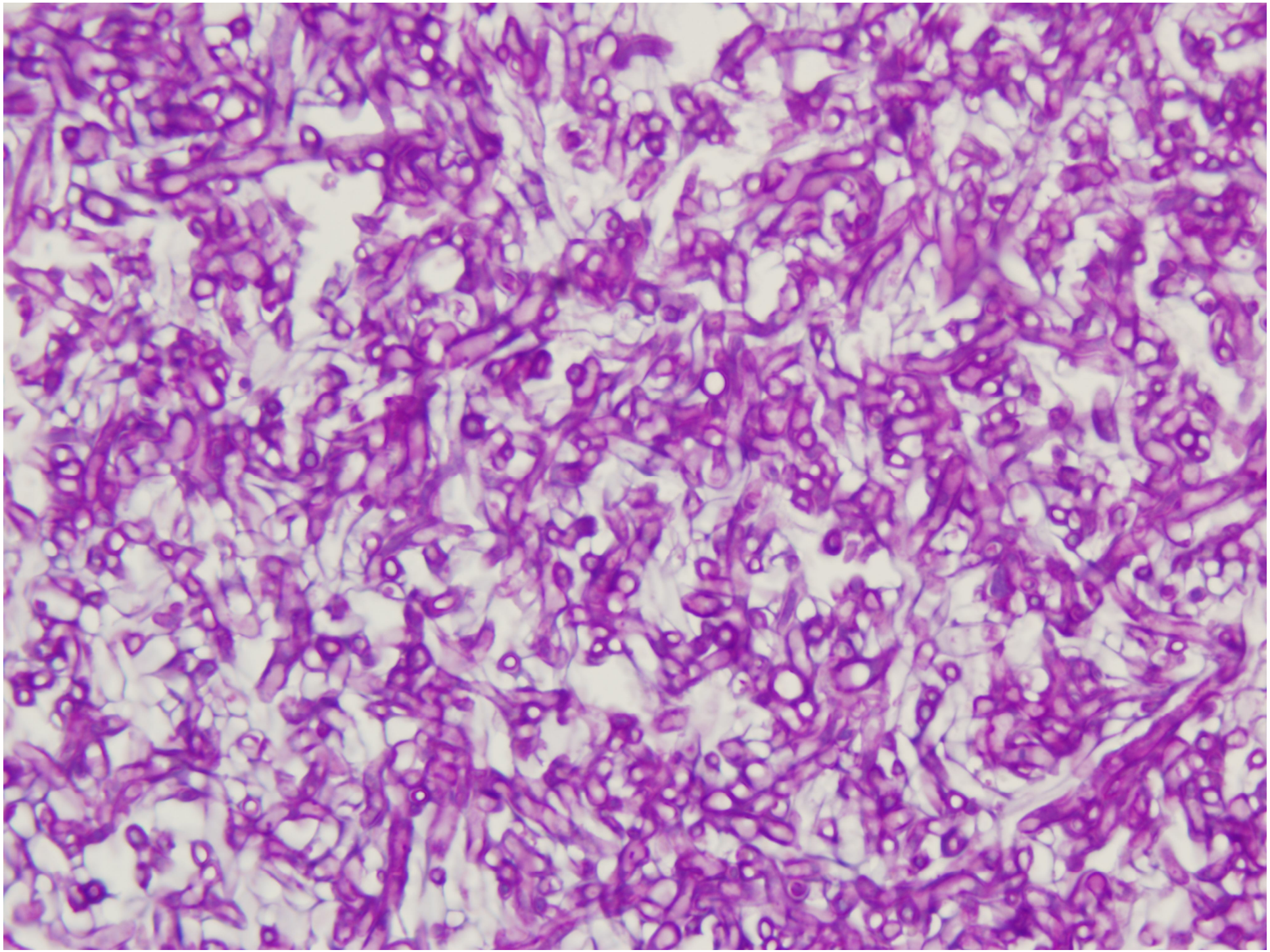
✓ Granülomatöz yangısal reaksiyon

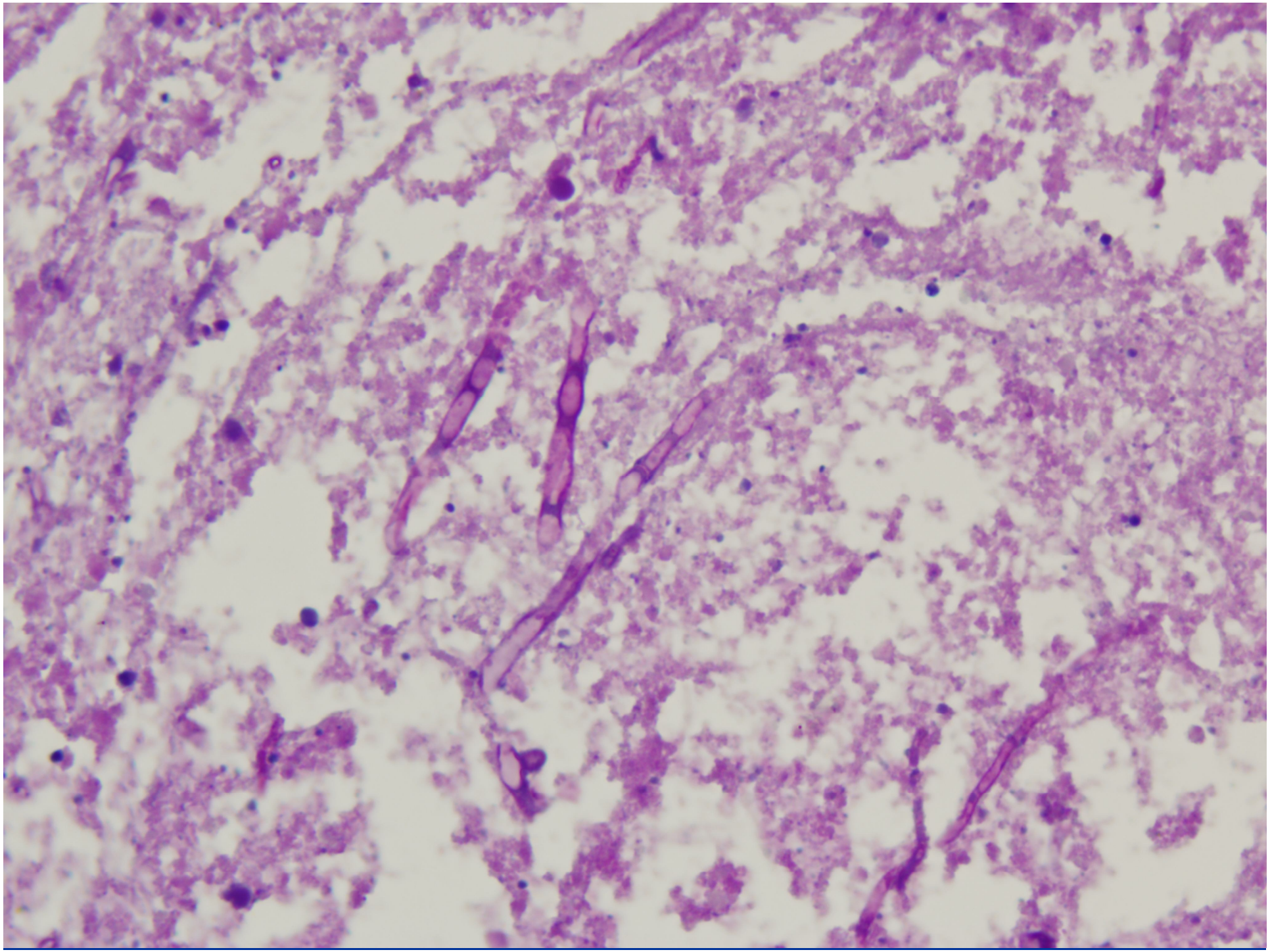
✓ Fokal nekroz ve fungal invazyon

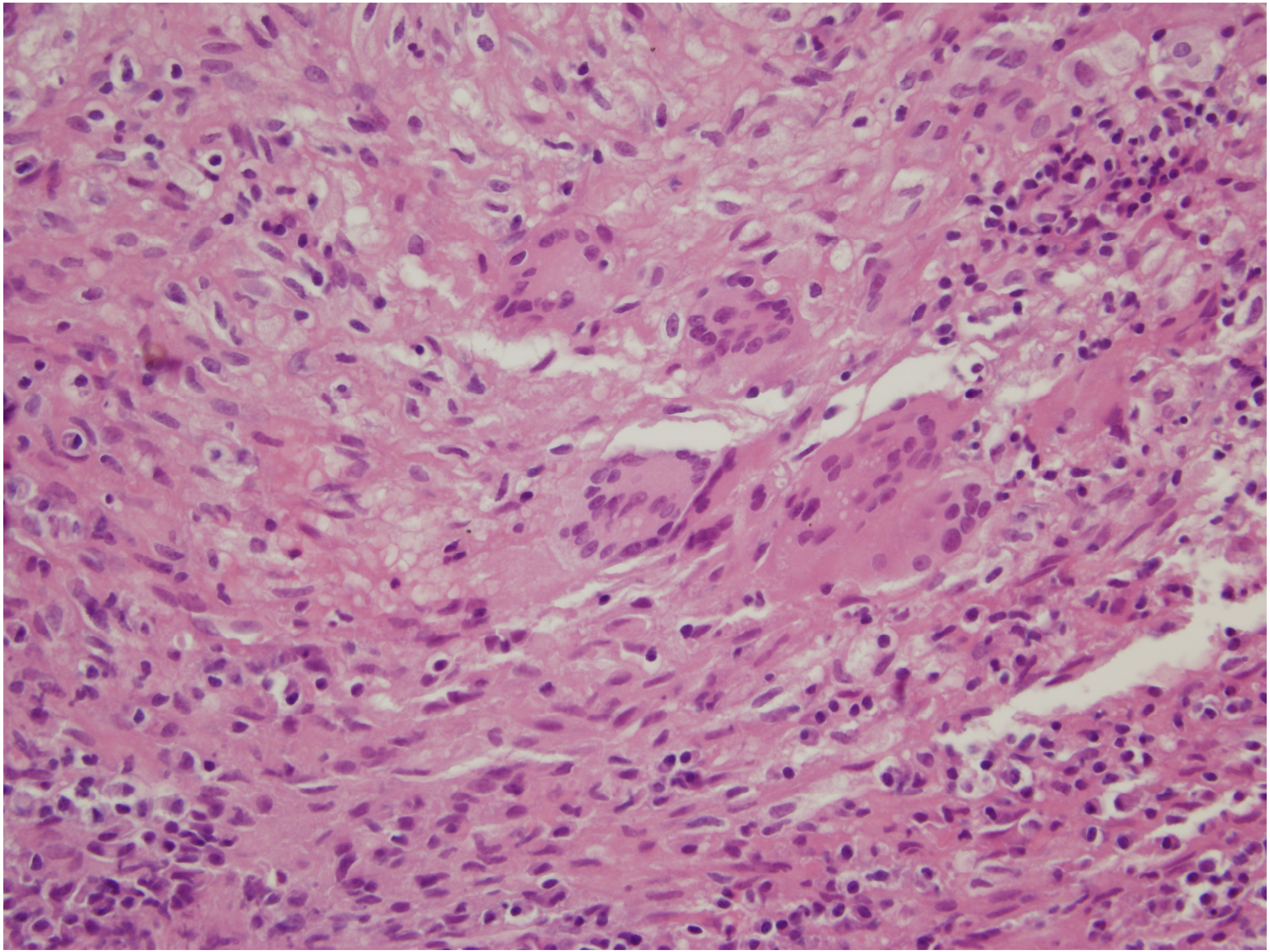












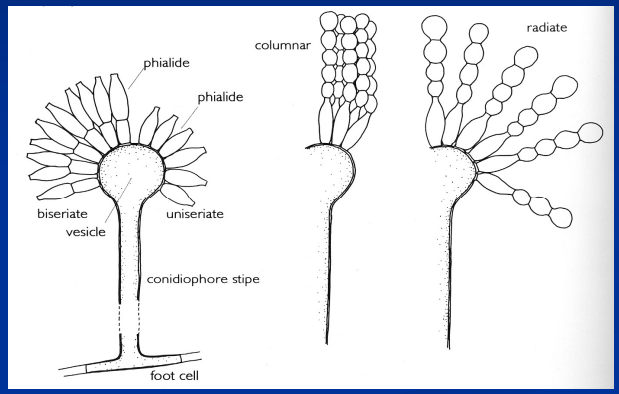
Patolojik Tanılar

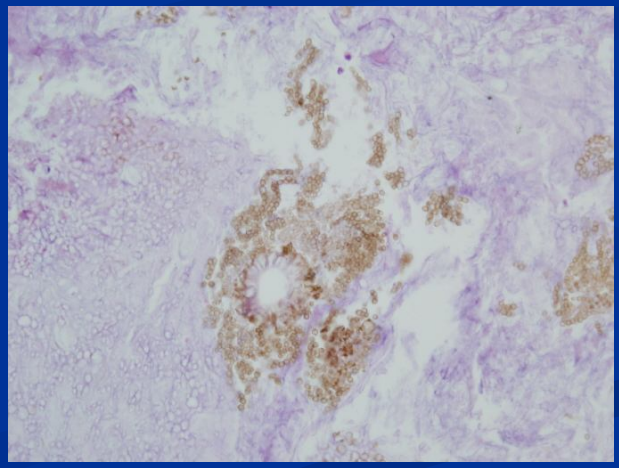
DEÜTF Patoloji AD Dr Uğur Pabuççuoğlu

- **Hiyalin septalı hiflerden oluşmuş fungal miçelyum (*Aspergillus* ?)**
- **Fokal nekroz ve fungal invazyon**
- **Granülomatöz yangısal yanıt** (Histokimyasal olarak ARB negatif)
- Ayırıcı tanıda : diğer bazı benzer hiyalin septalı fungal etkenlere bağlı infeksiyonlar

SONUÇ

- Olguda, hiyalin, septalı hiflerden oluşan bir fungus topu (olasılıkla aspergilloma) mevcut,
- Konidiforlar (konidial başlar) ya da oksalozis izlenmediğinden, aspergilloma histopatolojik tanısı kesinleştirilememekle birlikte, bu hif morfolojisi *Aspergillus*'da da izlenebilmektedir.
- Bu durumda mikolojik doğrulama önemli.





