Brain abscess: a cogent clarifier of the confused concept of immunity

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EXPERIMENTAL data suggest that the neuraxis is remarkably resistant to infection. The brain is resistant to abscess formation. With microbes triumphantly resistant to powerful antibiotics; with often fatal pyemias and septicemias rampant the globe over; with children in third-world countries experiencing head-region pyodermia often caused by bilateral purulent otitis media; and with parasal sinuses, which are also paracranial, recurrently full of resistant pus, the cool assertion of the brain’s immunity to abscess formation arrives as a welcome surprise. A leading, intellectually jarring note, marking this celebration, is the spate of specialty papers, clinical as well as experimental, in which authors consider immunity itself as pathogenic in brain abscess—a “j’acuse” that perpetuates the confusion even more.

One definition of the term immunity—from im (not) and munis (service) (hence, municipality)—is “exemption from public service, especially military service.” Immunity implies worklessness. No wonder, until today, those active in modern medicine have not known whether immunity is a friend or a foe. Immunity, as a concept, has yet to be defined. Medawar, the co-Nobel Prize winner with Burnet, has described immunology as ailing from “bare-faced empiricism and embarrassingly silly terminology.” Immunity, it would seem, is a force that runs with the hare to hunt with the hounds, a situation reminiscent of the Big Brother in Orwell’s novel 1984: “He was the tormentor, he was the protector, he was the inquisitor, he was the friend.” Immunity-wise, “Nature seems diabolical.”

Nature is not malicious, provided we differentiate immunity from reactivity. Immunity, in its quintessence, is an aristocracy of being that refuses to react to a situation, avoids a showdown or a fight, and lets irritants pass by. Reactivity is the body’s reasoned reaction to an antigen, microbe, graft, and so on. The brain is aristocratic enough to exhibit lofty immunity, but when need be, partakes in reactivity that spawns an inflammation, pus, and abscess.

Even in such cases that it capitulates, there is method in the brain’s seeming madness: pre-gnomically, BRAIN reads Balanced Reactivity And Immunity Noticeable—a judicious mix of the body’s bittersweet while dealing with ubiquitous microbes.

Ropper and Brown have written, “In most instances of bacteremia or septicemia, the nervous system seems not to be infected... With respect to the formation of brain abscess, the resistance of cerebral tissue to infection is notable.... The arachnoid membrane (in fulminant meningitis) tends to serve as an effective barrier to the spread of infection into the brain substance.... Only rarely does acute bacterial meningitis result in a brain abscess.” Thus, the brain can wear an intimate garb loaded with virulent microbes and yet stay clear of them.

The brain in fact has learned this trick from the human body. “As many as 100 trillion viruses and bacteria live on each of us. However much we wash, there are always ten million or so bacteria on every square centimeter on our skin.” The human body has 10^{12} number of cells and 10^{13} number of microorganisms. This blanket of life covering our skin and mucosae is the human body’s “surfinsic/surfe-rior” milieu, endowed soon after birth and symbiotically coexisting with each one of us unto the grave.

If, as Lovelace wrote in the 17th century, “stone walls do not a prison make,” then the loads of microbes painting our surfaces do not infection beget. Massive microbial symbiosis is the hallmark of human health. The ability of the human body to live in peace with 10 microbes per every human cell is a state of genuine immunity, wherein the body exercises a holy indifference to the resident microbes, to...
gain therefrom freedom from any reactivity against the obviously non-self microbes. The joint Nobel Prize winners (for discovery of acquired immunological tolerance) with Burnet, Medawar brought to the fore the realization that the so-called immune system reacts against any element it perceives as non-self, through a wide assortment of cells (“reactocytes”) and humors (“reactins”). The reactivity cascade, by and large, results in the rejection of the non-self focus.

Burnet has extensively elaborated on the fact that the human immune system is not so much antimicrobial as it is anti–non-self, for the integral body is uninterruptedly comprised of self-units that dialog with one another to hold a 10-trillion cell economy into a gestalt whole without any screws, tape, or adhesives. Cells and fluids move with stellar ease in the individual body-universe.

