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ARAYIŞLAR VE ÇALIŞMALAR

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IN HEALTH SCIENCES

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Bölüm 1

DEMANSLI YAŞLIYA BAKIM VEREN AİLE ÜYELERİNİN DESTEKLENMESİ İÇİN KULLANILABİLECEK MÜDAHALELER

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GİRİŞ

Günümüzde artan yaşlı nüfus için evde yalnız yaşamak bir tercih olsa da, evde yaşayan yaşlıların bir kısmı aile üyelerinden bakım desteği almak zorunda kalmaktadır (National Institute of Nursing Research, 2001). Değişen toplumsal yapıya rağmen ülkemizde ve gelişmiş ülkelerde güçlü aile ilişkileri varlığını devam ettirmektedir ve yaşlı bireylerin bakım sorumluluğunun yaklaşık %60-80'i aile bireyleri tarafından yerine getirilmektedir (Aile ve Sosyal Politikalar Bakanlığı Demans Bakım Modeli Raporu, 2017). Yaşlılar için aile bakımının varlığı yaşam kalitesini iyileştiren, bağımsızlığı destekleyen, işlevselliği arttıran, kurumsallığı azaltan ve böylece sağlık harcamalarından tasarruf ettiren (Kelley et al., 1999) bir yapı sunmaktadır. Ancak bu olumlu yönlerinin yanında yaşlının özellikli durumlara sahip olması bakım veren aile üyeleri için çeşitli sorunları da beraberinde getirebilmektedir. Bu özellikli durumlardan biri de damarsal ve dejeneratif değişimlere bağlı olarak gelişen demanstır.

Demans, bilişsel işlevlerdeki düşüş ile ilişkili semptomlar için kullanılan, ilerleyici bir hastalık grubunun genel adıdır. Bu hastalık grubunda alzheimer, vasküler demans, frontotemporal demans gibi birçok farklı demans türü bulunmaktadır (Department of Health, 2013). Tüm dünyada çeşitli demans türlerinin görüldüğü 65 yaş ve üstü birey sayısı 2015 yılı verilerine göre yaklaşık 47 milyondur (WHO, 2015) ve bu sayının yaşlı nüfusun artışına paralel olarak artacağı öngörülmektedir. Semptomlar demans türüne göre değişse de genel olarak özellikle kısa süreli hafızada kayıplar, iletişim ve yargıda bulunmada güçlükler, kişilik yapısında değişimler (Garrod et al., 2019) ve kişinin günlük aktivitelerini yönetmesinde zorluklar şeklinde görülmektedir (Administration for Community Living U.S. Department of Health and Human Services, 2018).

Demans sadece demanslı kişinin değil aynı zamanda bakım veren aile üyelerinin ve diğer bakım verenlerin hayatının çeşitli yönlerini de etkileyebilir. Ücretli bakım sağlayanlar ile aile üyeleri, demanslı bireye ev işlerinde yardım, tıbbi durum yönetimi, uygulamalı kişisel bakım, sürekli denetim ve saldırganlık veya gezinme gibi davranışsal semptomlara yanıt verme dahil bakım ve desteğin çoğunu sağlamak durumu ile karşılaşabilirler (Administration for Community Living U.S. Department of Health and Human Services, 2018). Alzheimer hastası ve diğer demans hastaları genellikle evde ücretsiz aile üyelerinden bakım görürler (Alzheimer's Association, 2012). Bu durum bakım verenlerin demanslı bireye bakım vermeden kaynaklanan sorunlarla daha fazla karşılaşacağı sonucunu ortaya çıkarabilir.

Demanslı bir bireyle birlikte yaşamak ve ona bakmak bakım verenler için son derece zorlayıcı ve zaman alıcı bir durum haline gelebilir. Demanslı bireye bakım vermek aile üyeleri için çoğu zaman fiziksel olarak zor veya rahatsız edici görevlerin yerine getirilmesini de gerektirebilir. Bu süreç aile rutinlerini ve dinamiklerini sıklıkla kesintiye uğratar ve ailede bakım veren birçok kişinin ailenin diğer üyelerinden ve arkadaşlarından soyutlanmasına neden olabilir. Dahası, bakım veren aile üyeleri sevdikleri birinin kaybıyla karşı karşıya kalabilir ve yeni ailevi rollere adaptasyonu güçleşebilir (Eisdorfer et al., 2003). Bağımlı bireye günlük 5 ile 20 saat bakım sağlayan aile üyesinden aynı anda başka birçok rolü de yerine getirmesi beklenebilir (Marziali ve Donahue, 2006). Sonuç olarak, pek çok bakım veren aile üyesi ciddi bir yük ve stres yaşar ve buda aile üyesinin fiziksel ve zihinsel sağlığının bozulmasına neden olabilir (Eisdorfer et al., 2003). Aile üyesi uykusuzluk çekebilir, yorgunluk, kaygı, depresyon yaşayabilir ve bozulmuş immünolojik tepkiler gösterebilir (Marziali ve Donahue, 2006).

Bakımın kronik stresi ile ilişkili olduğu ileri sürülen depresyonun (Dura et al., 1991) görülme sıklığının bakım verenler arasında %22 yaşlı bireylerde ise %11 olması (Vitaliano et al., 2003) dikkate değerdir. Kadın bakıcıların erkek bakıcılara göre (Anthony et al., 1988), eşlerin diğer aile üyelerine göre daha depresif olma eğiliminde olması (Dura ve diğerleri, 1991) da dikkat çekilmesi gereken diğer bir konudur. Özellikle demanslı kişilerin bakıcıları arasında depresyon yaygınlık oranlarının %30'dan %83'e kadar yükselebildiği (Drinka et al., 1987) bildirilmektedir. Bakım verenlerde yaşanan depresyonun sadece bakım veren sağlığını değil aynı zamanda bakım sağlamaya devam etme yeteneğini de etkileyeceği (Czaja et al., 2000), ayrıca alzheimer hastasında da depresyona yol açarak işlev bozukluğu düzeyinin hastalığın kendisiyle ilişkili olanın ötesine geçmesine neden olabileceği (Teri ve Uomoto, 1991) ileri sürülmektedir.

Üstelik bakım verenler ve bakım alan yaşlı bireylerin coğrafi konumu arasında mesafe olduğunda bakım verme sürecinin fiziksel ve sosyal boyutlarını desteklemek adına ek yardımlara ihtiyaç duyulabileceği (Morgan, 2004) de öngörülebilir.

Genel olarak, bakım verenlerin sağlığının olumsuz etkilenmesi durumunda bakım alanların da sağlık durumunun tehlikeye girebileceği ve bunun da bakım alanlar için erken kurumsallaşmayla sonuçlanabileceği (Marziali ve Donahue, 2006) göz önüne alındığında bakım verenlere yönelik çeşitli müdahaleler geliştirmenin üzerinde durulması gereken bir konu olduğu görülmektedir.

Bu müdahalelerden yüz yüze ve evde bakım modellerinin yanı sıra teknoloji odaklı müdahaleler, kronik engelli bireylerin bakım veren aile

üyelerine bilgi ve destek hizmetleri sağlamak için giderek daha fazla kullanılmaktadır (Czaja ve Rupert, 2002). Bakım verenler için çok sayıda çevrimiçi destek programı olmasına rağmen, çoğu bakım verenlerin stresini ve yükünü azaltmadaki etkileri ile diğer alanlar açısından değerlendirilmemiştir (Burdick ve Kwon, 2004). Bu çalışmada demanslı yaşlıya bakım veren aile üyelerinin bakım ve diğer uygulamalarda desteklenmesi için kullanılabilecek teknoloji odaklı ve diğer müdahaleler ve etkilerinin gözden geçirilmesi amaçlanmıştır.

1. BAKIM VERENLERE YÖNELİK MÜDAHALELER VE ETKİLERİ

Demanslı bireye kurumda bakım vermenin yüksek maliyeti nedeniyle, evde bakım verenlerin davranış değişikliği ve artan sosyal destek yoluyla psikososyal durumlarını iyileştirmek için çok sayıda müdahale geliştirilmiştir. Bu müdahalelerden bazıları bireysel ve/veya grup seansları halinde yüz yüze, bazıları müdahale uzmanının bakım verenin evine gitmesi veya telefonla müdahale etmesi gibi bir ya da birkaç müdahalenin birlikte uygulanması şeklindedir.

Bazı çalışmalar (Godwin et al., 2013) demanslı bireye bakım verenlere en iyi müdahale yöntemini belirlemek amacıyla kanıtlar sunmaktadır. Demanslı bireye bakım verenlere yönelik müdahale çalışmaları çeşitli yüz yüze müdahale modellerinin bakım verenlerin yaşadığı sıkıntılar (örneğin depresyon) ve yaşam memnuniyeti, bakım ve bilgi edinme ile ilgili önemli faydalar sağladığını (Chu, Edwards, Levin ve Thomson, 2000; Sorensen, Piquart ve Duberstein, 2002) göstermiştir. Engelli bireye bakım verenler için, engelli bireyin davranış sorunlarına odaklanan bireysel davranışsal yönetim terapilerinin bakım verenlerin ruh sağlığını iyileştirdiği (Selwood et al., 2007) belirlenmiştir. Ayrıca bakıcılara hem bireysel hem de grup seansı formatlarında başa çıkma becerilerini öğretmenin bakım verenlerin psikolojik sağlığını iyileştirmek adına destekleyici sonuçlar (Thompson et al., 2007) ortaya koyduğu belirlenmiştir.

Literatürde ev tabanlı müdahalelerin başka bir yerde yapılan müdahalelere kıyasla daha az külfetli olması bakımından daha yaygın kullanıldığı görülmektedir. Ancak bakım verenler için zamanlamada yaşanan zorluklar nedeniyle elverişsiz olabileceği de (Godwin et al., 2013) belirtilmektedir.

2. BAKIM VERENLERE YÖNELİK TEKNOLOJİ ODAKLI MÜDAHALELER VE ETKİLERİ

Teknoloji odaklı müdahaleler bilgisayar veya web tabanlı uygulamaları kullanan müdahalelerdir (Murray et. al., 2005). Teknoloji odaklı müdahaleler,

- Otomasyon ve tele-sağlık (Morgan, 2004),
- Bilgisayar ağı (Brennan et al 1995, Czaja ve Rubert, 2002, Morris ve Lundell, 2003),
- Televideo (Czaja ve Rubert, 2002; Morris ve Lundell, 2003) gibi bileşenlerden oluşmaktadır.