FUNGAL İNFEKSİYONLAR

- Akciğerlerde nadir görülen infeksiyonlar
- Genellikle bakteriyel pnömonilerde tedaviye yanıt alınamadığında düşünülürler
- Tanı genellikle geç konmakta ve problem oluşturmakta
- Klinisyenin etkeni tanıma ve tedavi etmedeki başarısı mortalite ve morbiditeyi etkilemekte

Aspergillozis - klinik

- Allerjik değişiklikler (ABPA, allerjik aspergillus sinüziti)
- **Kolonizasyon aspergillozisi = Aspergilloma**
  Önceden oluşmuş patolojik kavitelerin kolonizasyonu (fungus topu).
- İnvaziv aspergillosis : Akciğerler ve diğer organlarda invaziv, yangısal, nekrotizan hast.

ASPERGİLLOMA “mantar topu”

- Altta yapısal akciğer hastalığı olan hastalarda oluşan saprofitik infeksiyon
- Genellikle normal bağışıklık sistemine sahipler
- Kavite içerisinde mantar hifi, hücre debrisi, müküs birleşmesinden oluşur
- Kavite duvarı fibröz doku, inflamatuvar hücreler ve granülasyon dokusu
- %90 büyümeden kalır, %10 tedavisiz iyileşir
- Seyrek olarak kr.nekrotizan, daha nadiren de invaziv forma dönüşebilir.

ASPERGİLLOMA

- Sıklıkla hastanın pozisyonunu değiştirmekle kavite içerisinde yer değiştirirler
- Genellikle üst loblarda plevraya komşu yerleşirler
- Plevrada kalınlaşma olabilir
- Mantar topu ile kavite arasında mantar lifleri uzanabilir
- En sık semptom hemoptizi (%20-30 hayatı tehdit eden)

  Kavite damarları invazyonu, hasarlanma ve mantardan hemolitik toksin salgılanması ??
- %90> serumda aspergillus presipitinleri pozitif
- Balgamda mantar kültürü olguların %50'inde pozitif

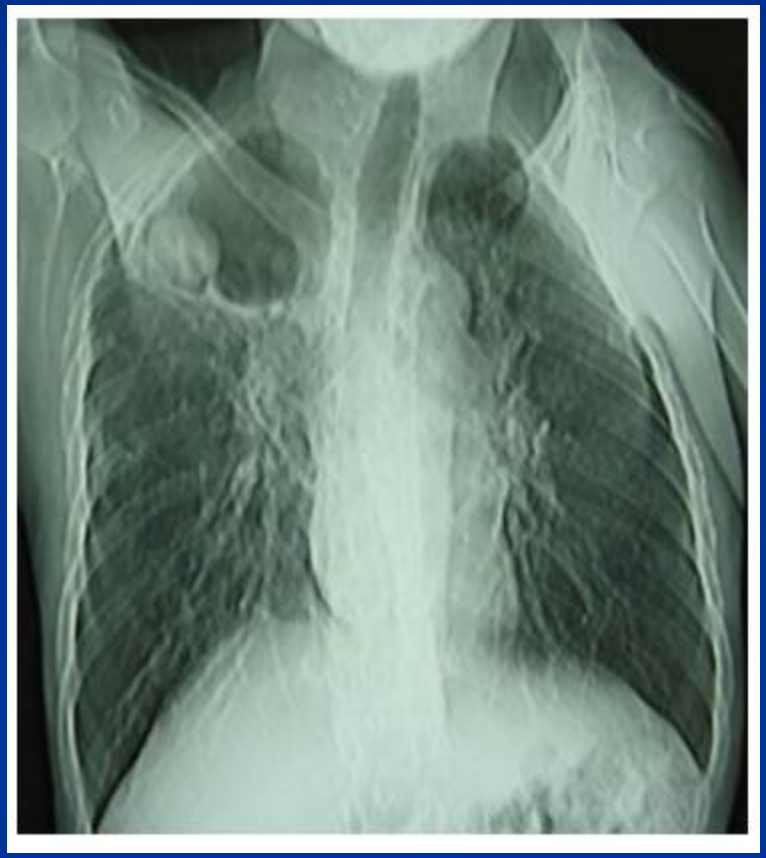
ASPERGİLLOMA

- En sık görülen altta yatan hastalıklardan **tüberküloz** geçirmiş olgularda **kaviter** hastalık
- Sarkoidoz 2.sıklıkta
- Ankilozan spondilit, maliğnite, akciğer infarktı, bül, abse, kist ve bronşektazi
- Yuvarlak veya oval bir kitle kısmen kaviteyi doldurur.
- Hava içeren yarım ay görünümü yapar (monod belirtisi)
- Kaviteyi tam doldurursa bu oluşmaz

