The immunosuppression road movie: a pictorial review of CT findings

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Learning objectives

The aim of this educational exhibit is to expose a pictorial review of Computed Tomography (CT) findings of some of those conditions that, despite being uncommon in general population, have a significant incidence among immunosuppressed patients, and that may require urgent attention at Emergency Department. Patients presenting in an immunocompromised state merit special consideration when being evaluated.
Background

Immunosuppression (or immunodeficiency) refers to the state in which the immune system is dysfunctional, lowering the ability to combat infection. Immunosuppression itself does not cause pathology but does leave the patient prone to infection and other disease conditions.

Most cases of immunodeficiency are acquired (secondary), being it also possible as a consequence from a defect in the immune system (primary immunodeficiency).

There are therefore a large number of immunodeficiency syndromes and conditions: congenital immune defects, Acquired ImmunoDeficiency Syndrome (AIDS), hematologic malignancies and other cancer types by themselves or by means of them immunosuppressive treatments, including also therapies for autoimmune disorders and prevention of rejection in transplantation.

The actual tendency towards chronicity of some oncologic patients, the increasing availability of biological treatments and extensive use of other immunosuppressive drugs such as corticosteroids, together with other patient groups (HIV acquired immunodeficiencies, poorly controlled diabetes mellitus, end-stage renal disease...) make the immunosuppressed patients group a heterogeneous population.

A variety of immunodeficient conditions and their respective therapies exert numerous systemic effects that may lead to multiorgan dysfunction, facing those patients a common set of entities that are less frequent in the general population and that may present acutely or require urgent attention. This is the main reason why patients presenting in an immunocompromised state require special consideration when being evaluated, meriting a comprehensive and multidisciplinary approach in which Imaging plays a key role in early diagnosis, being also often determinant in therapeutic management.
Findings and procedure details

In this educational exhibit we describe some examples of presentation of herpes encephalitis, brain, epidural and transcranial abscesses, central nervous system lymphoma, neurocysticercosis, toxoplasmosis, spondylodiscitis, pulmonary aspergillosis, mycotic aortic pseudoaneurysm, acute pericarditis, gastrointestinal tuberculosis, gastrointestinal lymphoma, typhlitis, emphysematous Cholecystitis, xanthogranulomatous pyelonephritis (XGP), emphysematous cystitis and Fournier gangrene.

- **Central nervous system (CNS).**

Patients with immunodeficiency are at risk of a wide range of neurologic disorders including infections, neoplasms, and toxicity or other complications of therapies. CNS infections are rare in immunocompetent hosts due to the blood-brain barrier, but more frequent in immunocompromised patients. Different infective agents have been reported to cause neurological disorders, including viral infections (herpes simplex virus, varicella zoster virus, cytomegalovirus, JC virus), bacterial infections (Staphylococcus, pneumococcus, haemophilus, Listeria, norcadia, mycobacterium tuberculosis and mycobacterium Avium/Intracellulare Complex), fungal infections (Cryptococcus neoformans, Aspergillus spp, Candida albicans, Coccidioides, Zygomycetes) and parasitic infections (toxoplasma gondii).

**Herpes encephalitis.** Herpes encephalitis (Herpes simplex virus type 1 accounts for 95% of all cases of encephalitis), usually resulting from reactivation of the latent ganglion infection, is the most common cause of viral encephalitis. Although MRI is the most sensitive modality for evaluating the brain, CT scans may reveal some findings that support the diagnosis (Fig. 1). Classically, hypodensity in the temporal lobes either unilaterally or bilaterally may be seen. This classic involvement of the medial temporal and frontal lobes is consistent with intracranial spread along the small meningeal branches of the fifth cranial nerve. Hemorrhage is usually not observed. A gyral or patchy parenchymal pattern of enhancement is observed.