Bu müdahaleler engeli bulunan bireye bakım verenlerde bakım uygulamalarında bulunmak için uygun ve düşük maliyetli alternatifler sunmaktadır. Ayrıca sosyal destek veya davranış değişikliği desteğinin yanında sağlık bilgileri sağlayabilmektedir. Web tabanlı ve diğer teknolojik uygulamaları kullanan müdahalelerin bir faydası da bakım verenin uygun bulunduğu gün veya gecenin herhangi bir saatinde kullanılabilir olmasıdır. Bu tür müdahalelerin diğer faydaları arasında, çeşitli formatlarda (yani metin, grafikler, video ve ses) bilgi aktarma yeteneği, bilgi sağlanması yoluyla bilinçli karar vermeyi sağlamak, bilgiyi artırarak sağlık davranışlarını teşvik etmek ve akranlar arasında bilgi alışverişini ve duygusal desteği teşvik etmek yer almaktadır (Murray et. al., 2005). Otomasyon ve tele-sağlık teknolojileri dahil olmak üzere çok sayıda teknolojik yardımın coğrafik olarak aralarında mesafe bulunan bakıcı ve bakım alan yaşlı bireyler için bakıcı desteğini sağlama potansiyeline sahip olduğu da (Morgan, 2004) bildirilmiştir. Teknolojiye dayalı müdahaleler sanal olarak bakıcı ve yaşlıyı birbirine bağlarken aynı zamanda yaşlıların fiziksel, duysal, sosyal ve bilişsel bozukluklarını ele alan uzaktan bakım için güçlü destek sağlamada güçlü kanıt sunmaktadır (Mynatt et al., 2001; ETAC, 2004). Yaşlıların fiziksel ve bilişsel yetenek düzeyine göre uyarlanmış iki yönlü video bağlantıları, yaşlıları sosyal ve bilişsel uyarımla meşgul edebilir. Aktivite işaretleme, televideo izleme gibi akıllı yardımcı teknoloji uzaktan sağlık kontrolüne yardımcı olabilir, bilgi ve karar desteği sağlayabilir ve sağlık veya işlevsel durumdaki değişiklikleri değerlendirmek için uzaktan bakım gereksinimlerini karşılayabilir (Czaja ve Rubert, 2002; Morris ve Lundell, 2003).

Literatürde olası yararları, sağladığı kolaylıklar ve düşük maliyetleri nedeniyle teknoloji odaklı bileşenlerle engelli bireye bakım verenler için uygulanan müdahaleler (Godwin et al., 2013) ile yapılan çalışmalar mevcuttur. Bu müdahalelerin kullanıldığı çalışmalardan birinde bilgi, iletişim ve karar desteği olmak üzere üç ana bileşeni olan bir bilgisayar ağı kullanılmıştır (Brennan et al., 1995; Bass et al., 1998). Burada demansın en sık nedenlerinden olan alzheimer hastalığının yönetimi ve tedavisi, bakım verenlerin öz bakım hakkında bilgi edinmeleri ve toplum hizmetleri elektronik bir ansiklopedi aracılığıyla sağlanmıştır. Bakım verenler diğer bakım verenlerle halka açık bir forum aracılığıyla veya e-posta yoluyla özel olarak iletişim kurabilmiştir. Soru-cevap forumu bir

hemşire tarafından yönetilmiştir. Karar destek bileşeni de bakım verenlerin problemlerle kendi değerlerini ödünleştirmelerini sağlamada rehberlik etmiştir. Bilgisayar ağı engelli birey ile yalnız yaşamayan ve gayri resmi desteğe sahip olan bakım verenlerde belirli türlerdeki gerginliği azaltmada başarılı olurken (Brennan et al., 1995), bakım verenlerin karar verme sürecinde de iyileşme sağlamıştır (Bass et al., 1998). Bir diğer müdahale (Beauchamp et al., 2005) ise deney ve kontrol grubu olmak üzere iki grubun yer aldığı bir çalışma yapılmıştır. Önemli hafıza kaybı olan kişilere bakım verenlere olumlu bakım stratejileri sunmak ve demansla başa çıkmak için metin ve video mesajlar yoluyla web tabanlı bir multimedya müdahalesi kullanılmıştır. Bakım verenler özel endişelerine ve aile üyelerinin hafıza kaybı derecesine göre programı kişiselleştirebilmişlerdir. Müdahaleyi uygulayan bakım verenlerde öz-yeterlilik, destek alma niyeti ve bakım vermenin olumlu yönlerine ilişkin algı önemli ölçüde artmıştır. Deney grubundaki bakım verenlerde kontrol grubuna kıyasla stres, gerginlik, anksiyete ve depresif belirtilerde istatistiksel olarak anlamlı azalmalar saptanmıştır.

Bir başka çalışmada (Marziali ve Donahue, 2006) nörodejeneratif hastalığı olan yaşlı yetişkinlerin bakıcıları için “Başkaları için Bakım” internet tabanlı çevrimiçi grup müdahale modeli uygulanmıştır. Müdahalede internet tabanlı video konferans formatında toplantı yapılmış, grup üyelerinin birbirleri hakkında empatik anlayış geliştirerek karşılıklı destek ve anlayış geliştirmeleri sağlanmıştır. Bu modelin, özellikle hizmetlere çok az erişimi olan veya hiç olmayan uzak bölgelerde yaşayan aile bakıcılarına eğitici ve destekleyici müdahaleler sağlamanın etkili bir yolu olarak umut vadettiği vurgulanmıştır.

Alzheimer’da Bakıcı Sağlığını İyileştirmek İçin Kaynaklar (REACH) (Resources for Enhancing Alzheimer’s Caregiver Health) araştırmasında yer alan çalışmalarda, bakım verenlere yönelik Telefonla Bağlantılı Bakım (Telephone-Linked Care) (TLC), Yapısal Ekosistem Terapisi (Structural Ecosystems Therapy) (SET) ve Bilgisayar Telefonu Entegre Sistemi (A Computer Telephone Integrated System) (CTIS) uygulamaları yer almıştır. Araştırmada yer alan tüm çalışmalar bir bilgi ve sosyal destek bileşeninden oluşmuştur. Uygulamalar sunum ve içerik açısından farklılık göstermiştir (Godwin et al., 2013).

Telefonla Bağlantılı Bakım, bakım verenlere sorunlu davranışları yönetme konusunda stres izleme ve danışmanlık bilgileri sağlayan etkileşimli sesli yanıtı telefon ağı sisteminden, Alzheimer hastalığı uzmanlarına kişisel sesli bağlantılardan, sesli posta telefon destek grubundan ve Demanslı bireyler için bir dikkat dağıtma çağrısından oluşmaktaydı (Mahoney et al., 2003). Araştırma kapsamında yapılan çalışmalardan birinde ilk 6 ay boyunca haftalık, sonraki 2 ay boyunca

iki haftada bir ve son 6 ay için aylık oturumlar şeklinde evde bulunan bakıcılara aile terapisi yapılmıştır. Hem Telefonla Bağlantılı Bakım hem de Yapısal Ekosistem Terapisi ve Bilgisayar Telefonu Entegre Sistemi uygulamaları bakım verenin depresyonunu önemli ölçüde iyileştirdiği (Mahoney et al., 2003) saptanmıştır. (REACH) Telefonla Bağlantılı Bakım müdahalesi daha az bakım deneyimi olanlar için depresyona ek olarak rahatsızlık ve kaygı üzerinde önemli bir etkiye (Mahoney et al., 2003) sahip olmuştur. (REACH) Yapısal Ekosistem Terapisi ve Bilgisayar Telefonu Entegre Sistemi müdahalesi sadece depresyonu iyileştirmekle kalmamış aynı zamanda yüksek sosyal destek müdahalesi ile bakıcı desteğini sürdürmeyi sağlamıştır. Müdahale ayrıca bakıcıların güveninde ve bakım alan kişiye bakım sağlama becerisinde olumlu bir gelişme ile de (Finkel et al., 2007) sonuçlanmıştır. Bilgisayar Telefonu Entegre Sistemi uygulamasının tek başına kullanımının yüksek düzeyde sosyal desteğe sahip olan bakıcıların fazla mesai desteğini sürdürme olasılığını arttırdığı (Finkel et al., 2007) sonucunu ortaya koymuştur. Araştırma kapsamındaki bir çalışmada teknoloji kullanılarak yapılan müdahaleler ile bakım verenlerde zorlanmada önemli bir iyileşme (Beauchamp et al., 2005) bildirilirken diğer bir çalışmada genel gerginlikte hiçbir iyileşme olmadığı ortaya koyulmuştur. Ancak eşler ile olan ilişki geriliminde azalma ve gayri resmi destekle bakıcılar için duygusal gerginlikte azalma olduğu (Bass et al., 1998) rapor edilmiştir.

Çalışmalarda özellikle bakıcıların çevrimiçi eğitime (Glueckauf, et al., 2004; Chiu, et al., 2009) internet tabanlı destek gruplarına (Glueckauf, et al., 2004; Marziali ve Garcia, 2011), bilgisayar aracılı etkileşimli sesli yanıt sistemlerine (Mahoney et al., 2001) ve çevrimiçi beceri geliştirmeye (Lewis et al., 2010) olumlu yanıt verdikleri görülmüştür. Buna ek olarak, teknolojiye dayalı müdahalelere ilişkin çalışmaların çoğu, iş yükünde azalma (Glueckauf, et al., 2004; Chiu, et al., 2009), genel ruh sağlığında iyileşme (Marziali ve Garcia, 2011), bakım verme becerilerine olan güvenin ve yetkinliğin artmasıyla (Lewis et al., 2010) ilgili dikkate değer sonuçlar da ortaya koymuştur.

Tüm bu yararlarının yanı sıra ileri teknolojik müdahaleleri kullanmanın birtakım zorlukları da vardır. Teknolojik yetenekleri gerçek bakım ihtiyaçlarıyla eşleştirmek, insanların teknolojiyle etkileşim kurma tercihlerini anlamak ve teknoloji kullanımıyla ilişkili yeni yükler getirmeden bakıcıların ve yaşlıların hayatlarına nasıl uyum sağladığını öğrenmek (Morris ve Lundell, 2003; Dishman, et al., 2004) bunlardan birkaçıdır.

SONU

Engeli bulunan bireylere bakım verenlere ynelik geliřtirilen teknoloji odaklı mdahaleler ierdikleri bilgi, sahip oldukları (grafik, video ve sesli yanıt gibi) destek saęlayıcılar ve uygunluk bakımından geleceęe ynelik umut vermektedir. stelik mevcut alıřmalar hem yz yze hem de teknoloji tabanlı destekleyici mdahalelerden aile yelerinden oluřan bakıcıların yararlandıęını ve teknoloji odaklı, bilgisayar tabanlı mdahalelerin de engelli bireye bakım veren bakıcılar arasında kabul edilebilir olduęunu gstermiřtir. Ancak bu alıřmaların bazı olumlu sonuları olmasına raęmen, lkemizde řu anda demanslı birey bakıcıları iin teknoloji odaklı mdahaleleri desteklemek veya rtmek iin yeterli kanıt bulunmamaktadır. Gelecekte, lkemizde demanslı bireye bakım veren aile yeleri iin en iyi teknoloji odaklı mdahaleleri aıklıęa kavuřturmak adına alıřmalar planlanmalıdır.