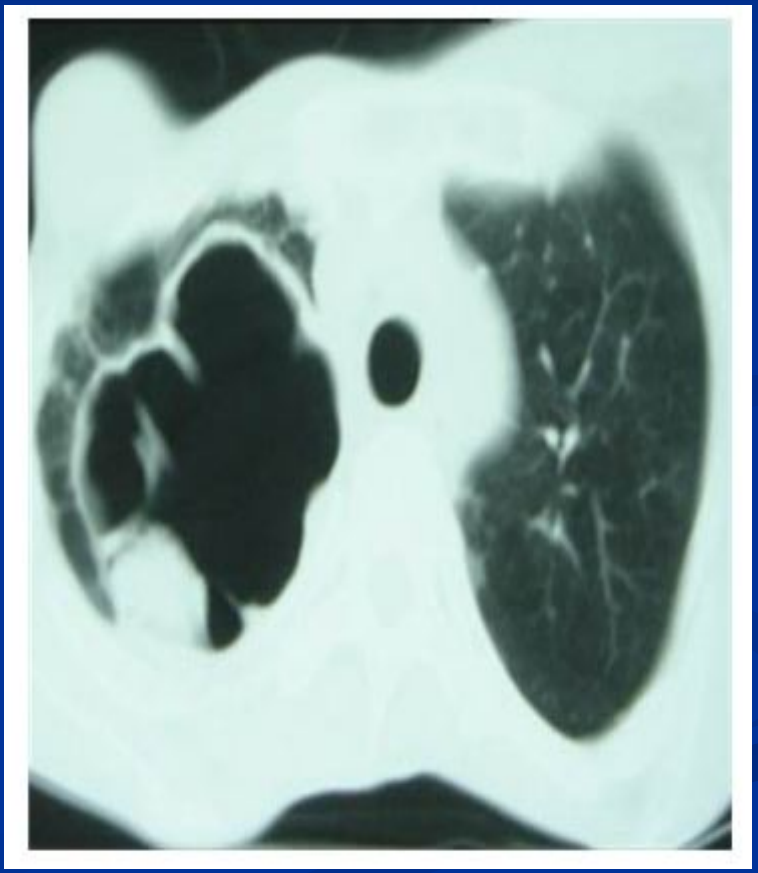
ASPERGİLLUS TBC

- The most common presenting symptom is haemoptysis, which is reported to be seen in 50-80% of patients . Most patients will experience mild haemoptysis but massive and life threatening haemoptysis may occur particularly in patients with underlying PTB .
- In a study of 544 patients with pulmonary cavities, secondary to tuberculosis, 11% had radiological evidence of aspergilloma

- **The Internet Journal of Radiology 2007. Volume 6 Number 1**



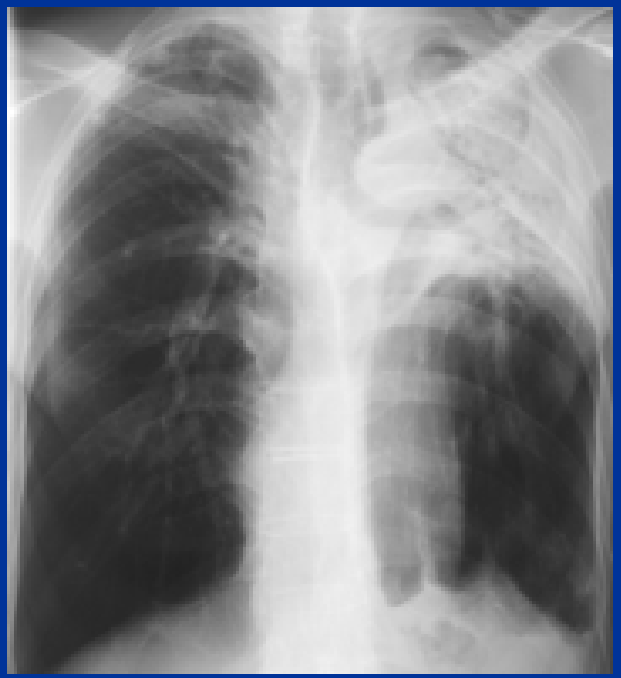
- A Case Report On Pulmonary Aspergilloma **Biva Shrestha Khan**

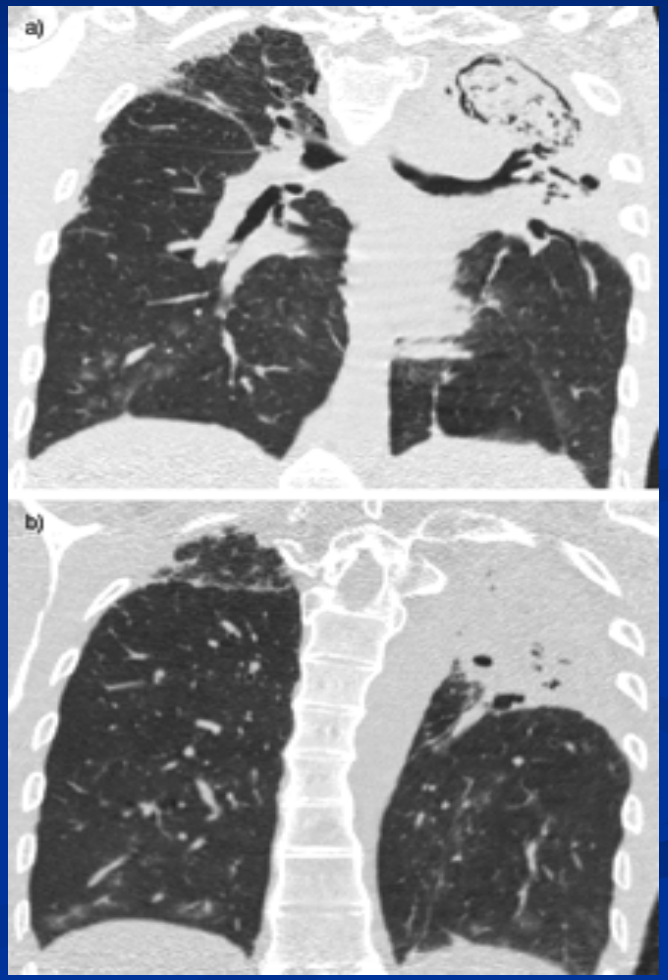


Left apical fibrocavitary disease with saprophytic aspergilloma in a patient with ankylosing spondylitis

