The immunological nature of the pathological effects of SARS-CoV-2 and other pathogens

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Abstract

The results of the investigation of the exact nature of the mechanisms that ensure the organism's survival in the face of the pathogen's pathological effects reveal those severe co-occurring manifestations that are temporally linked to a pathogen, such as those which appear in COVID-19 patients, to be manifestations of different diseases which are brought about through the same pathway under the influence of different causes which include the pathogen. Since the single pathway through which all of such diseases, which have the same "immunological nature," are brought about must be blocked for the attenuation of the influence of the pathogen to bring about the remission of the disease it causes, such diseases will undergo simultaneous remission when conditions permit immune mechanisms to attenuate the causative influence of the pathogen. And since the pathway must be blocked for the disease the pathogen causes to be cured, severe manifestations that are linked with a pathogen persist despite treatments that reduce pathogen load when conditions do not permit immune mechanisms to attenuate the influence under which any of the diseases in the same "immunological spectrum" as this disease is produced through

the pathway, a persistence which we attributed to the pathogen's resistance to treatment. These results throw light on the different immunological phenomena, from those that inspired variolation and vaccination to those remissions that are temporally linked with infection.

Keywords: Immunology; immunity; autoimmunity; infection; inflammation; vaccination

Introduction

The immunological nature of the pathological effects of pathogens, the nature that permits immune mechanisms to protect organisms from such pathological effects, has been considered to be that which requires pathogens to be perceived as invaders, detected and eliminated and mechanisms which eliminate pathogens have since been referred to as "resistance" or "defense" mechanisms.[1,2] But what has been observed is that tolerance mechanisms, which we normally do not think of as "immune" because they do not eliminate pathogens, are the ones that ensure survival in the face of diseases that are caused by pathogens and the effects of such mechanisms which reduce disease severity without affecting pathogen load[3] have also been observed during the present pandemic.

In some cases of severe COVID-19, loads of SARS-CoV-2 are lower than those observed in some mild and asymptomatic cases.[4] These observations, have led clinicians to the theoretical picture that severe disease is a consequence of hyperinflammation which is brought about by SARS-CoV-2 through effects that depend on the vulnerability of the individual instead of effects

of direct viral toxicity.[5] And indeed, what these observations suggest is that rather than reducing pathogen load, the mechanisms that protect us from the diseases that are caused by pathogens reduce the vulnerability of organisms to the pathological effects of such causes so that the severity of such diseases reduces until they are rendered mild or asymptomatic irrespective of how high the pathogen load may be.

When we consider them with minds that are detached from the preconceived notion that the nature of the pathological effects of pathogens is that which requires immune mechanisms to reduce pathogen load in order to protect us from such effects, a hypothesis of the immunological nature of the pathological effects of pathogens crystallizes out of such observations. This hypothesis proposes that the immunological nature of the pathological effects of pathogens, the nature of such effects which permits immune mechanisms to protect organisms of diverse kinds against them, is not one that depends on a nature that is uniquely possessed by pathogens but rather one which depends on a nature which pathogens share with sterile causes so that such mechanisms could neither detect nor destroy pathogens and therefore could not reduce pathogen load to bring about their effects.

The consequences of this empirically-grounded hypothesis have been observed. In bats, the study of Matae Ahn and coworkers revealed a key mechanism that dampens the inflammation that occurs in response to infections with three different zoonotic RNA viruses as well as sterile factors without affecting the viral loads in cells which we have referred to as “immune” cells[6] on the basis of the assumption that the reduction of pathogen loads which we have observed in them

are brought about by immune mechanisms that protect organisms from disease. The conclusion to which this consequence of our empirically grounded immunological hypothesis leads is that those cells, which we refer to as “immune” when the pathogen loads in them are reduced, do not perform functions that protect the organism from disease but rather functions which we are yet to discover.

The effects of such mechanisms which permit bats to host large loads of viruses while dampening the inflammation through which severe diseases are brought about in response to both viruses and sterile factors, asymptomatic and mild disease in the face of high loads of viruses in the sera or tissues[6] must also be observed in humans when immune mechanisms protect them from disease despite high viral loads. And indeed, even though they were mysterious in the absence of the empirically-grounded hypothesis that predicts them, observations which revealed large amounts of SARS-CoV-2 in some children who experienced none of the symptoms of COVID-19[7,8] have been made during the present pandemic.

It has been concluded that the most important barrier to the understanding of the disease tolerance through which immune mechanisms protect against disease without affecting pathogen loads might be that it requires studies of the whole physiological response of a body in which organismal function is investigated in parallel to biological mechanisms and not the study of isolated cells[3] which we refer to as immune cells on the basis of the assumption that the reduction of pathogen loads that are observed in such cells are brought about by immune mechanisms for the purpose of protecting organisms from disease. Indeed, instead of the significant overlap

which Ayres and coworkers expected to find between genes that ensure the survival of the organism in the face of disease which they investigated and those which were considered to be immunity genes when they were identified in studies of isolated cells, what they found was none.[9]

While their findings, just like those of Matae Ahn and coworkers, lead us the conclusion that those cells which we refer to as “immune” do not perform functions that protect the organism from disease when we view them through the lens that our empirically-grounded immunological hypothesis holds before us, these researchers concluded that the interactions between the host and pathogen are complex.[9] Here, we present the results of an investigation that has the capacity to reduce this complexity in the direction of which this empirically-grounded immunological hypothesis points us.