A non-self focus can arise from without and/or within. A surfinsic virus/microbe/fungus can turn intrinsic through a breached epithelial barrier. A splinter or thorn may serve the same purpose. A wound, small or large, would contain damaged/dead tissue of one’s own but no longer self. Thyroid or, say, gastric cells, may mutate to pose as non-self. A grafted kidney is a large non-self locus. The body’s reactive repertoire contends with each of the aforementioned in a prototypical way: Recognize, React, Reject, Repair, and Restore to status quo ante as best as possible. The vector assembly to achieve this is CelluloHumoral Reactivity Insuring Selfsame Totality, or CHRIST for short. Little wonder that processes as diverse as microbial infection, wound healing, graft rejection, or the so-called autoimmune phenomenon are mediated by what we call, for want of any other term, inflammation, eupologized by Nobel Prize–winner Florey as “the backbone of pathology.” Inflammation, a gift from CHRIST, is the animal body’s greatest invention and one’s only license to survive the rough and tumble of life, manage severe infections, heal massive traumatic/operative wounds, and peremptorily throw away well-intended but non-self grafts. The fact that the human body exhibits no reactivity to, much less rejection of, one’s own cancer proves that cancer is part of the self. No wonder, Maclean qualifies a cancer cell as a “superdifferentiated normal cell.”

The massive drug market for antiinflammatory agents reflects medicine’s poor appreciation of the inflammatory gift and is tantamount to crucifying CHRIST. It is the same for an angel called pain. It would be no exaggeration to see Inflammation and Pain as the twin guardian angels of the human body.

Abscess and pus are the children of inflammation and, like Quasimodo in The Hunchback of Notre Dame, have a bizarre demeanor but a heart of golden benevolence. Both abscess and pus are discussed pejoratively and, therefore, stand forever condemned. In abscess, abs (away) and cess from cedere (to go) connote something that goes/drain away. From Skt. puyati (to stink) comes the word “pus,” meaning something foul, putrid, or rotten. If, in the famous Hollywood musical My Fair Lady, Mr. Doolittle, the lovable rascal and father to Eliza, had to have biological clarity, he would have described his own abscess and pus as “Me own flesh and blood.”

Let us now picture how abscess and pus, the two powerful arms of Vis Medicatrix Naturae (“the natural curative power inherent in the organism”) work. The CHRIST detects a splinter, a modicum of microbes, or a bit of dead tissue and sets into motion “cellulohumorovascular” reaction to occasion the classical Celsusian signs of inflammation—namely calor, rubor, tumor, dolor, and the Galenical functio laesa. If the inflammatory cellulitis cannot dispose of the non-self focus, CHRIST sets about throwing a fibrous barricade—the wall of the upcoming abscess. The CHRIST knows that the only way to discharge the non-self focus to the exterior is to spawn a fluid-filled cavity, under tension, by, if need be, lysing the patient’s own tissues. Just as the solid fetus is delivered after its bag of water dilates the maternal passage, so does the fluid-filled abscess strive to find a path to the exterior, throw away the non-self material, and then heal the gap left behind. Even a brain abscess is known to have spontaneously healed this way. To make the saga complete, it pays to study the typical composition of pus: “A liquid inflammation product made up of cells (leukocytes) and a thin fluid called liquor puris.” The brain, in its innate wisdom, largely denies itself the hydrodynamic option of a fluid-filled tense cavity, making the abscess focus more solid than fluid because the brain knows that any such venture could direct the abscess to burst into a ventricle (IVROBA) with disastrous consequences. The brain prefers a pyoma to a pyoecele, and a mycoma to a mycocele.

Incidentally, brain abscess, more as a pyoma than a pyoecele, is best suited to underscore the dual definitions that the word “abscess” enjoys. In Celsusian sense, apostem/a postema/apsestum is abscessus (a pyocele). However, Marcus Aurelius Severinus used “abscessus” to connote a tumor or new growth, not excluding cysts. The universally established resectability of a brain abscess can be summed up as a pyomectomy and, likewise, mycomectomy.