- **Eur Respir J 2004; 23:488-489**

- A patient with ankylosing spondylitis and recurrent haemoptysis
- T. Franquet1, N.L. Müller2 and J.D. Flint3





LİTERATÜR

- **Clinical Rheumatology 2004**
- **Case Report**

A patient with ankylosing spondylitis who presented with chronic necrotising aspergillosis Report on one case and review of the literature

- Ömer Nuri Pamuk[1] -, Orbay Harmandar[2], Birsen Tosun[3], Yener Yörük[4] and Necati Çakır[1, 5]
- (1) Department of Rheumatology, Trakya Medical Faculty, University of Trakya, Edirne, Turkey

Abstract

- **Upper lobe fibrobullous disease is a well-known finding in advanced stages of ankylosing spondylitis (AS).** In this report, we present a 57-year-old male patient who was diagnosed with a **right apical cavitary lesion** after coming to us with the complaint of **haemoptysis**. The patient underwent **upper lobe segmentectomy and an aspergilloma was detected**. Histologic findings were in favour of necrotising *Aspergillus* pneumonia. It was interesting that the patient had not been diagnosed with AS before and presented initially with chronic necrotising *Aspergillus* pneumonia. **In the literature, there are recently published series of pulmonary high-resolution computed tomography (HRCT) in AS which claim that parenchymal abnormalities are quite frequent. Although the clinical significance of these abnormalities is not known with certainty, it has been reported that they might be seen even in early-stage patients.** It is suggested that the pulmonary involvement in AS might be affected by mechanical factors related to limitation of motion of the thoracic cage and also by parenchymal inflammation. Here, we review the series of pulmonary HRCT in AS patients.

DİSCUSSİON

- **Fibrobullous disease is a late complication of AS: it is characterised by slowly progressive fibrosis of the upper pulmonary zones and develops nearly 2 decades after the onset of AS** [6]. **It is seen as linear or patchy opacities on chest X-ray and later a cavity with cystic appearance develops. These cavities might be colonised with *Aspergillus*** [1, 9]. Our patient had upper lobe fibrocavitary disease and later developed *Aspergillus* superinfection in the cavity. Chronic necrotising *Aspergillus* pneumonia was confirmed histopathologically; however, we could not determine its exact classification because the cultures were negative. It has been reported that the presence of ***Aspergillus* antibodies in the serum** support the diagnosis and **are positive in 83–100% of cases** [13]. We could not perform these tests because they were unavailable at our centre. Our case was interesting because although the patient s clinical radiographic findings were typical, he had not been diagnosed with AS for a long time and he presented with haemoptysis and constitutional symptoms.

DİSCUSSİON

- Although some studies [2] reported **chronic *Aspergillus* colonisation in a significant proportion of AS patients (50–65%), symptomatic pulmonary *Aspergillus* infection is rare [1]. In one AS series, pleuroparenchymal manifestations were detected in 28 of 2080 patients (1.3%) and most of these were associated with upper lobe fibrobullous disease** [1]. **Aspergillomas** were detected in 5 of those 28 patients **(0.24%).** Cases of pulmonary aspergillosis have also been reported—although less frequently than in AS—in rheumatoid arthritis (RA) localised in rheumatoid nodule-associated cavities [14] and in systemic lupus erythematosus (SLE) patients using high doses of immunosuppressive drugs [15].

DİSCUSSİON

- Recent studies showed that **pulmonary findings, other than fibrobullous disease, might be seen in AS.** This is **because of HRCT being used, which is an especially sensitive method for evaluating the pulmonary parenchyma**. Table 1 summarises recent studies on HRCT in AS patients. Here, the factor which draws most attention is that **there is a high frequency of HRCT abnormalities in patients with normal chest X-rays.** When we consider all HRCT series summarised in Table 1, we see that **upper lobe fibrosis was detected in 11 of 220 cases; however, aspergilloma was present in only 1 case. Pathologies such as upper lobe fibrosis/cavity formation, which might have clinical significance, are seen in rather late stages of AS.** This is supported by these findings being absent in two studies in Table 1 which included AS patients with relatively shorter disease duration—less than 15 years [*8*, *10*]. Our patient had a cavitary lesion and a 30-year history of inflammatory back pain. However, **probably some pulmonary changes—other than cavities—occur in early disease stages and they progress with time**. This was demonstrated in two recent studies [*9*, *10*].

DİSCUSSİON

- **The clinical significance of abnormalities detected by HRCT or PFT** in studies presented in Table 1 is not clear. Although HRCT abnormalities were frequent in the patients, impaired PFTs were encountered less often. The percentage of lung-related symptoms is even lower as seen in Table 1. Therefore, we might conclude that most of the abnormalities on thorax HRCT in AS do not cause clinical symptoms.
- **There are different explanations for the presence of an increased frequency of HRCT abnormalities in AS patients.** One study [*8*] claimed that **mechanical reasons such as thoracic cage rigidity were responsible for the restrictive problem.** Contrarily, two different studies [*6*, *12*] stated that the pulmonary findings in AS were inflammatory and not mechanical. In addition to limitation of thoracic cage movements, probably interstitial inflammation plays an important role in pulmonary lesions [*16*].

Treatment

- The treatment for symptomatic aspergilloma is administration of **antifungal drugs**. In cases **where medical therapy is insufficient, there is an indication for thoracic surgery** [*2*]. **Haemoptysis, a common symptom, is experienced by the vast majority of patients with aspergilloma** [*17*]. As the prognosis of symptomatic aspergilloma is poor, surgical resection is indicated in such cases [*18*]. Our patient underwent thoracic surgery and a cure was obtained.
- **The upper lobe fibrocavity formation and *Aspergillus* superinfection present in our case are rare complications which might be seen in advanced stages of AS**. Generally, AS is a progressive disease with an insidious course and clinical findings might be misleading and noninformative for a long time; therefore, the diagnosis might be delayed. Similar to our case, patients might rarely present with pulmonary symptoms. **With the use of HRCT becoming more common in recent years, it is now understood that the lungs are involved quite commonly even in early stages of AS.** However, there are different ideas about the clinical significance and pathogenesis of pulmonary findings seen during the course of the disease and these should be clarified.