**Brain, epidural and transcranial abscesses.** Brain abscess is a focal infection of CNS that evolves from inflammation of parenchyma, cerebritis phase, into a necrotic collection of pus surrounded by a well-vascularized capsule. Immunocompromised patients have increasing incidence of brain abscess, often with fungal or protozoan organisms. CT imaging characteristics depend on the stage of the abscess formation, from normal findings or just subcortical hypodense areas to a relatively thin, well-delineated capsule that marks the final stage of a fully formed abscess. The so called Pott puffy tumor (fig. 2), when scalp swelling is associated to the infection of the epidural space, is an uncommon complication of trauma, previous surgery or hematogenous spread. It can also result from spread of infection to the epidural space.
from the paranasal sinuses, middle ear, orbit, or mastoids. Virulence of the organism and the resistance of the host influence the outcome of this condition significantly.

**CNS lymphoma.** This entity is strongly related to immunosuppression states, being its incidence parallel to that of AIDS and the increasing use of immunosuppressive treatments and chemotherapy. MRI is the examination of choice for CNS lymphoma. Nonenhanced CT images typically show focal nodular areas of high attenuation (Fig. 3, Fig. 4), representing high tumor cellularity, with ill-defined margins and little surrounding vasogenic edema. Contrast-enhanced CT images usually demonstrate diffuse enhancement of the lesions, although ring-enhancing lesions can also be possible due to central areas of necrosis.

**Neurocysticercosis.** Cysticercosis is the most common parasitic infestation affecting the CNS. Meningeal cysts form mostly in the basal meninges, sometimes causing stroke and hydrocephalus. Parenchymal cysts are usually found in the cerebral cortex, including the cortical-subcortical junction, while the white matter is rarely involved. Ventricular cysts are also possible, which may cause intermittent hydrocephalus. The imaging findings vary depending on the stage of infection. The viable cyst appears as a thin-walled fluid-filled cyst (vesicular stage, Fig. 5), a mural nodule (scolex) may also be seen at CT and MRI images; at this stage the cyst causes no inflammatory reaction, for this reason there is no edema and it does not enhance. When the parasite dies, 2-6 years after infection, the disintegration of the parasites produces an intense tissue reaction, the cyst is encapsulated presenting ring enhancement and associated edema. As the cysticercus becomes fibrotic or collapses, a focal area of enhancement suggestive of granuloma is seen (granular-nodular stage) and, finally, a focal area of calcification appears, typically measuring 2-10 mm in diameter.

**CNS Toxoplasmosis.** It is caused by an obligate intracellular rotozoal parasite, *Toxoplasma gondii*. In adults, most infections are subclinical, but severe infection can occur in immunocompromised patients. AIDS-associated *Toxoplasma* encephalitis results from reactivation of chronic latent infection in more than 95% of patients. CT images may show single or multiple thin-walled cavitating nodular lesions with ring enhancement, more frequently involving the basal ganglia. Edema of the surrounding white matter is often depicted as well.

**Spondylodiscitis.** Pyogenic spinal infections most commonly are caused by *Staphylococcus aureus* and *Enterobacter* spp. Other pathogens to cause it are *Salmonella*, *Pseudomonas aeruginosa*, *Serratia* spp, and *Candida* spp in patients with a history of intravenous drug abuse. *Mycobacterium tuberculosis* causes most nonpyogenic spinal infections; however, fungi like *Cryptococcus* spp, *Aspergillus* spp and *coccidioidomycosis* also may cause nonpyogenic infections. MRI is the modality of choice for evaluating spinal infections, CT scans may appear normal early in the course of disease. Disk-space narrowing, destruction of the vertebral body and paravertebral soft tissue lesions or collections support the diagnosis (Fig. 6).
After the administration of iodinated contrast material, the abnormal disk space, vertebral marrow, or paravertebral soft tissues may enhance.

- **Respiratory and cardiovascular system.**

Patients with immunodeficiency are at risk of a wide variety of infectious and noninfectious lung conditions. Being infections the most common cause of lung diseases in immunocompromised patients, they have an increased risk for uncommon opportunistic infective agents but also for common infections implicated in community acquired pneumonia. Among these pathogens are Streptococcus pneumoniae, Klebsiella pneumonia, Haemophilus influenza, Pseudomonas aeruginosa, actinobacterspp, fusobacteriumnucleatum, bacteroidsmelaninogenicus, bacteroidsfragilis, mycobacterium tuberculosis, mycobacterium aviumintracellulare, pneumocystis jirovecii, Norcadiaspp, Coccidomycesspp, Aspergillus spp, Rhodococcusequi etc. The infections usually present as pneumonia, interstitial lung disease and obstructive lung diseases. But immunocompromised patients also suffer from noninfectious lung injury and their clinical manifestations and imaging findings may mimic infections.