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Bölüm 2

SPONTAN İNTRAABDOMİNAL HEMORAJİNİN NADİR BİR NEDENİ: RENAL HÜCRELİ KARSİNOMUN KARACİĞER METASTAZI

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Giriş

İntraabdominal Hemorajiler(İAH), erken tanı ve tedavi yapılmazsa morbidite ve mortalitesi yüksek olan acil hayati durumlardır. İAH'ya neden olan durumlar iatrojenik veya spontan kanamalardır. İatrojenik nedenler batına penetran ve künt batın yaralanmalardır. Spontan İAH'ya neden durumlar genellikle oral antikoagulan kullanımı, batın içi kist veya tümörün rüptürüne bağlıdır. Olgumuzda , spontan yaygın intraabdominal hemoraji nedeniyle akut karın gelişen ve opere edilen 64 yaşında erkek hastayı takdim edeceğiz

Acil servise ani başlayan karın ağrısı, halsizlik, karın şişliği ile başvuran hastanın anemnezde geçirilmiş ameliyat öyküsü ve bilinen hastalığını olmadığını ifade etmiştir. Yapılan fizik muayenesinde akut karın ve hipovolemik şok tablosu görülmüştür. Acil şartlarda yapılan görüntülemelerde intraabdominal hemoraji rapor yazılan ve acil opere edilen hastanın, kanamaya sebep olan karaciğerde metastatik kitleye bağlı olduğu görülmüştür. Karaciğer kitlenin eksizyonu patolojik değerlendirilmesinde Renal hücreli karsinom metastazı rapor edilmiştir. Özellikle özgeçmiş ve soygeçmişinde akut karın sebep olan etyopatogenetik faktör anamnezi olmayan acil durumlarda karaciğer metastatik kitle rüptürüne bağlı hemoraji akılda tutulmalıdır.

Olgu

Ani başlayan karın ağrısı, halsizlik, karın şişliği ve baş dönmesi şikayetleri ile acil polikliniğimize başvuran 64 yaşında erkek hastanın yapılan fizik muayenesinde hastanın derisi soğuk ve nemli, nabız hızlı ve zayıf karakterde, bulantı kusma, hipotansif ve hipovolemik şok tablosunda olduğu gözlemlendi. Batın muayenesinde yaygın hassasiyet, defans ve rebound gözlemlendi. Laboratuvar incelemesinde Hb 8.6g/dl , Htc: %24 , diğer laboratuvar değerleri normal sınırlarda kabul edildi. Acil şartlarda batın ultrasonografisinde batın içinde yaygın sıvı tespit edildi. Çekilen İ.V. Kontrastlı abdominopelvik bilgisayarlı tomografi(BT)'de aksiyel plandaki BT kesitlerinde karaciğer sol lob segment 4A'da ağırlıklı yerleşimi olan, subkapsüler lokalizasyonlu, anterior duvar bütünlüğü yer yer net olarak izlenemeyen, yoğun heterojen içerikli 58x50 mm boyutlarında ve yapılan dinamik incelemede ise özellikle arterial fazda periferik duvar kontrastlanması gösteren hemorajik kitle lezyon tespit edilmiştir(Şekil-I). Daha sonra yapılan Manyetik rezonans görüntüleme(MRG)'da Aksiyel plandaki İ.V. Kontrastlı Dinamik MRG kesitlerinde bir kısmının kalın mural yapılarında periferik heterojen kontrast tutulumu izlenen renal kistik lezyonlar ve karaciğer sol lob segment 4A'da subkapsüler lokalizasyonlu, dinamik incelemede ise arteriyel fazda parsiyel ring tarzında periferik duvar kontrastlanması

gösteren santrali hemorajik intra-hepatik kitle lezyon görülmüştür(Şekil-II). Genel durumu kötüleşen hastaya acil operasyona karar verildi. Acil şartlarda acil opere edilen yapılan ilk eksplorasyonda batın içinde yaygın yaklaşık 2500 cc hemorajik sıvı olduğu gözlemlendi. Hemorajik sıvının aspirasyonu takiben yapılan detaylı laparotomi muayenesinde karaciğer segment 4’de anterior yüzeyde yaklaşık 5x4x3 cm çapında aktif kanayan tümoral kitle olduğu görüldü(Şekil -III). Karaciğerin diğer bölgelerinde ve batında başka patolojiye rastlanmadı. Karaciğerdeki tümoral kitle total eksizyonu sonrası kanama kontrol altına alındı. Postoperatif takiplerinde herhangi bir komplikasyon görülmeyen hasta şifa ile taburcu edildi. Karaciğerdeki kitlenin histopatolojik değerlendirilmesinde Renal Hücreli Karsinom metastazı ile uyumlu rapor edilmesine takiben hasta ileri tetkik ve tedavi amacıyla medikal onkolojiye yönlendirilmiştir.

Tartışma

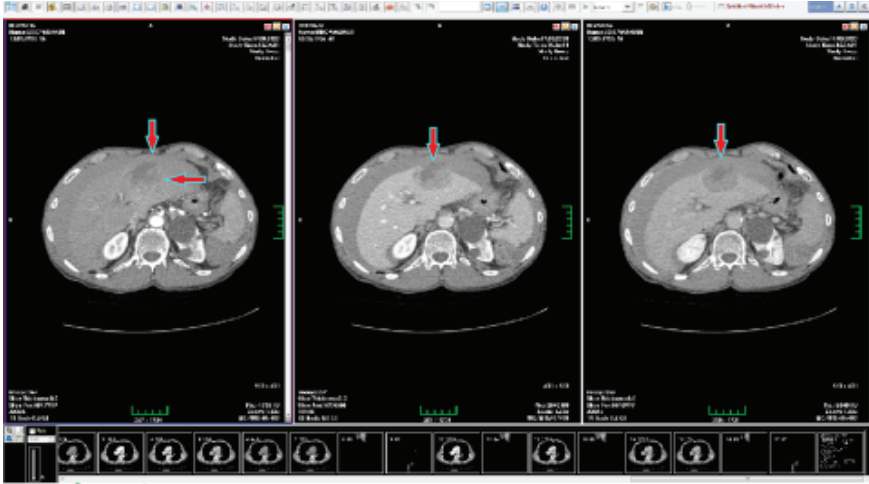
Spontan intraabdominal hemorajiler travmaya bağlı kanamaların aksine nadir görülen acil durumlardır. Spontan İAH hemorajilerin sebepleri arasında oral antikoagulan kullanımı daha fazla olmakla birlikte nadir de olsa batın içi tümoral kitle veya kistin rüptürüne bağlı hemorajiler görülebilir. Profilaktik olarak düzenli oral antikoagulan kullanan hastalarda intraabdominal hemorajiler görülmüştür(1). Aslında tümör kanaması altta yatan bir malignitenin ilk belirtisi olabilir. Spontan tümör kanamasının geniş bir semptom ve klinik prezantasyonu vardır. Kanamanın semptomları spesifik olmamakla birlikte, lokalize veya yaygın karın ağrısı sıktır. Bu semptomlara ilave olarak mide bulantısı, halsizlik ve hipotansiyon ve şok tablosu içerebilir(2). Gastrointestinal kanama ve hematüri sırasıyla gastrointestinal ve üriner sistemin tümörlerinin prezantasyonu olabilir. Asemptomatik olgular yalnızca görüntüleme tesadüfen fark edilebilir ve erken tedavi edilmezse hipovolemik şoka kadar ilerleyen ölümcül tablo ile karşımıza çıkar. Bizim olgumuzda kesin tanı intraoperatif ve histopatolojik değerlendirme sonucunda konulmuştur. Spontan tümör kanamasının mekanizması tam olarak bilinmemektedir ve muhtelemen birden fazla faktöre bağlıdır. Hepatosellüler kanser, erişkin yaş grubunda en sık görülen primer karaciğer tümörüdür. Genellikle siroz zemininde gelişir. Spontan intrahepatik veya intraabdominal kanama, Hepatosellüler kanserin iyi bilinen bir komplikasyonudur(3). Metastazlar en sık görülen habis tümörlerdir. Karaciğere metastaz yapan en sık görülen primer tümörler kolorektal, meme, mide, pankreas ve akciğerdir(4). Çok sayıda farklı primer tümörler spontan kanamaya sebep olurken en sık akciğer, renal hücreli karsinom ve melanom gibi hipervasküler lezyonların karaciğer metastazlarında olmaktadır(5). Altta yatan bir maligniteye bağlı kanamaların sebepleri arasında; koagülopatiye bağlı kanama, salınan büyüme faktörlerinden kaynaklanan neovaskülarizasyon,

metastatik kemik iliği invazyonu ve mikroanjiopatiye bağlı olarak gelişir. Lokal damar sistemi üzerindeki etkilerin de kanamada muhtemelen rolü vardır. Tümör kitlesi tarafından mekanik baskı veya iltihaplanma reaksiyonundan kaynaklanan vasküler erozyon, damarların yırtılmaya yatkın hale getirebilir(6). Karaciğerin diğer primer tümörleri olan hepatik adenomlar, hemanjiyomlar ve anjiosarkomlar nadirde olsa spontan batın içi kanamaya sebep olurlar.

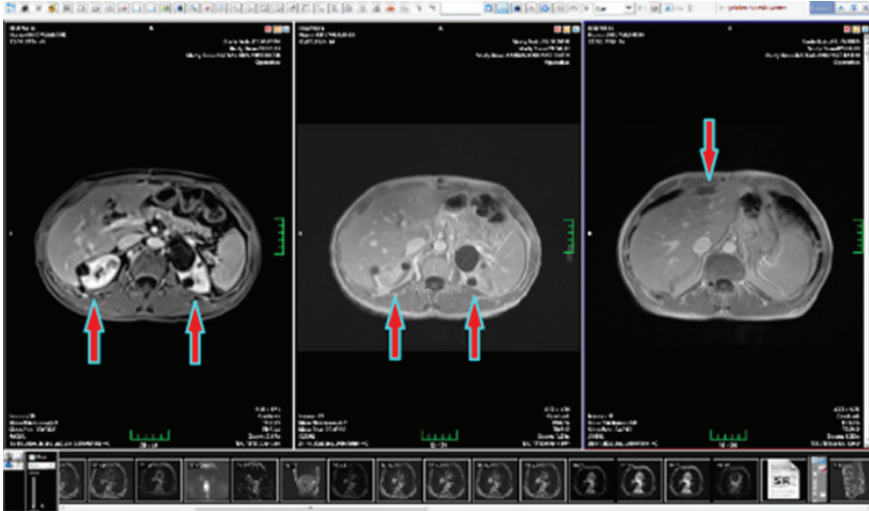
Ultrasonun intraabdominal kanamanın değerlendirmesinde, stabil olan hastalarda rutin kullanıma girmiştir. Ultrasonun avantajı kolay kullanılabilirlik, noninvaziv ve FAST(Travma için odaklanmış Sonografi) tekniği ile karın içi serbest sıvının tanımlanmasında yüksek duyarlılık ve özgüllük göstermesidir. Bilgisayarlı tomografi(BT) spontan tümör kanaması değerlendirmesinde hızlı ve yaygın kullanılabilirliği nedeniyle ilk tercih edilebilir. Hastalar özgü olmayan abdominal semptomlarla başvurabildiğinden, çoğunlukla tek fazlı ve kontrastlı BT ile tanı konabilir. Manyetik rezonans görüntüleme(MRG) spontan tümör kanamasında ilk tercih edilecek modalite olmamasına rağmen tümör kanamasının değerlendirmesinde önemli bir role sahiptir. Ayrıca MRG abdominal malignitelerin, diğer tümörlerin saptanmasında ve altta yatan kitleyi komşu kanamayı ayırmaya yardımcı olduğunu görülmüştür(7).