İnvaziv Aspergillozis

- Akciğer grafisinde çok çeşitli görünümler
- Kavitasyon, tabanı plevraya oturmuş kama şeklinde lezyonlar
- Sık olarak kavitasyon gösteren " hilal belirtisi=air crescent sign" veya göstermeyen nodüler " halo işareti" lezyonlar
- Nadiren diffüz infiltrasyonlar
- Ayırıcı tanı için tanısal girişimler (HRCT, FOB, BAL %30-70 tanı koydurucu, TBB) yapılmalı
- Hasta serumlarında Elisa yöntemi ile Aspergillus'un hücre duvarının komponenti galaktomannan antijeninin %90 üzerinde sensitivite ve spesifitesi

YARI-İNVAZİV ASPERGİLLOZİS

- KOAH, düşük doz kortikosteroid kullanımı, alkolizm, Tbc, Diyabet, kollajen vasküler hastalıklarda
- Pnömokonyoz ve RT gibi akciğerlerde yapısal değişiklikler oluşmasında risk daha da artar
- Aktif Tbc'u taklit edebilir
- Düzensiz üst lob konsolidasyonu, plevral kalınlaşma yavaşça (hf-aylar..) ilerler , kavitasyon gelişir, kavite içinde mantardan oluşan internal opasiteler görülür.Düzensiz iplik şeklinde yapılar kavite duvarına uzanır

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Akciğer grafisi ve HRCT

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HRCT

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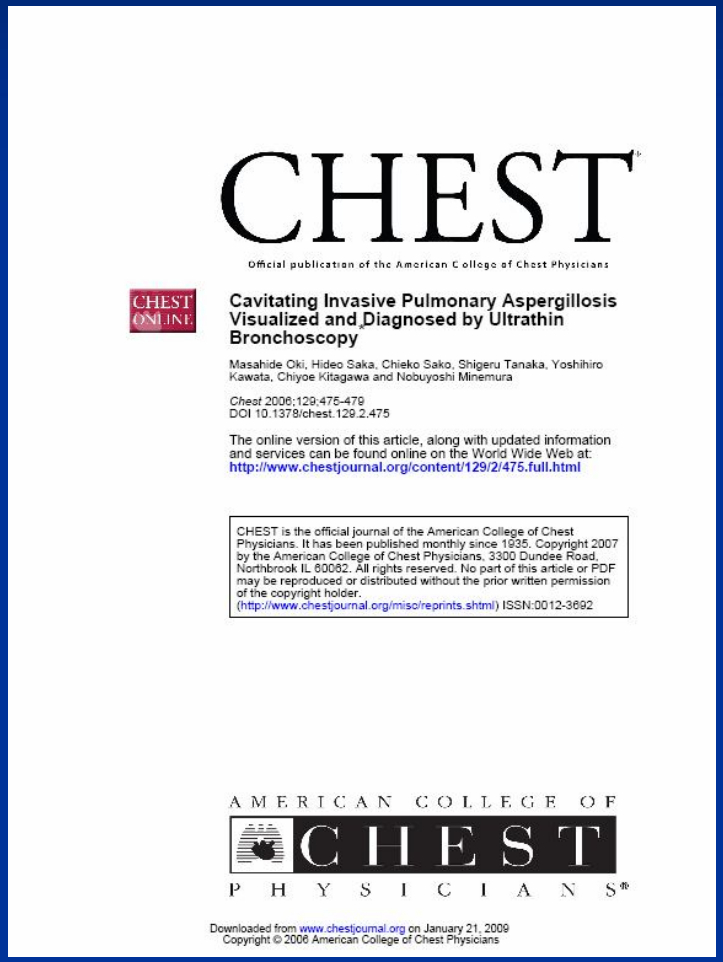
PULMONER ASPERGİLLUS FOB



CHEST

Official publication of the American College of Chest Physicians

CHEST ONLINE

Cavitating Invasive Pulmonary Aspergillosis Visualized and Diagnosed by Ultrathin Bronchoscopy

Masahide Oki, Hideo Saka, Chieko Sako, Shigeru Tanaka, Yoshihiro Kawata, Chiyoe Kitagawa and Nobuyoshi Minemura

Chest 2006;129:475-479
DOI 10.1378/chest.129.2.475

The online version of this article, along with updated information and services can be found online on the World Wide Web at:
http://www.chestjournal.org/content/129/2/475.full.html

Cavitating Invasive Pulmonary Aspergillosis Visualized and Diagnosed by Ultrathin Bronchoscopy*

Masahide Oki, MD; Hideo Saka, MD, FCCP; Chieko Sako, MD; Shigeru Tanaka, MD; Yoshihiro Kawata, MD; Chiyoe Kitagawa, MD; and Nobuyoshi Minemura, MD

A definitive diagnosis of invasive pulmonary aspergillosis (IPA), which usually occurs in immunocompromised patients, is often difficult. We report two cases of cavitating IPA in a peripheral pulmonary region in patients who were receiving corticosteroids, in whom the cavity was successfully visualized and sampled during ultrathin bronchoscopy. Ultrathin bronchoscopy provides a new option for definitive diagnosis of cavitating IPA.
(CHEST 2006; 129:475–479)

Key words: bronchoscopy; cavity; invasive pulmonary aspergillosis; transbronchial biopsy; ultrathin bronchoscope

Abbreviations: IPA = invasive pulmonary aspergillosis; TBB = transbronchial biopsy

Invasive pulmonary aspergillosis (IPA), which commonly occurs in immunocompromised patients, is a life-threatening infectious disease. Not only are such patients difficult to treat, the diagnosis is especially difficult. Although bronchoscopic procedures such as BAL and transbronchial biopsy (TBB) have been used to establish the diagnosis of IPA, their diagnostic yield is insufficient.[1] The diagnostic yield of TBB is particularly low,[2] so its value for the diagnosis of IPA remains controversial.[3]

Recently, ultrathin bronchoscopes offering a smaller outer diameter and higher image quality have been developed. Such a bronchoscope with an outer diameter of 2.8 mm is now commercially available and permits the observation and manipulation of more peripheral bronchi than was previously possible with a standard bronchoscope. The ultrathin bronchoscope has been reported to be a valuable diagnostic tool for peripheral pulmonary lesions.[4–6] Although various diseases can be diagnosed histologically using the ultrathin bronchoscope, there is, to our knowledge, no report in the literature about its contribution to the diagnosis of IPA. We herewith report two cases of IPA diagnosed in patients were receiving corticosteroids, in whom the cavity was visualized and sampled during ultrathin bronchoscopy.