Methods

The reality that exists in organisms when immune mechanisms reduce the severity of the disease a pathogen causes and render it mild or asymptomatic without affecting pathogen load so that pathogen loads are lower in some cases of severe disease than in some asymptomatic and mild cases was illustrated with the aid of an experiment which was conducted in the mind since such a reality could not be illustrated in laboratory experiments.

The following are the conditions which permit us to conduct the thought experiment. Let the space in front of a row of porous houses which all have dogs within them be the place on earth where extraterrestrial beings from a planet where animals do not exist have decided to rest. Let the aliens be repeatedly disturbed by a certain kind of rage that is produced in porous house A only after the entry of a particular cat and never when the cat is outside the house. Let the aliens assume that the nature of the disturbing rage which would permit certain immune mechanisms to exempt the occupants of porous houses from it is that which depends on the nature of the cat and conclude on the basis of this assumption that such mechanisms must achieve this desired result by eliminating cats from porous houses.

We are able to investigate the immunological nature of the pathological effects of pathogens which permit immune mechanisms to protect organisms from such effects without affecting pathogen loads when we sufficiently consider the following results of the thought experiment. When the aliens observe that while a disturbing rage repeatedly follows the entry of a single cat into porous house A, the entry of several cats into a porous house B is not followed by any disturbance at all, they must necessarily be surprised until the reality illustrated by a thought experiment reveals the nature of the effects through which cats cause the disturbing rage in porous houses which permits occupants of such houses to be protected from them to be that which does not depend on the nature of cats since it is a nature that makes them prefer to ignore or escape at the sight of the dog,[10] the source of such effects which they could not know in the absence of this thought experiment.

As soon as this reality reveals the source of the disturbing rage as an animal which could either be sociable or aggressive in its response to the presence of the cat,[10] the aliens realize that the nature of the effects that bring about the disturbing rage in porous houses, which permits the occupants of porous houses to be protected from such effects, depends on a causative influence that cats exert on dogs. They realize that when immune mechanisms are exposed to conditions that permit them to reduce this influence, the disturbing rage will not be produced in a porous house, irrespective of how great the number of pets in the house may be or how different the nature of such pets may be, if they all exert causative influences on the dog that have the same protection-permitting nature so that when the pathway through which the disturbing rage is produced by the dog in response to any of them is blocked, the influences of the others will not cause the disturbing rage because it is through the same pathway that the dog responds to them. And they are able to expect that when the conditions that permit protective mechanisms to reduce influences of such a nature disappear and the pathway through which the dog responds to them is unblocked, the dog will produce a rage in response to every single one of the pets in the porous house that exerts such an influence on it.

Results

The investigation of the immunological nature of the pathological effects of SARS-CoV-2 and other pathogens, which the results of the thought experiment above enable us to carry out in our minds, yields the following results.

1. The immunological nature of the pathological effects of a pathogen depends on the nature of the influence it exerts on a gravity-like unobservable that produces diseases of different kinds in response to the influences of different causes

Our investigation reveals the immunological nature of the pathological effects of the pathogen to be that which does not depend on the invasive and destructive nature of the pathogen but rather on the nature of the influence which the pathogen exerts on an unobservable which produces pathological effects of different kinds through its mechanisms in response to the influences different causes exert on it. Since the differences in the strengths of the pathogen's influence under which the mechanisms of this unobservable produce different levels of disease severity, from most severe through mild to asymptomatic, do not have their origin in differences in the load of the pathogen to which the organism is exposed just as the different strengths of the sun's influence under which the mechanisms of the physical unobservable known as gravity produce different amounts of perihelion shift do not have their origin in differences in the mass of the sun to which the fabric of space is exposed but rather in differences between the distances of the orbits of different planets from the sun so that the greatest amount of perihelion shift occurs in the orbit of Mercury which is the closest to the sun,[11] we shall refer to this biological unobservable as the gravity-like unobservable. What this similarity demonstrates is that the mechanisms that bring about both physical and biological phenomena are similar.

2. All diseases which have already been brought about through causative influences of the same nature as that of the infectious agent will be reduced in severity when immune mechanisms reduce at least one of such influences and their manifestations will disappear

Since different causes which bring about pathological effects of the same immunological nature as the pathological effects of a pathogen must necessarily influence this gravity-like unobservable to bring about different diseases through the same pathway, this pathway will become obstructed when conditions permit immune mechanisms to attenuate the influence of at least one of such immunologically-linked causes. Therefore, a consequence of this result of our investigation is that all that are present among the diseases in the immunological spectrum to which the disease that is caused by a pathogen belongs will be simultaneously reduced in severity. It follows, therefore, that if such protective conditions persist long enough, such diseases will all be rendered asymptomatic and no new disease will be produced through the same pathway when the body becomes exposed to their causes because the influence of such causes will also be attenuated. This result finds representation in two kinds of phenomena.