Sonuç

Karaciğerin primer ve sekonder tümöral lezyonların tedavisinde cerrahi rezeksiyon ve transplantasyon halen optimal tedavi tercihleri olarak karşımızda bulunsa da; olguların büyük bir bölümü tanı konduğu anda cerrahi şansını kaybetmiş durumdadır. Bizim olgumuzda olduğu gibi nadir de olsa renal hücreli karsinomun karaciğer metastazına bağlı intraabdominal hemoraji ile karşımıza çıkmaktadır.



ŞEKİL – I İ.V. Kontrastlı aksiyel plandaki BT kesitlerinde karaciğer sol lob segment 4A'da ağırlıklı yerleşimi olan, subkapsüler lokalizasyonlu, anterior duvar bütünlüğü yer yer net olarak izlenemeyen, yoğun heterojen içerikli (iç yapısı 29-33 HU dansitede ölçülen) 58x50 mm boyutlarında ve yapılan dinamik incelemede ise özellikle arterial fazda periferik duvar kontrastlanması gösteren hemorajik kitle lezyon tespit edilmiştir.



ŞEKİL-II Aksiyel plandaki İ.V. Kontrastlı Dinamik MRG kesitlerinde bir kısmının kalın mural yapılarında periferik heterojen kontrast tutulumu izlenen renal kistik lezyonlar ve karaciğer sol lob segment 4A'da subkapsüler lokalizasyonlu, dinamik incelemede ise arteriyel fazda parsiyel ring tarzında periferik duvar kontrastlanması gösteren santral hemorajik intra-hepatik kitle lezyon oklar ile gösterilmektedir.

řekil III: Renal Hücresel Karsinomun Karacięer Metastazının makroskopik görünümü



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Bölüm 3

COMPUTED TOMOGRAPHY (CT) FINDINGS OBSERVED IN COVID-19

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1. INTRODUCTION

Covid-19 (coronavirus disease 2019) is a viral infectious disease caused by a strain of coronavirus, Severe Acute Respiratory Syndrome Coronavirus 2 (**SARS-CoV-2**). It was declared as a pandemic by the World Health Organization (WHO) on 11 March 2020 **(1)**. Although multisystemic involvements have been recognized as the pandemic progresses, the primary involvement is the upper respiratory tract disease progressing to pneumonia in most of the cases. Definitive diagnosis is made by a positive real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) test on respiratory specimens or gene sequencing **(2)**. However, the results are not available immediately to allow quick assessment of the patients. Chest computed tomography (CT) with its high sensitivity plays an important role in the management of the patients by revealing the pneumonia instantly, but it is not recommended in the screening and diagnosis of Covid-19 due to the lack of specificity. Although the rRT-PCR test is very specific, its lower sensitivity may be associated with false negative initial results making chest CT especially important in these patients by demonstrating typical findings of the pneumonia and providing early management. Chest CT is also useful in the identification of the alternative diagnosis of similar clinical presentations in the acute settings. In addition, it is valuable for the detection of complications during the follow up. We present the most frequently encountered chest CT findings of Covid-19 pneumonia in our patients with rRT-PCR test-confirmed Covid-19. In addition, we presented less frequently described pulmonary and extrapulmonary imaging findings of the disease observed in our patients.

2. EARLY STAGE CHEST CT FINDINGS OF Covid-19 PNEUMONIA

A wide variety of chest CT findings are encountered in patients with Covid-19 pneumonia which are neither pathognomonic nor specific for Covid-19 pneumonia. However, some of these findings are very commonly observed as the typical features for the Covid-19 pneumonia. In addition, although rarely encountered, some characteristic patterns are observed in Covid-19 pneumonia more frequently than the other pathologies.

2.1. Ground Glass Opacity (GGO)

GGO is resulted from partial filling/collapse of the airspaces or interstitial thickening and appears as an area of increased attenuation with preserved bronchovascular structures on CT. GGO is the most common and the earliest chest CT feature of Covid-19 pneumonia. Peripheral/subpleural distribution is more common and the lower lobes and posterior

parts are affected more frequently. In majority of the cases bilateral and multifocal involvement is observed (3,4)(figure 1).

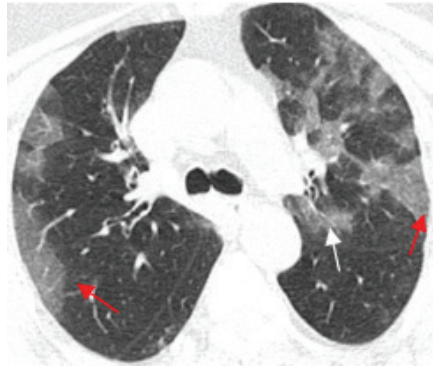


figure 1: axial chest CT image shows peripheral subpleural (red arrows) and central peribronchovascular patchy GGOs (white arrow).

2.2. Consolidation

Consolidation is resulted from complete filling of the alveolar airspaces by fluids or cells and manifested as increased attenuation areas with obscuration of underlying bronchovascular markings on CT. Consolidative infiltrations have been reported as a worse prognostic factor seen in death patients more frequently than survival patients (3) (figure 2).

Consolidations usually accompany the GGOs, both of which are usually patchy in shape, sometimes showing confluence but nodular/round-shaped opacities with varying sizes can also be identified (5). These infiltrations may show a totally solid appearance or may have a surrounding areas of GGO called “halo sign” (4, 6) (figure 3, 4).



figure 2:axial chest CT image shows peripheral subpleural patchy GGOs (white arrows) and consolidation (red arrow).

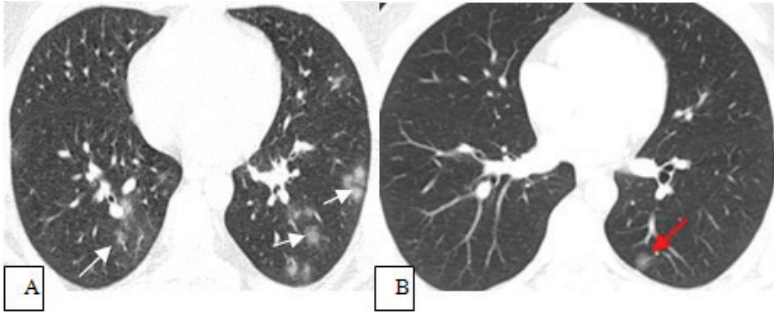


figure 3: A,B) axial chest CT images show nodular multiple GGOs in a patient (A, white arrows) and a solitary GGO in another patient (a ground glass nodule) (B, red arrow)

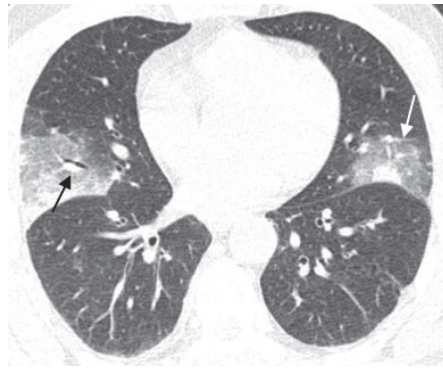


figure 4: axial chest CT image shows a central consolidation surrounded by GGO which is called as “halo sign” (white arrows). Note also the presence of air bronchogram sign and prominent pulmonary vessel sign within the GGO in the right lung (black arrow)

2.3. Reticulation

Reticulation is defined as thickening of the inter/intralobular septa. In Covid-19 pneumonia, it is observed more commonly with superimposition on GGOs resulting in **crazy paving pattern** (5, 7) (figure 5). If the thickened interlobular septa are superimposed on the triangular or angular GGOs forming a web like appearance, then it is called as **spider web sign** (7)(figure 6).

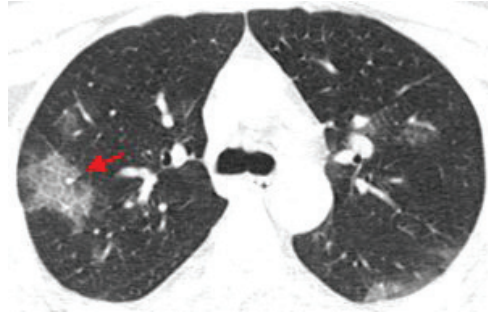


figure 5:axial chest CT image shows thickened intralobular septa superimposed on GGOsresulting incrazy paving sign(red arrow).

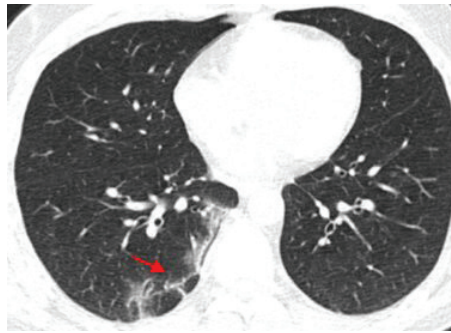


figure 6: axial chest CT image shows thickened inter/intralobular septa superimposed on GGOs forming a web like appearance, which is called as spider web sign (red arrow).

2.4. Associated Findings

In Covid-19 pneumonia, the frequently observed perilesional CT findings in association with the GGOs and consolidations are **air bronchogram sign** and **prominent pulmonary vessel sign (4,6,8)**. The classical definition of air bronchogram is air filled patent airway within a lesion area. However studies about Covid-19 autopsy series demonstrated this findings as low attenuation airways filled with gelatinous mucus instead of air and often associated with some degree of bronchioloectasis/ bronchiectasis. (9).**Pulmonary vascular prominence** is the enlargement of the pulmonary vessels within or around the GGOs and consolidations. It is resulted from inflammatory capillary wall edema. It is a quite common finding in many cases of Covid-19 pneumonia. It has been revealed that it is one of the more prevelant finding when compared with non-Covid viral pneumonia (10, 11)(figure 7).

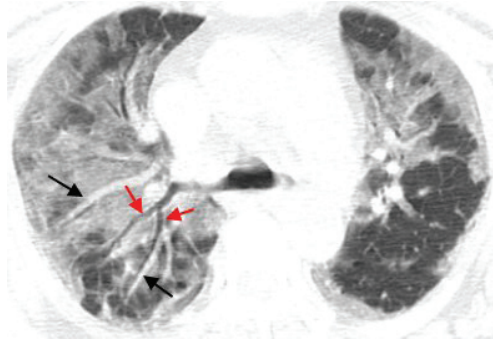


figure 7: axial chest CT image shows air bronchogram sign (red arrows) and prominent pulmonary vessel sign (black arrows) within the GGO

2.5. Covid-19 pneumonia in cases with emphysema

In patients with emphysematous pulmonary parenchyma, the superimposed Covid-19 pneumonia creates a different appearance that not seen in the normal pulmonary parenchyma. It is characterized with the increased concentration of consolidations at the circumferences of the emphysema areas and is resembled the swiss cheese sign (12) (**figure 8**).