Case Reports

Case 1

A 57-year-old man with dermatomyositis was referred for bronchoscopic evaluation of progressive radiographic changes consisting of an enlarging cavity despite antibiotic therapy. For 3 months, he had received prednisolone, 40 to 80 mg/d, and azathioprine, 100 mg/d, for intractable dermatomyositis. Two weeks earlier, he complained of fever, increased cough, purulent sputum, and dyspnea. The chest radiograph showed a cavity with surrounding infiltrates in the upper lobe of the right lung. Sputum cultures grew *Pseudomonas aeruginosa* and *Candida glabrata*. The patient had been treated with IV cefozopran and fluconazole for 2 weeks without any clinical improvement.

A CT scan of the chest the day before bronchoscopy revealed a thick wall cavity in the anterior segment of the right upper lobe that had not been present 2 months previously (Fig 1). Bronchoscopic examination using a standard bronchoscope with an external diameter of 6.1 mm (BF-6C240; Olympus; Tokyo, Japan) [Fig 2] was first performed. The bronchoscope reached the segmental bronchus of the right upper lobe and revealed no abnormalities. Then, for peripheral investigation, a 2.8 mm in diameter ultrathin bronchoscope with a 1.2-mm working channel (BF-XP40; Olympus) [Fig 2] was employed. The ultrathin bronchoscope was inserted into the right B3 and advanced through the fifth-generation bronchus under direct observation, and then entered a cavity, as confirmed by fluoroscopy (Fig 3). A whitish intracavitary lesion was seen (Fig 4, *left*, *A*). Biopsies using a minforceps (FB-56D-1; Olympus) and washing were performed with bronchoscopic visualization, and then amphotericin B, 5 mg, was instilled into the cavity through the ultrathin bronchoscope for treatment of a presumptive fungal infection. Biopsy specimens showed septate-branching hyphae suggestive of aspergillosis and cultures of the cavital washing grew *Aspergillus flavus*. Unfortunately, 9 days later the patient suddenly died of cerebral hemorrhage.

Case 2

A 69-year-old man with systemic lupus erythematosus was admitted to the hospital with cough, bloody sputum, fatigue, decreased appetite, and enlarging left lower lobe pulmonary cavity. For 6 months before hospital admission, he had received prednisolone, 20 to 30 mg/d, for systemic lupus erythematodes. Two months earlier, he complained of bloody sputum, and a chest CT showed cavitary infiltrates in the superior segment of

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A comparison of bronchoscopes. *Left*: a standard bronchoscope with an external diameter of 6.1 mm and a working channel of 2.0 mm (BF-6C240; Olympus); *right*: an ultrathin bronchoscope with an external diameter of 2.8 mm and a working channel of 1.2 mm (BF-XP40; Olympus).

CHEST

Official publication of the American College of Chest Physicians

CHEST ONLINE

Pulmonary aspergilloma diagnosed by fiberoptic bronchoscopy.

R L Smith, M J Morelli and C P Aranda

Chest 1987;92;948-949
DOI 10.1378/chest.92.5.948

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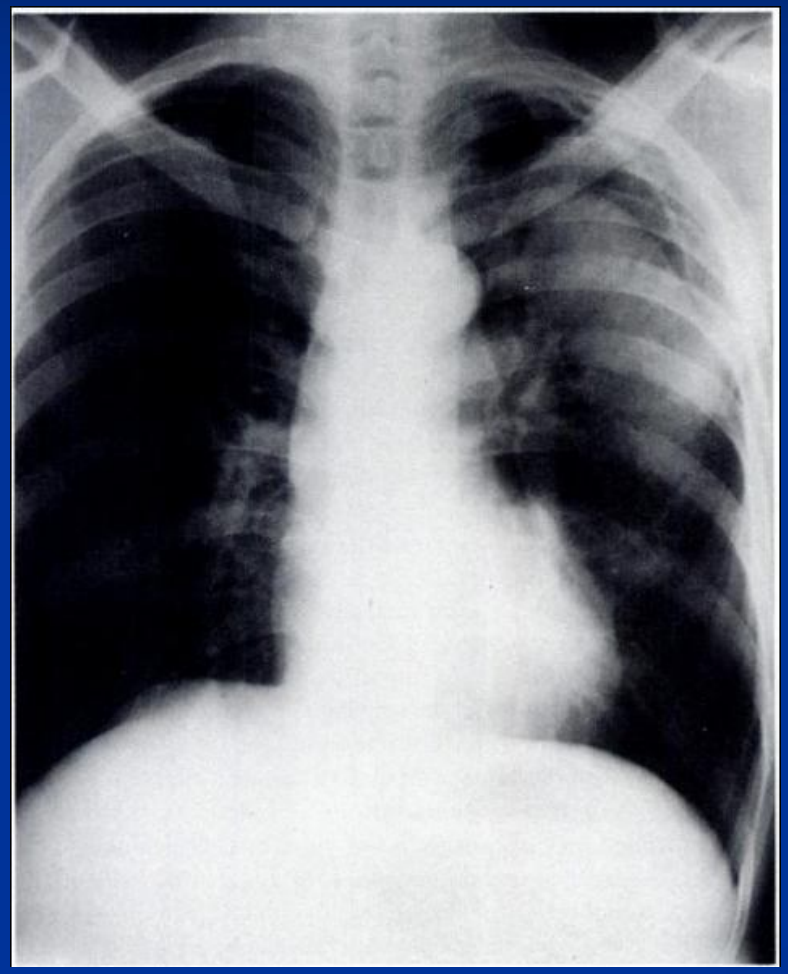
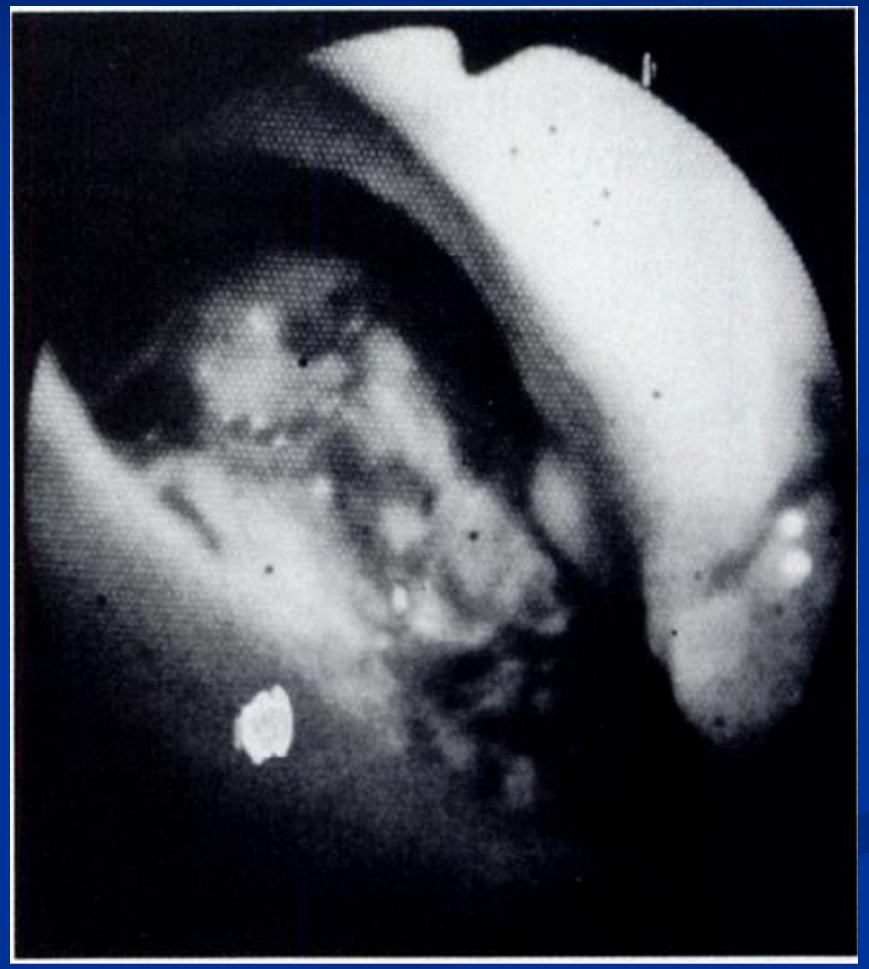