Having glimpsed the raison d’etre of the 2 bioinventions called pus and abscess, it is now time to allow the brain abscess itself to turn into a teacher that helps medical science distinguish immunity from reactivity.

Let us focus on the so-called immunology of brain abscess. An extensive review charges “inappropriate glial activation” as perpetuating antibacterial immune response that ends up contributing to disease pathogenesis. Another extensive review holds them responsible for both defense against, and neuropathogenesis of, central nervous system infections. The review concluded, “The evidence to date suggests that activated microglia functions as ‘double-edged sword’ with neuroprotective features predominantly in the healthy nervous system and neurodestructive properties observed in various states.” Because the review does not explain the neuroprotective features of microglia, the microglia end up being neurodestructive in conditions as apart as abscess and Alzheimer disease. Microglia—the immunocytes of the central nervous system—run with the hare and hunt with the hounds.

Bengalese writer Rabindranath Tagore bemoaned, “We read Nature wrong, and then blame her.” The truth is that immunity, true to its meaning, is an innate, lofty, nonreactivity that thrives on the principle that the best battle is one (or won) that is never fought.

Any thing or event from without and/or within that breaches the self-same cellular continuity of the body gets vigorously addressed by cells and humors generally called immunocytes and antibodies. The non-self is eliminated and self-sameness is restored through what can be called reactivity. Reactivity entails fever, inflammatory cellulitis,
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pus formation, abscess formation, and graft rejection, all seen through medical eyes as “abnormalities” to be treated, nay, combated. “In the years to come,” Raeburn24 mused, “the story of antibiotics may rank as Nature’s most malicious trick” on mankind, ushering in unintended immunodeficiencies. Reactivity, like pain, is our license to survive, nay thrive, and does so with the sole aim of sustaining the human being.

A brain abscess is a brilliant illustration of the coexistence of immunity and reactivity, the former striving to stay away from the abscess and the latter fighting to do its very best to save the precious neuraxis. Let us detail how.

Toward a Synthesis of Immunity, Reactivity, and Brain Abscess

The infrequency of brain abscesses in the midst of microbial crisis, locally, focally, or systemically reflects the brain’s immunity to abscess formation. When an abscess does develop, however, the various processes that go into making and manifesting it comprise the brain’s reactivity. An expanded appreciation of the following may help a neurosurgeon understand why an abscess does not occur and when it does, as well as how and why.

The What and Why of the Brain’s Immunity to Abscess Formation

First, the brain—as the experimental psychologist R. L. Gregory said, “like nothing so much as a lump of porridge”—is innately strong. Ropper and Brown25 have written, “Direct injection of virulent bacteria into the brain of an animal seldom results in abscess formation. In fact, this condition has been produced consistently only by injecting culture medium along with the bacteria or by causing necrosis of tissue at the time bacteria are inoculated.”

Second, the brain’s immunity to abscess formation is 2-fold: it is so despite intimate contact with inflamed and infected arachnoid (vide supra), and it is so despite direct planting of virulent microbes into its substance.

Third, a leading reason for the aforementioned nonreactivity is that the whole neuraxis, during embryonic ontogenesis, “escapes” tolerance in the thymus, thus acquiring “immune privilege,” which suggests the neuraxis’ ability to ignore reactive (antigenic) stimulus in the form of microbes.

Fourth, as Male and colleagues21 have written, “Immune privilege is clearly designed to dampen down inflammatory responses in certain vital organs. The same suppressive mechanism would apply equally to inflammation caused by infectious or self-antigen.”

Both the third and fourth points support the brain’s deliberate “nonreactivity,” heretofore incorrectly called “immune privilege” for privilege as a word could mean indolence, irresponsibility, and unaccountability, and hence access to hyperreactive/inflammatory response.