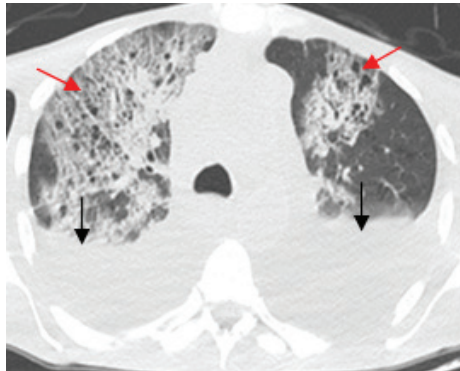


figure 8: axial chest CT image shows increased concentrations of consolidations surrounding the emphysema areas (red arrows) resulting in the swiss cheese sign. Bilateral presence of large amount of pleural effusion in this patient is also showed (black arrows)

3. ADVANCED (PROGRESSIVE AND PEAK) STAGE CHEST CT FINDINGS OF COVID-19 PNEUMONIA

In the classical course of **COVID-19** pneumonia four stages are usually observed; the early stage lasting approximately till the 5th days, the progressive stage (about 5th to 8th days); aggravation and extension of the lesions, the peak stage (about 9th to 13th days); a more slower increase

toward the maximum involvements, the recovery stage which may or may not be accompanied by irreversible pulmonary (5, 13). However, a distinct pattern and time course of evolution is observed depending on the severity of the disease and the state of the underlying pulmonary parenchyma. It is worth to note that, the expected progression of the chest CT findings during the classical of the disease should be differentiated from the findings of poor prognosis. Therefore, if there is no clinical/laboratory deterioration CT examination would be unnecessary and may be misleading by showing aggravation of the imaging findings of the classical course in some cases. However, for the detection of complications like pulmonary embolism during the disease course, chest CT plays a crucial role.

3.1. Organising Pneumonia

In the progressive and peak stages of the disease, in addition to the increase in GGOs (with or without reticulation) & consolidations, **organizing pneumonia pattern** may develop and appears usually as irregular, frequently linear consolidative opacities (5, 13)(figure 9). It is a common but a nonspecific pattern of alveolar inflammation since it can be caused by various infectious and noninfectious etiologies. In association with organising pneumonia pattern, **bronchial changes** including **bronchial wall thickening** and **bronchiectasis** may occur, due to the inflammatory damage of bronchial wall. These changes have been more frequently reported in critical cases (4, 6, 14) (figure 10).

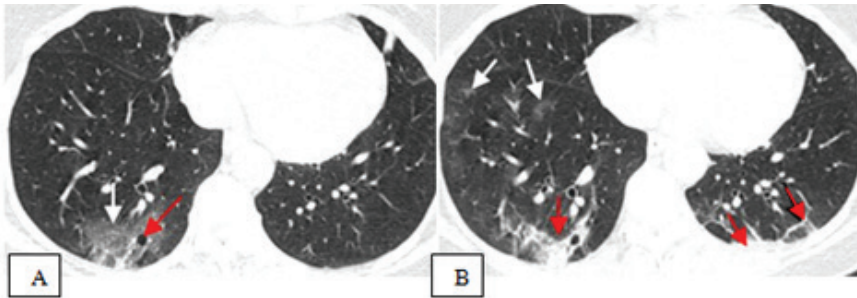
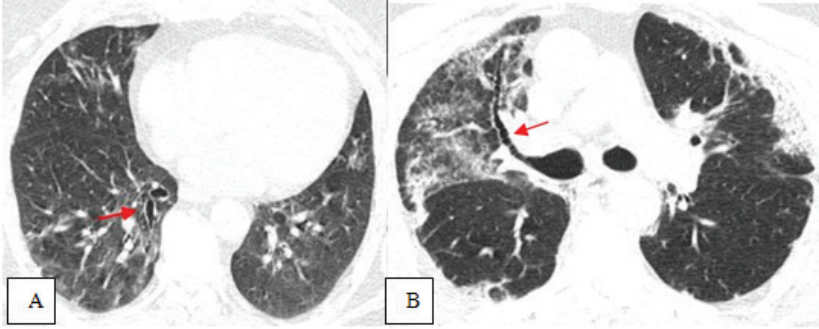


figure 9: A,B) axial chest CT images of a patient at presentation (A) and follow-up after 10 days performed due to clinical deterioration (B) show the evolution of the GGO into organising pneumonia with the development of irregular consolidations (red arrows in A and B). Newly developed GGOs on follow up are also seen (white arrows in B).

figure 10: (A, B) axial chest CT images show dilated bronchi in a patient (red arrow in A) and a distorted bronchi in another patient (red arrow in B).



3.2. Reversed Halo Sign

A **reversed halo sign**, also known as **atoll sign** indicates an area of GGO surrounded by a complete/incomplete ring of consolidation (**figure 11**). It is actually a nonspecific pattern of organising pneumonia and has been reported variably in patients with Covid-19 (**15**). The mechanism of this sign is not clear. Some studies argued that it depicts disease progression that makes the consolidation developed around the GGO. In contrast, others opined that it is related with absorption in the lesion leaving a decreased attenuation in the center.

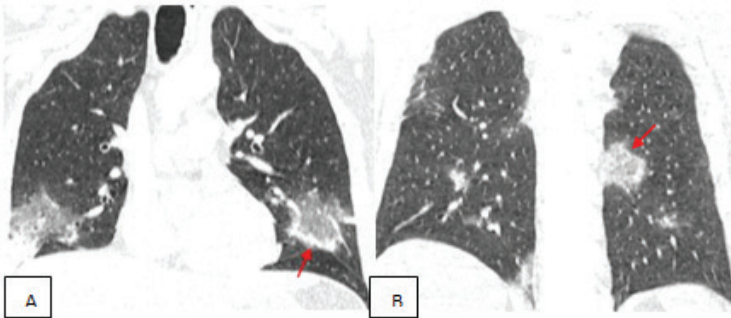


figure 11: (A, B) coronal chest CT images show an area of GGO surrounded by a complete/incomplete ring of consolidations, resulting in reversed halo sign in two different patients (red arrows).

3.3. Perilobular Pattern

A **perilobular pattern** is another type of organising pneumonia, which is composed of a polygonal shape linear/curvilinear opacities thicker than the linear opacities of reticulations(**16**) (**figure 12**).

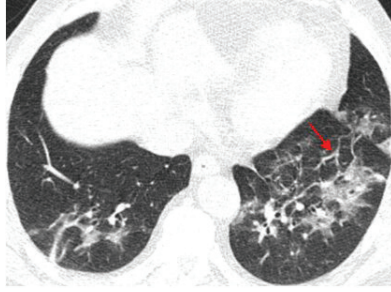


figure 12: axial chest CT image shows a polygonal shape linear/curvilinear consolidations which is called as peribular pattern of organising pneumonia (red arrow).

4. RECOVERY STAGE (ABSORPTION PHASE) CHEST CT FINDINGS OF Covid-19 PNEUMONIA

During the recovery stage, the GGOs and consolidations are gradually reabsorbed with or without persistent pulmonary changes. The healing of the pulmonary inflammation may be ended with total recovery of the pulmonary parenchyma or may leave behind persistent pulmonary changes like **fibrosis** and **cystic formations**.

4.1. Pulmonary Fibrosis

Pulmonary fibrosis which is defined as scarring of the lung interstitium with or without associated tractional bronchiectasis. Whether this indicates a good prognosis due to control and recovery of the ongoing pulmonary inflammation or worse prognosis due to putting the patient at risk of chronic interstitial diseases in the future **(13)**. **Fibrotic streaks** are encountered usually due to scarring (fibrosis), but it may also be a finding of pulmonary edema in the early stages **(17)(figure 13)**. **A subpleural curvilinear line**, a curvilinear opacity with a few millimeters of thickness, close to the pleural surfaces, is among the rare CT features observed in Covid-19 pneumonia and may reflect fibrosis or can also be seen due to pulmonary edema in the proliferative stages **(7, 17) (figure 14)**.

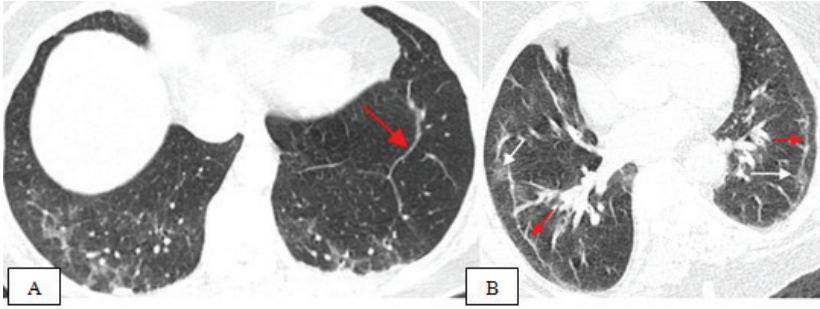


figure 13: *A,B)axialchest CT images show a thin lineer consolidative opacity, which is called as a fibrotic streak that can be seen both in recovery stages due to fibrosis (red arrow in A) and also in proliferative stages due to pulmonary edema (red arrows in B). In the second patient the GGOs of the proliferative stages are also shown (white arrows in B)*

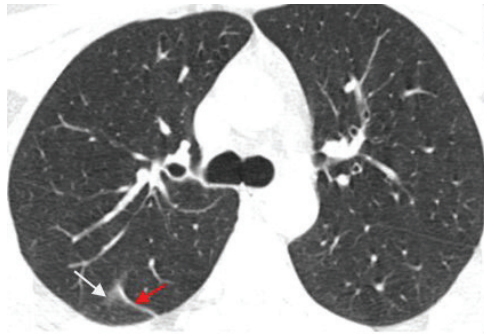


figure 14: *axialchest CT image shows a subpleural curvilinear opacity with a few milimeters of thickness, which is called as subpleural curvilinear line (red arrow). The associated GGO of proliferative stage in this patient is also seen (white arrow).*

4.2. Cystic Air Spaces

Cystic air spaces may also develop during the recovery stage of the pulmonary infiltrations, usually in the subpleural areas due to the predominant involvement of the lesions in the subpleural regions (**figure 15**). These subpleural cystic air spaces are assumed to be associated with increased risk for spontaneous pneumothorax (**18**). They should not be confused with air bubbles within the lesion that disappear with the reabsorption of GGOs and consolidations at the recovery phase or may

represent pathological dilatation of physiological air spaces during the proliferative phases (13).

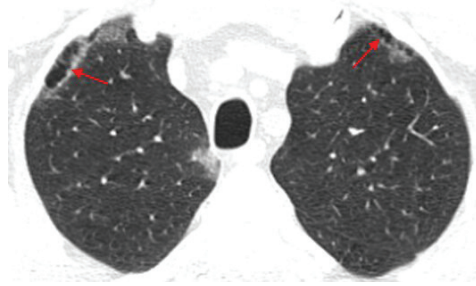


figure 15: axialchest CT image shows bilateral subpleural cystic air spaces developed during the absorption of the GGOs in the late stages (red arrows).