**Pulmonary aspergillosis.** Aspergillus spp cause a spectrum of mycotic diseases at respiratory system. This fungus is commonly found in the sputum of healthy individuals. However, in immunosuppressed hosts, its ability to invade the arteries and veins facilitates its hematogenous spread, depending the development of disease and its histologic, clinical, and radiologic manifestations on the virulence and, more importantly, on the patient's immune status. The fungus, depending on the host immune response, may take any of the following forms: allergic bronchopulmonaryaspergillosis (ABPA), aspergilloma (Fig. 6, Fig. 7), noninvasive and involves colonization of preexisting cavities, chronic necrotizing aspergillosis, angioinvasiveaspergillosis.

**Mycotic aortic pseudoaneurysm.** Mycotic pseudoaneurisms are a common complication of the hematogenous spread of bacterial infection. The most common cause of mycotic aneurysm is the hematogenous infection of atherosclerotic vessels (Fig. 9). CT findings of mycotic aneurysm of the aorta include an aortic wall rupture, which may show gas-forming inflammation around the aneurysm.

**Acute pericarditis.** Suppurative pericarditis (Fig. 10) is caused by organisms that may arise from direct extension, hematogenous seeding or lymphatic extension. Immunosuppression facilitates this condition. Pericardial effusion with gas-filling images suggest the diagnosis.

- **Gastrointestinal system.**

The gastrointestinal associated lymphoid tissue constitutes the largest immune compartment in the body. However the gastrointestinal tract is particularly at risk of infectious and noninfectious injuries because of its close proximity to the external environment.
The infections may be bacterial (Clostridium difficile, Salmonella spp, Shigella spp, H. pylori, Escherichia coli, Campylobacter spp, Yersinia enterocolitica, Mycobacterium tuberculosis, Mycobacterium aviumintracellulare complex), viral (cytomegalovirus, herpes simplex, human papilloma virus, ebstein-barr virus and rotavirus), fungal (histoplasmacapsulatum, candida albicans, candida tropicalis, mucormycisspp), or parasitic(cryptosporidium, microsporidium, entamoebahistolytica, giardia lamblia, Strongyloidesstercoralis) and may infect one or more gut segments between the mouth and anus.... The gastrointestinal infections have varying presentations but the commonest presentation is diarrhea.

There is increase in prevalence of both common and uncommon gastrointestinal malignancies in patients with immunodeficiency. Decreased immune surveillance and ingestion of carcinogens, continuous mucosa inflammation, gastrointestinal infections, are some of the factors suspected to be responsible for the higher prevalence of malignancy in this population.

Other common locations affected include theoesophageal and anorectal regions, the most exposed areas to external insults. The oesophagealopathologies include oesophageal candidiasis, oesophageal herpes simplex, cytomegalovirus, aphthous ulcer, malignancy, and reflux oesophagitis manifesting as dysphagia and odynophagia. The anorectal lesions which are usually seen in immunocompromised patients with AIDS include herpes simplex infection, gonorrhoea, syphilis, anal wart(condylomata) and Chlamydia.

The gastrointestinal malignancies that have been associated with immunosuppression include Kaposi sarcoma, colorectal carcinoma, post transplantlymphoproliferative lymphoma, gastric mucosa associated lymphoma. The clinical presentation is usually asymptomatic, but can lead to perforation, obstruction or gastrointestinal.

Immunodeficiency states have been associated with hepatobiliary disease. These disorders that have been reported in immunocompromised patients include infectious hepatitis, granulomatous hepatitis, alcoholic liver disease, cholangiopathy, cholecystitis,hepatocellular carcinoma, schistosomiasis, haemangioma and hepatic adenoma.

Acute pancreatitis in immunocompromised patients areless common, but it increases significantly the morbidity and mortality when associated with immunodeficiency.