Fifth, neurons, like muscle cells, belong to the category of perennial/immortal/postmitotic cell populations wherein cell multiplication ceases soon after birth.23 The cells tend to be very large. Both nondivisibility and large size endow nonreactivity.

Sixth, the endothelium lining the entire neuraxial vascu-
game) connoting Speedily Locate Adroitly Manage. The simple-looking CSF examination fails to help for 2 reasons: it chooses to get unaffected, and a thoughtless tap could precipitate herniation. A quartet of adroit management is Antimicrobialize, Aspirate, and/or Ablate and over an extended time Antiepilepticize. Needless to say, THEOS-SLAM-AAAA comprises “the basic principles of abscess management.”

The first A in AAAA, for want of any sensitivity-guidance, has to be a strong cocktail led by penicillin, and fortified by others, including metronidazole. The second A may entail repeated aspiration under image control. The third A is capable of teaching a neurosurgeon that the oma-like abscess tends to be isolated from brain tissue and lends itself to ready enucleation. The fourth A is a protracted must. The first 3 As must be in hurried succession. The antimicrobial cocktail gets replaced by a specific one on identifying the visitor. The factors that almost conspire to help the patient and the surgeon comprise some self-evident truths as follows.

Incidence: Amazingly Low

“The incidence of brain abscess has remained stable in the antibiotic era; nevertheless it is generally regarded as a rare disease, with large autopsy series reporting an occurrence rate of 0.18 to 1.3 percent.... brain abscess remains a significant problem in the developing world, particularly children living in poverty.... male:female ratio of 2:1. In some series, brain abscess secondary to otitis media displays a bipolar age distribution, with peak in children and after 40. In contrast, brain abscess secondary to paranasal sinuses usually occur between 10 to 30 years of age.”

Routes: Continuity, Contiguity, Circuitry, and Crypticality

Direct, clear continuity between pathogen(s) and parenchyma produces poor abscessing. No wonder, despite their enormous numbers, head injuries and procedural-operative trauma remain immune to abscess. Contiguity accounts for the largest number of brain abscesses, neighbored, as the brain is, by usually infected paranasal sinuses and the commonly infected middle ear. The brain’s infected neighbor decides which part of it abscesses. Otogenic brain abscesses are most commonly located in the temporal lobe or cerebellum; conversely, 85–95% of cerebellar abscesses are associated with ear or mastoid infections. Usually these lesions are solitary. Little wonder the occipital lobes, for want of an infected neighbor, never abscess by continuity.

The brain’s circulatory oneness with the rest of the body renders it susceptible to abscessing in pyemia, septicemia, fungemia, lung abscess, pelvic infections, and so on. The immunity—nonreactivity—that neurangiothelium exhibits against widely circulating microbes accounts for the freedom that the neuraxis enjoys. In 15–20% of the cases the brain abscess is cryptic—that is, you cannot guess the source. Presumably the route is vascular, often an undetected periodontal sepsis.

Sources and Species

In an order of decreasing frequency, brain abscesses are rhinogenic, otogenic, hemogenic, and cyanogenic. Cyanotic heart diseases presumably devitalizes the neuroangiothelium rendering the brain susceptible to abscessing.

Since the brain abscess behaves in a prototypical fashion throughout the course of disease, details on the menagerie of microbes that visit the brain singly or severally remains an academic issue.

SICKness of Compromised Immunity

The tandem terms immunocompromised and opportunistic microbes beg for clarity. How come an immunologically depressed person develops multiple abscesses, elsewhere and in the brain, to paradoxically exhibit intense “immunoreactive” processes in the form of abscessing, and so often by fungi. The reality is that the culprit microbes are not opportunistic, but are “opportunized” by the loss of surface integrity, largely because of drugs, be it in cases of cancer, transplantation, or AIDS. The “opportunization” starts with the person’s Surface/Somatic Integrity Compromised by Khemicals, a SICK syndrome wherein the culprit is hardly the microbe. Even then, whatever the abscess(es), the response to therapy is highly satisfying, a credit more to the brain’s balanced immunity and reactivity.