5. EXTENT OF THE DISEASE

Extent of the disease at presentation can widely vary ranging from unifocal small nodular involvement, to severe, diffuse pneumonia resulting in **white lung** appearance on chest CT (**figure 16**). In addition, the progression may occur in a very short time on re-examination CT scans progressing to white lung after initial focal presentations in a few days.

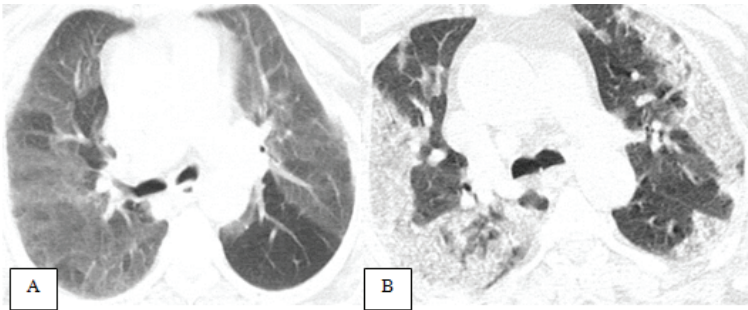


figure 16: A, B)axialchest CT images show diffuse GGOs (A) and consolidations (B) resulting in white lung appearance at presentation in two different patients.

6. EXTRAPARENCHYMAL FINDINGS ON CHEST CT

6.1. Pleural and Pericardial Manifestations

Isolated extraparenchymal manifestations are rare to be identified in chest CT of Covid-19 patients and usually observed concomitantly with pulmonary disease. Pleural pathologies are particularly more frequent and include **pleural thickening** and **pleural effusions**. **Pleural thickening** is seen in the pleura adjacent to Covid-19 pulmonary infiltrations or

interlobar pleural parts can be thickened (**figure 17**). **Pleural effusion** has been variably reported in Covid-19 patients and is thought to be associated with poor prognosis (**8**) (**figure 8, 18**). Complicated pneumonia with **spontaneous pneumothorax** is rare (**figure 19**). It may also occur in the recovery stages or later as a result of subpleural cystic formations, causing a potential risk to rupture into the pleural cavity (**18**). **Pericardial effusion** is also rare and may be associated with myocardial injury (myocarditis) or can be the sign of acute pericarditis (**figure 20**).

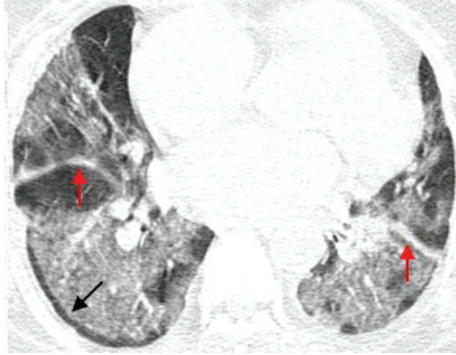


figure 17: axial chest CT image shows interlobar pleural thickening (red arrows). Also note the presence of subpleural sparing seen in association with the right lower lobe GGO (black arrow)

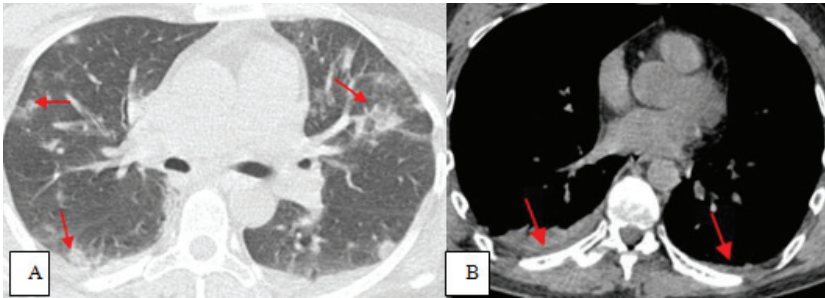


figure 18: A,B) axial chest CT images show bilateral areas of GGOs (red arrows in A) associated with small amounts of pleural effusion in the same patient (red arrows in B).

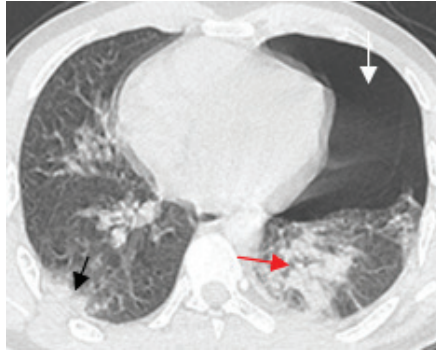


figure 19:axial chest CT image shows bilateral areas of peripheral subpleural (black arrow) and central peribronchovascular consolidations (red arrow) complicated with left sided pneumothorax during the proliferative phase of the Covid-19 pneumonia (white arrow).

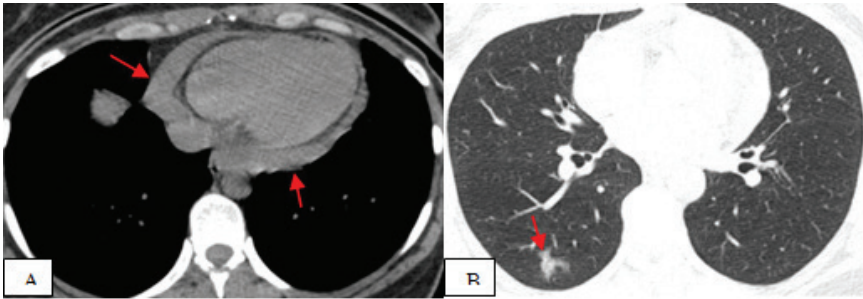


figure 20: A,B) axial chest CT images at mediastinal window (A) show pericardial effusion greater than 1.5 cm in thickness that developed during the Covid-19 pneumonia (red arrows in A). Note the peripheral pneumonic consolidation at parenchymal window (B) in the same patient (red arrow in B).

6.2. Mediastinal Lymphadenopathy

Mediastinal lymphadenopathy with short axis diameter greater than 1 cm is rare to be observed in association with Covid-19 pneumonia. However, highly sizeable mediastinal lymph nodes have been reported in Covid-19 patients, particularly in severe cases (7, 19). (figure 21).

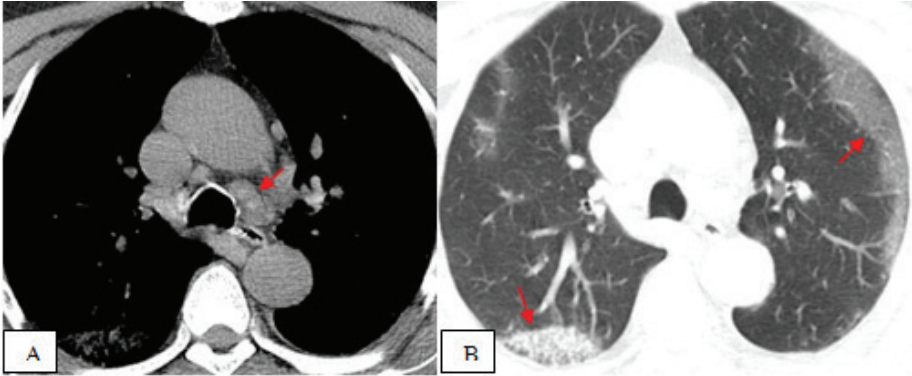


figure 21: A,B)axial chest CT images at mediastinal window (A) shows mediastinal LAP greater than 1 cm in short axis diameter (red arrow in A). Note the peripheral subpleural GGO and consolidation at parenchymal window in the same patient (red arrows in B).

6.3. Pulmonary Thromboembolism

Covid-19 patients are at increased risk of both microcapillary and large vessel thrombosis due to disturbed coagulation functions making the patients prone to acute thromboembolic complications (20). The most frequent of these complications are **deep vein thrombosis** and **pulmonary embolism**(figure 22). Therefore, in cases with clinical suspicion for pulmonary embolism, pulmonary CT angiography (CTA) should also be performed. In addition, cerebral and myocardial acute ischemic complications are also common especially in patients with pre-existing cardiovascular risk factors(21).

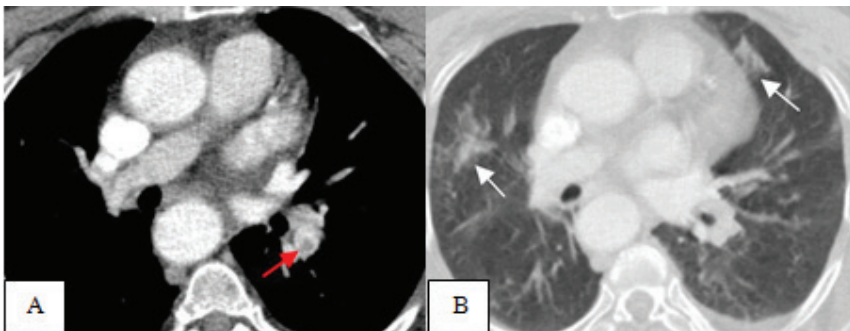


figure 22: A,B) contrast enhanced axial chest CT images at show an acute pulmonary embolism in the left interlobar artery (red arrow in A). Note also the presence of peripheral GGOs in the same patient (white arrows in B).

7. UNEXPECTED CT MANIFESTATIONS IN COVID-19

Focal segmental or lobar consolidations, multiple small **centrilobular nodules** and **tree in bud** appearances are not expected to be identified in viral pneumonia and so also in Covid-19 pneumonia. However, **superinfections** are common particularly in severely ill Covid-19 patients with much greater frequency in the intensive care unit (ICU). Although reported in a few cases of Covid-19 pneumonia, **pulmonary cavitation** is also uncommon to be identified in viral pneumonia (22, 23). In these cases, bacterial superinfection should always be considered before assuming the necrotising pneumonia as the consequence of Covid-19 itself, as in our one case demonstrating a large sized pulmonary cavity when he was in ICU, who was evaluated with bronchoscopy that revealed *Acinetobacter* in bronchoalveolar lavage (BAL) culture (24) (figure 23). A relatively rare CT feature is **air bubble sign** also named as **vacuolar sign** which refers to a small, round shaped air space within the lesion (figure 24). It should also not be confused with a pulmonary cavity. The differentiation can be made with the much thinner walls of these air spaces that can be encountered as a part of the reabsorption of GGOs and consolidations during the recovery phase or may represent pathological dilatation of physiological air spaces (13).

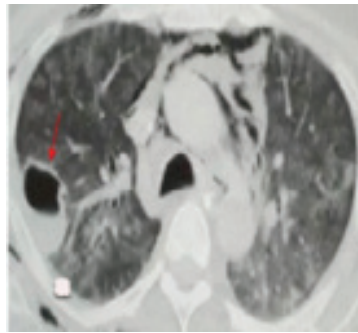


figure 23: Axial chest CT image shows a pulmonary cavity (red arrow) in the right lung in association with GGOs of Covid-19 pneumonia. It was diagnosed with superinfection with growth of *Acinetobacter* in (BAL) culture. Pneumomediastinum and subcutaneous emphysema following bronchoscopy is also visible.