**Gastrointestinal tuberculosis.** Clinical features of intestinal tuberculosis include abdominal pain, weight loss, anemia, and fever with night sweats. Patients may present with symptoms of obstruction, right iliac fossa pain, or a palpable mass in the right iliac fossa. Hemorrhage and perforation are rare but have been described as complications of intestinal tuberculosis.

Ileocecal region involvement is seen in 90% of patients with gastrointestinal tuberculosis, while infection involving the jejunum is seen more commonly with M avium-intracellulare (MAI) complex infection.

CT images may show wall thickening of cecum and terminal ileum (Fig. 11) with enlargement and enhancement of ileocecal valve. Mesenteric lymphadenopathy with a characteristiclow-density center suggestive of caseation necrosis can also be depicted.
Gastrointestinal lymphoma. Is the most frequently occurring extranodal lymphoma and is almost exclusively of non-Hodgkin type. Primary gastrointestinal lymphoma most commonly involves the stomach but can involve any part of the gastrointestinal tract from the esophagus to the rectum. Immunosuppression is one of the main risk factors. Gastrointestinal lymphoma has a wide variety of imaging appearances. CT images may show a bulky mass, diffuse infiltration (Fig. 12) with preservation of fat planes and no obstruction, associated bulky lymphadenopathy. Imaging is also important in the detection of perforation or obstruction, and other complications.

Typhlitis. Is the inflammation or necrosis of the cecum, appendix, or ileum in patients generally immunosuppressed. CT images (Fig. 13) demonstrate circumferential low-attenuation colonic wall thickening. High attenuation within the thickened colonic wall may represent hemorrhage. Pericolonic fat stranding is also common.

Emphysematous Cholecystitis. Is an acute infection of the gallbladder wall caused by gas-forming organisms (eg, Clostridium or Escherichia coli). CT images (Fig. 14) show the presence of air within a thickened gallbladder wall or lumen. It is mostly associated with diabetes mellitus. Gallbladder ischemia due to vascular compromise of the cystic artery facilitates the proliferation of gas-forming organisms and bacterial translocation in the ischemic tissue with low oxygen saturation.

- **Urogenital system.**

The urinary and part of the genital systems are sterile tracts. In immunodeficiency state the urogenital tract are exposed to higher prevalence of both common and uncommon infections. The urogenital diseases that have been reported in immunocompromised patients include urinary tract infection (UTI), epididymitis, prostatitis, extensive condylomata of the urethra, renal abscess and other renal related diseases.

Of all the categories of immunocompromised hosts, the renal transplant patient is the one most susceptible to the direct and indirect consequences of urinary tract infections. The rates of UTI in these patientes are primarily determined by the degree and duration of urinary tract manipulation. Renal failure from opportunistic infections and drugs used in these patients has also been reported. A broad spectrum of renal diseases affecting glomerular, tubular and interstitial tissues had been documented in immunocompromised patients, especially HIV infected patients. Most of the renal manifestations represent complications of concurrent infections in a severely immunocompromised host or side effects of the treatments used.

Xanthogranulomatous pyelonephritis (XGP). XGP is a rare, serious, chronic inflammatory disorder of the kidney characterized by a destructive mass that invades the renal parenchyma. XGP is most commonly associated with Proteus or Escherichia coli infection. It is often associated with urinary tract obstruction, infection, nephrolithiasis, diabetes, and/or immunodeficiency.

The renal parenchyma is destroyed and is replaced by low-attenuating masses (xanthomatous tissue), being also possible an extrarenal extension of XGP. Enhanced
CT images (Fig. 15, Fig. 16) show ring enhancement in areas of granulation tissue and intrarenal abscesses, whereas the xanthomatous tissue does not enhance. Calculi are often associated with the central portion of the mass.

**Emphysematous cystitis.** It is an acute infection of the bladder caused by gas-forming organisms. Mostly associated with diabetes mellitus. CT scans help to localize de gas, making easier the diagnosis in a proper clinical presentation (Fig. 17).