Clinical Features: Cold Abscesses, Hot Tumor

The clinical course of a patient with a brain abscess may range from indolent to fulminant; however, the duration of symptoms is ≈2 weeks in about 75% of patients. In most cases, the prominent clinical manifestations of the brain abscess reflecting the expanding intracerebral manifestations are often nonspecific and depend on several variables (for example, the virulence of the infecting organisms, the patient’s immune status, the location of the abscess or abscesses, and the presence or absence of associated meningitis or ventricular rupture). Only a minority of patients exhibit the classic triad of fever, headache, and focal neurological deficit.

A brain abscess epitomizes focally fast-growing pyoma (which begins manifesting signs at the stage of cerebritis), a locale that is poor in reactivity (hence often sterile, uninformative CSF), and an unexplainable absence of systemic reactivity in terms of fever, leucocytosis, erythrocyte sedimentation rate, and C-reactive protein. Such a contrast may be present in as many as 50% of cases. However, all the symptoms and signs of SOL abound.

Compared with a cytoma (brain tumor) that is tardy in its growth, a brain pyoma/mycoma marks the rapidity of its expansion in terms of days. Any delay may mean disastrous coning or IVROBA. One can thus sum up brain abscess’ clinical picture as one of Cold Abscess, Hot (volcanic) Tumor. It is like a fire in an oil well, and all that you can do you must do at your speediest.

Teleological Pathogenesis: Obliging Oma

From the Greek word for goal, task, completion or perfection. Teleological explanations attempt to account for things and features by appeal to their contribution to optimal states, or the normal functioning, or the attainment of goals, of wholes or systems they belong to.

 Needless to emphasize, the pathogenesis, whatever it is, is not immunopathogenetic, but “reactopathogenetic.” Brain abscess exhibits, when single/multiple or unilocular/multilocular, 4 stages and 5 zones. Such an “idealized”
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picture is not always present, but it allows a working description of its evolution.

The 4 stages are early cerebritis (or cerebellitis), late cerebritis, early capsule, and late capsule, each discernible on neuroimaging. The 5 zones are: 1) a well-formed necrotic center; 2) a peripheral zone of inflammatory cells, macrophages, and fibroblasts; 3) a dense collagenous capsule; 4) a layer of neovascularity associated with continuing cerebritis; and 5) reactive astrocytes, gliosis, and cerebral edema external to the capsule. The denseness of the capsule is purposive. The final, or capsule stage, occurs from Day 10 onward and is associated with a well-vascularized abscess wall, in effect sequestrating the lesion to protect surrounding normal parenchyma from additional damage. The plane of cleavage between Zones 4 and 5 forms the bedrock of excisional ease and success.

The reactive wisdom shines out through 2 very discernible features. The denseness of the capsule is to the result of "an abundance of reactive collagen" that is produced by fibroblasts derived from the walls of blood vessels. The other teleological feature is that on the inner side of the capsule, and hence within the abscess, are the inflammatory cells, macrophages, and fibroblasts, whereas external to the capsule and separated from it by edema are the reactive astrocytes.

A vascular explanation has been generally advanced that the capsule tends to be thicker on the side of gray matter and relatively thin on the white matter side, because of the greater vascularity of the gray area. While this may well be true, sight should not be lost of the fact that the abscess guides itself in such a way that it chooses not to invade and not to rupture into the neuronal layers of the cortex. The price that it exacts is that the thinness renders the abscess able to advance toward and rupture into the ventricle.

The tenacity of the wisdom of the abscessing brain comes from a study entitled, "Improved survival in central nervous system aspergillosis: a series of immunocompromised children with leukemia undergoing stereotactic resection of aspergillomas." In each child reported in this series, and in every abscess, successful image-guided resection of the lesion was possible. "Complete resection of the abscess yielded gross findings of a viscous fluid contained by a firm rubbery wall surrounded by soft capsule." Even under SICKness (vide supra), the brain retains its balance between innate immunity and reasoned reactivity.

References


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