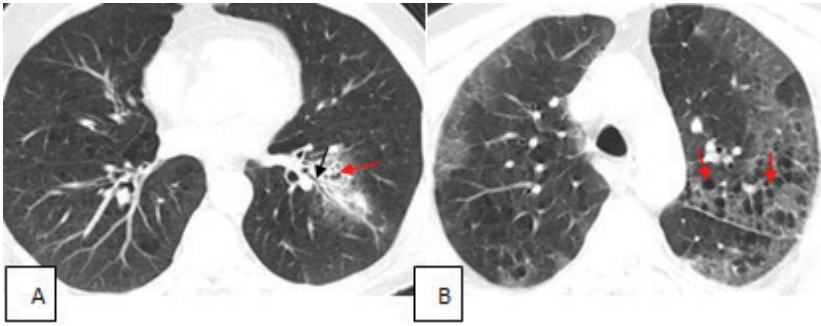


figure 24:A,B) axial chest CT images show multiple air bubbles within the peribronchovascular consolidation (red arrow in A) and within the peripherally located GGOs (red arrows in B). The air bronchogram sign is also visible within the consolidation (black arrow in A).

8. MIMICKERS OF COVID-19 PNEUMONIA ON CHEST CT

Especially in elderly patients with comorbidities like cardiovascular diseases with similar clinical presentations, some chest CT manifestations can mimic Covid-19 pneumonia. Among many others, **acute pulmonary edema** is the most frequently encountered noninfectious mimicker of the chest CT manifestations of Covid-19 pneumonia. The GGOs of acute pulmonary edema is usually accompanied by smooth interlobular septal thickening. However, these are more centrally distributed and associated with higher prevalence of pleural effusion and mediastinal lymphadenopathy (**figure 25**).

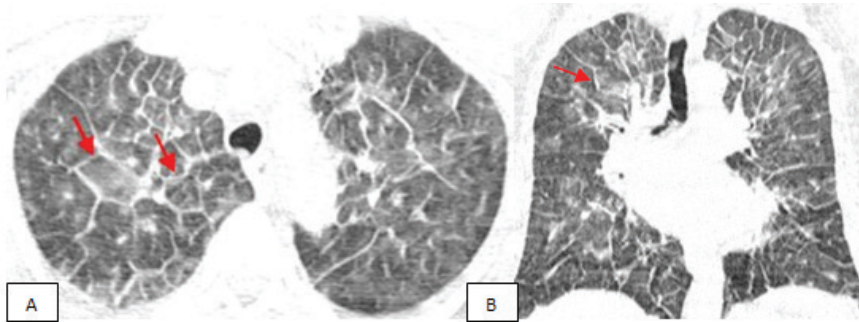


figure 25: Axial (A) and coronal (B) chest CT images of a patient with congestive heart failure show diffuse smooth interlobular septal thickening delineating secondary pulmonary lobules (red arrows in A and B) associated with areas of GGOs but predominating in the central parts.

A focal ground glass nodule can be an initial finding of early stages of Covid-19 pneumonia, but it may cause a diagnostic challenge particularly

when a solitary ground glass nodule is identified. Because, a solitary ground glass nodule may also be an incidentally found preinvasive lesion of the lung. For **ground glass nodules** measuring less than 5 mm, **atypical adenomatous hyperplasia** and for larger ones **adenocarcinoma in situ** should be kept in mind among the differential diagnoses. If they do not disappear after the treatment, follow up imagings with 3 months interval could be recommended (**figure 26**).

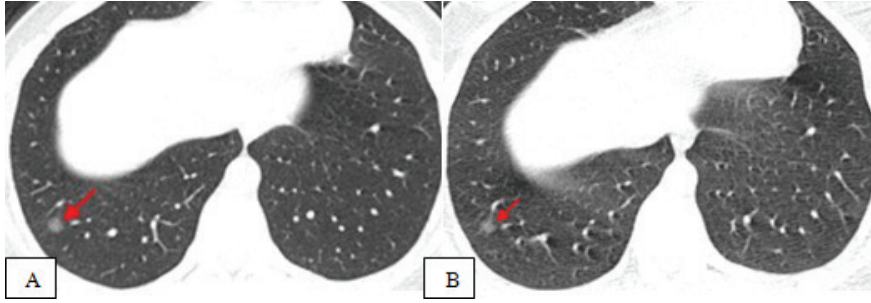


Figure 26: A,B, Axial chest CT images of a young female show a solitary ground glass nodule at presentation (red arrow in A) which is very similar to that seen in the Covid-19 pneumonia shown in figure 3b. She did not show any clinical progression and follow up imaging was recommended with consideration of an incidentally found atypical adenomatous hyperplasia. 3 months later, the re-examination chest CT showed no change in the lesion (red arrow in B).

9. NON-THROMBOTIC EXTRAPULMONARY COMPLICATIONS

Treatment related complications may occur in Covid-19 patients. The most common treatment related complication is hemorrhages in these patients. The increased risk of both microcapillary thrombosis and large vessel thrombosis are increased prophylactic anticoagulation especially in severe cases is recommended. However, in such critical patients hemorrhagic complications in various parts of the body including cerebral or abdominopelvic should also be considered, as one of our case presenting with right flank pain during the course of Covid-19 pneumonia whose abdominopelvic CT revealed a catastrophic large sized retroperitoneal hematoma. It may also involve the psoas muscle reported in some cases in the literature (25) (**figure 27**). In Covid-19 the state of immunosuppression and endotheliitis predispose to bacteremia from asymptomatic bacterial colonizations that may result in various severe pyogenic extrapulmonary complications(26). Secondary spinal infections including spondylodiskitis have been reported in few cases in the literature some of which complicated with epidural abscess (27).

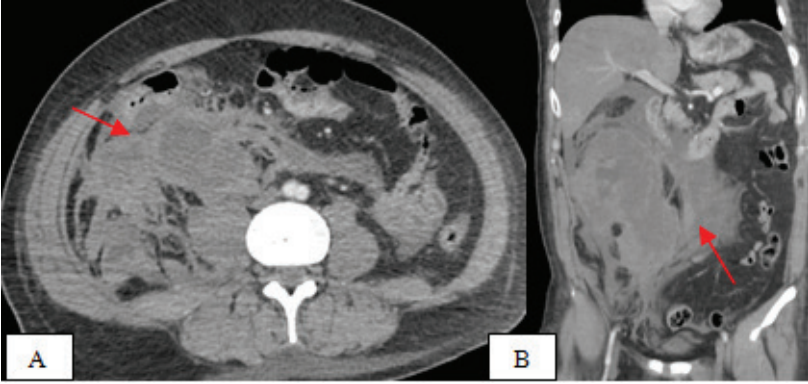


figure 27: Contrast enhanced axial (A) and coronal (B) abdominopelvic CT images of a patient with Covid-19 pneumonia presenting with a catastrophic right sided retroperitoneal hematoma that occurred under anticoagulant prophylaxis (red arrows in A and B).

10. CONCLUSION

Chest CT manifestations of Covid-19 pneumonia is not specific for Covid-19. The most common and main chest CT manifestations of Covid-19 pneumonia in our patients are multifocal ground glass opacities (GGOs) with predominantly peripheral/subpleural distribution at the presentation, with second most frequent is reticulation and consolidation. Perilesional findings including air bronchogram sign and prominent pulmonary vessel sign are frequently observed in association with these main lesions of Covid-19 pneumonia. In the course of the disease, CT manifestations show a distinct pattern and time course of evolution in survival patients. Complete reabsorption of the pulmonary infiltrations or persistence with irreversible changes as areas of pulmonary fibrosis or parenchymal cystic formations may occur depending on the severity of the disease and the state of underlying pulmonary parenchyma. Apart from the severe pneumonia, the increase risk of thrombosis may complicate with both severe acute thrombo-ischemic complications and also hemorrhagic complications in association with prophylactic anticoagulation. In addition, the state of immunosuppression and endothelitis make susceptible the Covid-19 patients for remote pyogenic infections via hematogenous spread from previously asymptomatic colonizations.

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Bölüm 4

OXIDATIVE STRESS: FREE RADICALS AND ANTIOXIDANTS

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Introduction

Oxidative stress is the imbalance between the production and accumulation of free radicals in a biological system and the ability to easily detoxify reactive intermediates or repair damage (Rao et al., 2011; Sevindik, 2019). Living organisms create a reducing environment in their cells, and this environment is protected by reduced enzymes (Xu et al., 2009; Jin et al., 2013). Toxic conditions can occur through the production of peroxides and reactive oxygen species (ROS) that damage all components of cells, including protein, lipid and DNA, through ongoing disturbances in the redox tissue state (Du Plessis et al., 2008; Kakadiya, 2009; Sevindik et al., 2020).

Chemically, oxidative stress is associated with increased production of oxidizing compounds or a decrease in the effectiveness of antioxidant defenses such as glutathione (Leeuwenburgh and Heinecke, 2001). The effects of oxidative stress that will occur depend on the magnitude of these changes. Living cells can suppress or eliminate minor irregularities (Du Plessis et al., 2008). On the other hand, cell death can be seen in oxidative stress situations that may occur more severely. In this context, even moderate oxidation can trigger apoptosis and more intense stress may cause necrosis (Kakadiya, 2009).

Oxidative stress occurs in living organisms when the antioxidant defense system is insufficient against free radicals (Aruoma, 1988; Bal et al., 2019). ROS specifically attack and oxidize cell components such as polyunsaturated lipids, proteins and nucleic acids. This causes tissue damage and, in some cases, regional injuries (Figure 1) (Kelly, 2003).

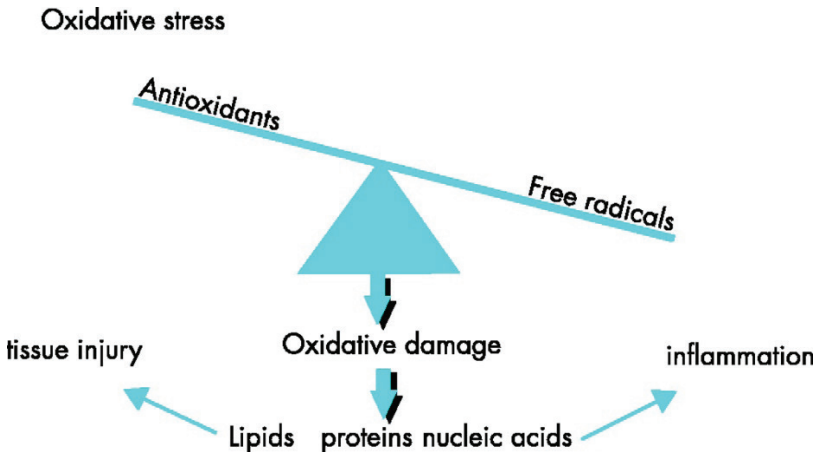


Figure 1. Oxidative stress (Kelly, 2003).