**Fournier gangrene.** It is a polymicrobial necrotizing fasciitis of the perineal, perianal, or genital areas. Impaired immunity (most commonly diabetes mellitus) is important for increasing susceptibility to Fournier gangrene. Infection of superficial perineal fascia (Colles fascia) may spread to the penis and scrotum via Buck and Dartos fascia, or to the anterior abdominal wall via Scarpa fascia, or vice versa. Testicular involvement is rare. CT images show necrosis of the superficial and deep fascial planes with asymmetric enhancement and fascial thickening, fluid and gas collections, subcutaneous emphysema (the hallmark of Fournier gangrene, but is not seen in all cases) and abscess formation.

- **Musculoskeletal system.**

There is increased prevalence of musculoskeletal diseases especially infections in immunocompromised patients. Musculoskeletal syndromes that occur in HIV-infected patients include manifestations of drug toxicity, reactive arthritis, Reiter's syndrome, infectious arthritis, and myositis. Post-transplant patients have developed myopathies and various bony and joint disorders. Myopathy and myositis have been reported in patients with diabetes mellitus and some primary immune deficiency disorders. Some other musculoskeletal disorders in patients with immunodeficiency include some syndromes with arthritis or myositis as one of the components eg Reitzers syndrome, Dermatomyositis, Sjogrens syndrome, Polymyositis and Psoriasis. The hallmark of the presentation is pain in the muscle, swelling of muscle, occasionally associated with fever and muscle atrophy. Arthralgia, swelling of the joint and when intervention is delayed distortion of the joint. Patient may develop cellulitis with or without abscess formation and osteomyelitis. There is need for prompt diagnosis and intervention as delay may lead to rapid spread of the infection in these patients.
Fig. 1: Unenhanced CT shows classical hypodensity in the right temporal lobe in a patient diagnosed as Herpes encephalitis.

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**Fig. 2:** Enhanced CT shows the so called Pott puffy tumor, when scalp swelling is associated to the infection of the epidural space. Transcranial abscess with bone destruction.

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Fig. 3: CNS lymphoma. Unenhanced CT shows nodular areas of high attenuation, representing high tumor cellularity, involving the splenium of corpus callosum. Note the ill-defined margins and little surrounding vasogenic edema.

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**Fig. 4:** CNS lymphoma. Nonenhanced CT shows an homogeneous high attenuation parietal mass with extracranial extension. Note the spiculated perpendicular (hair-on-end) periosteal reaction.

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**Fig. 5:** Vesicular stage neurocysticercosis at nonenhanced CT. Viable cysts appears as a thin-walled fluid-filled cyst. There is no inflammatory reaction.

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Fig. 6: Enhanced CT shows L2-L3 Spondylodiscitis and retroperitoneal abscesses caused by Mycobacterium tuberculosis.

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Fig. 7: Aspergilloma. Necrotic parenchimal consolidations with halo sign compatible with the clinical suspicion of fungal infection.

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**Fig. 8:** CT shows bilateral necrotizing pneumonia, with a halo sign, in a fungal infection.

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**Fig. 9:** Aortitis caused by Aspergillus flavus complex. Enhanced CT: aortic arch shows mycotic pseudoaneurism filled with contrast medium.

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**Fig. 10:** Suppurative pericarditis. Enhanced CT shows pericardial effusion with gas bubble images.

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**Fig. 11:** Enhanced CT shows bowel obstruction due to ileocecal tuberculosis. Note significant enhancement of the terminal ileum mucosa.

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**Fig. 12:** Enhanced CT shows diffuse infiltration and nodular areas of stomach and bowel with preservation of fat planes and no obstruction.

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Fig. 13: CT image shows perforated typhlitis caused by gas-forming bacteria.

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Fig. 14: Unenhanced CT shows the presence of air within gallbladder wall.

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Fig. 15: CT images show right renal parenchyma replaced by low-attenuating masses, also a renal calculus is depicted.
Fig. 16: Enhanced CT shows retroperitoneal and paravertebral abscess in a xanthogranulomatous pyelonephritis.

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Fig. 17: Enhanced CT images show the presence of air within bladder wall.

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Fig. 18: Enhanced CT shows subcutaneous emphysema and fluid and gas collections related to abscess formation.

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Conclusion

Radiologists should get familiarized with CT findings of those entities that, despite being uncommon in general population, have a significant impact on the different groups of immunocompromised patients and which may present acutely, demanding emergent attention.
References