TEDAVİ

- Optimal tedavi ??
- Belirti yok ise tedavi gerekmez, var ise tedavisi son derece zor
- Sistemik,intrakaviter veya inhalasyon yolu ile tedavi başarılı değil !
- Tedavi edilmemişlerde invaziv olanlarda mortalite %100'e yakın,
- Kısmi veya tam yanıt alınması sadece % 30,
- Konakçının immünitesine ve akciğerlerin durumuna, hemoptizi başta olmak üzere semptomların derecesine göre her birey için tek tek ele alınmalı

Tedavi

- Endobronşial haftalık amfoterisin B ve oral itrakonazol ?

  *Yamada H et al. Topical treatment of pulmonary aspergilloma by antifungals: relationship between duration of the disease and efficay of therapy. Chest 1993

  *Büyükşirin M et al. Endobronşial aspergillozis ile gizli akciğer kanseri ve topikal amfoterisin B ile oral itrakonazolün etkinliği. Toraks Dergisi, 2005

- Endobronşial haftalık flukonazol ve oral itrakonazol ?

  *Yoshitomi A et al. Lung cancer obscred by aspergillus hyphae. Nihon kokyuki gakkai zasshi 2000

- Birlikte sistemik Amfoterisin B tedavisi ?

Teşekkürler

Aspergillozis

- *Aspergillus* genusunun üyelerince oluşturulan hastalık grubu,
- İnvaziv hastalığa en sık neden olanlar

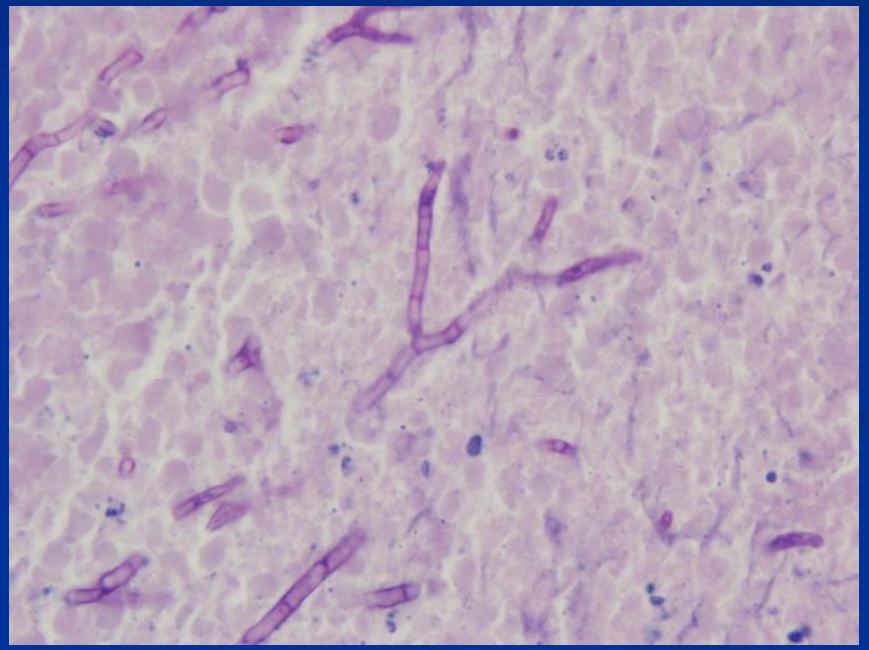
  A.fumigatus, A.flavus, A.niger, A. terreus ve A.nidulans
- Toprakta ve çürüyen bitkilerde yaygın olarak bulunurlar.

Aspergillozis'de klinik

- Allerjik değişiklikler (ABPA, allerjik aspergillus sinüziti)
- Kolonizasyon aspergillozisi=aspergilloma Önceden oluşmuş patolojik kavitelerin kolonizasyonu (fungus topu).
- İnvaziv aspergillosis : Akciğerler ve diğer organlarda invaziv,yangısal,nekrotizan hast.

Aspergillus histomorfolojisi

- Hiyalin septalı küflerdir.
- 3-6 µm genişlikte olan ve düzenli septasyon gösteren hiflerden oluşurlar
- 45 derecelik açı ile dikotom dallanma vardır
- Yalnızca hif morfolojisine dayanarak, *P. boydii* ya da *Fusarium* türleri gibi diğer hiyalin hyphomycetes'den kesin histopatolojik ayrımı zordur.



A.niger

- Kalsiyum okzalat kristalleri [Özellikle ***A.niger*** etken olduğu durumlarda].