The ground state oxygen in the atmosphere is quite distinctive from other gaseous elements by having two unpaired electrons. In this context, as long as it is not activated, this feature makes it less likely to participate in reactions with organic molecules (Ahmadi et al., 2008). The role of oxygen in aerobic life on earth basically plays an active role not only in energy metabolism and respiration, but also in many diseases and degenerative conditions (Kakadiya, 2009).

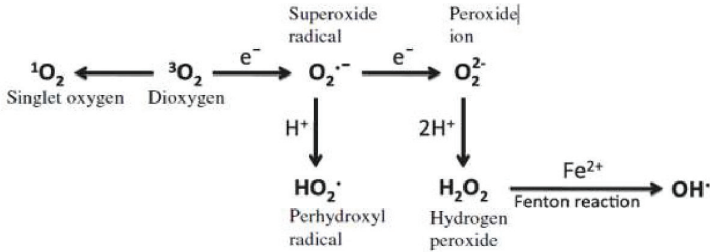


Figure 2. Reactive oxygen species (Abouzari and Fakheri, 2015).

Figure 2 shows the monovalent reduction of oxygen to form superoxide (O₂^{•-}), hydrogen peroxide (H₂O₂), hydroxyl radical (OH[•]) and finally water. H₂O₂ easily penetrates the membranes and is not divided into sections within the cell with this feature. A large number of enzymes are used as substrates in oxidation reactions involving the synthesis of organic molecules. Fenton discovered the oxidizing potential of H₂O₂ mixed with ferrous salts in the late 19th century (Figure 3). (Mckersie and Ya’acov, 1994). In the following years, the H₂O₂ radical was defined as the species responsible for oxidation in these reactions.

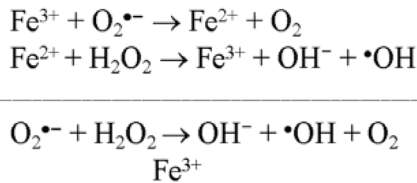


Figure 3. Fenton reactions (Rammouz et al., 2011).

The presence of ferrous ions in living organisms limits the reaction rate. In contrast, the recycling of iron from ferric to ferrous with a reducing agent can lead to the formation of hydroxyl radicals (Gligorovski et al., 2015). The suitable reducing agent is superoxide (O₂^{•-}) that participates in the general reaction as two half-reactions as seen in Figure 3. Due to all these conditions, in the presence of iron in the environment (O₂^{•-}) and H₂O₂, it interacts with the hydroxyl radical and initiates the

organic substrate oxidation. In addition, some metals other than iron can be involved in electron transfer reactions by participating in the cycle between oxidized and reduced states (Mckersie and Ya'acov, 1994; Rammouz et al., 2011).

Oxidation reactions of organic substances are seen in two possible ways. These are addition and abstraction reactions (Huysen, 1961). In addition reactions, the hydroxyl radical is added to an organic substrate, forming an oxidized product. This product then forms a hydroxylated product that is further oxidized by iron ions. In addition, this product has the ability to be broken down to form cross-linked products (Figure 4) (Mckersie and Ya'acov, 1994; Kakadiya, 2009; Chuang et al., 2016).

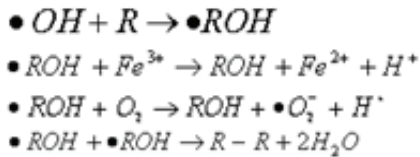


Figure 4. Addition reactions

In the Abstraction reaction, another organic substance oxidation reaction, the hydroxyl radical oxidizes water and an organic radical forming the organic substrate. The second product formed has a single unpaired electron. In this case, it can react with oxygen in the ternary ground state. The addition of ternary oxygen to the carbon radical can lead to the formation of a second carbon radical. This reaction can easily separate hydrogen from another organic molecule. These chain reactions are the reason why oxygen-free radicals cause more damage than their initial concentrations (Figure 5) (Mckersie and Ya'acov, 1994; Kakadiya, 2009; Chuang et al., 2016).

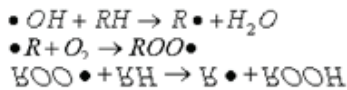


Figure 5. Abstraction reactions

Reactions of active oxygen with organic substrates are complex even with in vitro homogeneous solutions. On the other hand, due to the surface properties of cellular membranes found in living organisms, the binding properties of macromolecules have excessive complications arising from the partitioning of enzymes, substrates and catalyts (Romero et al.,

2018). Therefore, the structure and extent of the oxygen reactions of the cells may differ (Kakadiya, 2009).

Damage from oxidative stress leading to cellular death and damage is not clear. Mechanisms of damage to membrane lipids caused by oxygen radicals are generally known. Oxidative damage is often associated with peroxidation reactions in these membrane lipids (Riley, 1994). The lipid is unstable in the presence of hydroxyperoxide, iron or other metallic catalysts. These participate in the Fenton reaction resulting in the formation of reactive alkoxy radicals. For this reason, the presence of iron in reactions increases chain reactions (Wu and Cederbaum, 2003). In addition, Lipid hydroxyperoxide degradation products include malondialdehyde-like aldehydes and ethane and ethylene-like hydrocarbons. Peroxidation reactions in membrane lipids end when carbon or peroxy radicals are crosslinked to form non-radical conjugated products (Figure 6) (Kakadiya, 2009).

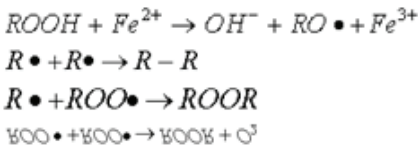


Figure 6. Membran lipitlerindeki peroksidasyon reaksiyonları

Oxidative action against proteins with high molecular weight results in regional amino acid modifications, cleavage of the peptide chain, accumulation of cross-linked reaction products, changing electrical charge, and increased susceptibility to proteolysis (Grune, 2000). Amino acids in peptide groups differ in susceptibility to oxidative effects. In addition, it may differ in terms of active oxygen forms and potential reactivity. The primary, secondary and tertiary structures of protein groups can cause changes in the sensitivity of amino acids (Davies, 2016).

Substances consisting of oxygen-free radicals can cause damage such as DNA deletions and mutations and different fatal genetic effects. This characterization of DNA damage demonstrates the susceptibility of sugars and base groups to oxidation. As a result, it can cause base degradation, single strand breakage, and protein cross-linking (Wickens, 2001; Valko et al., 2006).

Oxidative stress is the damage that occurs in the living cell through the oxidative process. Oxidation is a routine process and is constantly seen in the living body (Sevindik et al., 2018). In addition to this, the result of the disturbances caused by a free radical formed in the natural oxidation process is often toxic (Singh et al., 2019). Among the diseases caused by oxidative stress in humans, different diseases such as cancer, diabetes, autoimmune diseases, eye diseases, Parkinson's and Alzheimer's and cardiovascular diseases can be seen (Krupodorova and Sevindik, 2020). In addition, free radicals can be useful when used by the immune system in attack and fight against pathogenic groups. Also, another benefit is that it can be used in cell signaling (Yang et al., 2011; Nabi, 2014; Sevindik, 2018a).

Many diseases can occur even at an early age due to constant exposure to toxins or stress in the human body. Oxidative stress is caused by environmental and inherent factors such as environmental and air pollution, smoking, excessive stress, synthetic drugs, radiation, excessive exercise and direct and excessive exposure to sunlight (Scandalios, 2002; Pizzino et al., 2017).

Oxidation reactions are very important for survival. However, serious damage can occur due to the production and accumulation of many free radicals in their cells (Khansari et al., 2009). Plants, fungi and animals form peroxidases such as catalase and superoxide dismutase as well as vitamins C and E and glutathione, which have antioxidant properties. The presence of free radicals, especially at low antioxidant levels, causes oxidative stress (Sharma et al., 2012; Akgül et al., 2020). Molecules with antioxidant properties prevent oxidation. It terminates chain reactions by removing free radical intermediates. It also inhibits other oxidation reactions. They do this effect by oxidizing themselves (Lobo et al., 2010).

Thiols, ascorbic acid or polyphenols are good reducing antioxidant agents. In addition, superoxide dismutase (SOD), catalase and glutathione peroxidase enzymes are cellular antioxidants (Ighodaro and Akinloye, 2018). Paraoxonase, glutathione-S transferases and aldehyde dehydrogenases are other enzymes with antioxidant properties. These enzymes with antioxidant properties are more effective than supplementary antioxidants such as vitamins A, C and E, carotenoids and thiols, as they are biological catalysts. These enzymes can be used repeatedly against free radicals (Belinskaia et al., 2020). It can minimize the damage caused by free radicals by participating in the reaction in the early stages of the process (Phaniendra et al., 2015; Özaltun and Sevindik, 2020). In addition, in cases where antioxidant defense system elements are insufficient, supplemental antioxidants may come into play. Especially

in pharmacology, the use of antioxidants is tried in the treatment of stroke or neurodegenerative diseases (Ighodaro and Akinloye, 2018).

There are many chemically synthesized supplemental antioxidants. However, natural antioxidants are used more because of their possible side effects and partially inadequate (Gilgun-Sherki et al., 2001). In particular, antioxidant-effective plants, mushrooms and natural animal products are widely used to reduce the effects of free radicals (Sevindik et al., 2017; Pehlivan et al., 2018; Mohammed et al., 2018). In recent years, many studies have shown that different types of plants and mushrooms have antioxidant properties (Sevindik, 2021; Mohammed et al., 2019a). Traditional medicine has a very important place in the health system of people. Many natural products such as plants, mushrooms and animal products have a very important place in the oldest known health system (Sevindik, 2018b; Mushtaq et al., 2020). According to the World Health Organization (WHO), approximately 80% of the world population benefits from natural products in the treatment of diseases (Mohammed et al., 2019b). Throughout human history, plants have been used for different purposes such as shelter, food, fragrance, medicine, and spices (Mohammed et al., 2021). People belonging to different communities use herbs with medicinal properties in the treatment or prevention of diseases today (Mohammed et al., 2019c; Li et al., 2020). The use of medicinal plants is increasing in developed or developing societies. Medicinal plants are also used in the nutraceutical and cosmetic industries (Mohammed et al., 2020a). In addition, the use of medicinal herbs is based on many years of observations and clinical applications. It plays a very dominant role in the health system in underdeveloped countries. Different parts of plant species (aerial parts, root, leaf, fruit, flower, seed) are used in alternative medicine applications (Dar et al., 2017; Mohammed et al., 2020b). Plant parts can be used in the form of suitable preparation, tea, extract, oil, cream or tincture. Herbal medicines contain many phytochemicals, unlike synthetic drugs. Many studies have emphasized that herbs are natural sources of antioxidants (Anand et al., 2019; Mohammed et al., 2020c). It is known that the antioxidant properties of plants arise from the secondary metabolites they produce in their bodies. In this context, natural products can be used to reduce the effects of oxidative stress.

Conclusion

Oxidative stress is caused by the presence and accumulation of free radicals and causes serious discomfort. Oxidative damage can be reduced by paying attention to the factors that affect the formation of free radicals. In addition, materials with antioxidant properties taken from outside as a supplement to the antioxidant defense system may play a role in reducing the effect of oxidative stress.

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