The first are those remissions, which have continued to interest researchers because the manifestations they concern include malignancies which remain difficult to cure in spite of the many types of therapy that are available but yet have remained rare because the exact nature of the mechanisms that triggers the phenomenon remained a challenge.[12,14] The hypothesis that such remissions are caused by feverish infections which appeared to be suggested by the fact that they

are linked to such infections in time in a larger fraction of cases [13] is contradicted by the existence of cases in which there is no history of fever or infectious complications.[14]

But in the light of this result of the investigation of the exact nature of those immune mechanisms that ensure survival in the face of disease, we see that remissions are temporally linked with feverish infections in most cases which have been reported because in such cases, the conditions that permit immune mechanisms to block the pathway through which diseases in a particular immunological spectrum appear about the same time as one of the diseases in the spectrum, which manifests with a fever when the shared pathway is not blocked early enough, is produced by the gravity-like unobservable in response to the influence of a pathogen. It therefore follows that even if the one that appears among the diseases in a particular immunological spectrum at the time when protective conditions appear is not caused by a pathogen or does not manifest with a fever when the shared pathway is not blocked early enough, the shared pathway will still be blocked and the remission of all that are present among the diseases in the spectrum will occur without being linked with a feverish infection.

The phenomena of the second kind inspired different civilizations to inoculate the smallpox virus by means of variolation and Edward Jenner to inoculate other orthopoxviruses by means of vaccination.[15] And what occurs in such phenomena is the protection against diseases in the same immunological spectrum as the disease that is caused by a pathogen A (such as the smallpox virus) which follows previous infection with the same pathogen or infection with another pathogen B that causes one of the diseases in the same spectrum (such as the cowpox virus)

when conditions permit immune mechanisms to reduce the causative influence of pathogen A (in the case of the phenomenon that inspired variolation) or the influence of pathogen B (in the case of the phenomenon that inspired vaccination) and therefore to block the pathway through which all diseases in the spectrum are produced by the gravity-like unobservable.

The observation in the African nation of Uganda that patients with low versus those with high previous Plasmodium falciparum exposure have an increased frequency of severe or critical COVID-19, which was presented in a study that highlights the importance of understanding the potential clinical and therapeutic implications of overlapping co-infections,[16] when viewed in the light of the results of our investigation, leads us to the conclusion that malaria is one of the diseases in the immunological spectrum to which COVID-19 belongs. The consequence of this conclusion is that those who have survived despite high previous Plasmodium falciparum exposure are more likely to be exposed to conditions that permit immune mechanisms to reduce the severity of the diseases in that spectrum by blocking the pathway through which they are produced by the gravity-like unobservable in response to their different causes and therefore more likely to be those in whom the frequency of severe or critical manifestations of such diseases will be lowest. This consequence finds representation in the fact that the African region, which is at the most risk of malaria, has a comparatively lower COVID-19 disease burden than other regions of the world instead of the mass COVID-19 catastrophe which was predicted to be its fate on the basis of what was known about how the disease is transmitted and evidence of extensive SARS-CoV-2 spread in the region[17,18] and in the fact that the exception in the region is South Africa,[17] a nation which had low malaria levels by the time the pandemic began.[19]

And malaria is not the only disease which observations demonstrate to be part of the immunological spectrum to which COVID-19 belongs. The fact that a patient with systemic lupus erythematosus (SLE) and severe COVID-19 pneumonia who was managed conservatively without specific antivirals or steroids recovered spontaneously[20] demonstrates the multisystem manifestations that are seen in SLE to be manifestations of different diseases in the immunological spectrum to which COVID-19 belongs. And the fact that all evidence of hematological malignancy disappeared in two patients who presented with acute myeloid leukemia and relapsed acute lymphoblastic leukemia concomitantly with COVID-19 pneumonia despite the fact that they chose to have only supportive care until recovery from COVID-19 demonstrates that such cancers are also diseases that belong to the immunological spectrum of COVID-19.[21]

3. Manifestations of different diseases appear concomitantly when immune mechanisms no longer block the pathway through which they are all produced under influences of the same kind as the influence of the pathogen

Upon the disappearance of the conditions that permitted immune mechanisms to block the pathway through which different diseases are produced by the gravity-like unobservable in response to influences of the same nature as the influence of the pathogen, such diseases will produce their manifestations concomitantly if their causes are already present even if the pathogen is not present at such a time. It therefore follows that for as long as the pathway remains unblocked, such manifestations will persist and new manifestations will be produced through the pathway as the organism becomes exposed to causes which were absent when protective conditions disappeared.

This result finds representation in the broad spectrum of manifestations which we have observed in patients with the disease known as COVID-19 which SARS-CoV-2 causes, co-occurring manifestations which led us to the conclusion that this disease, which initially appeared to be just an upper respiratory disease when the pandemic began, is a multi-organ disease.[22] It also finds representation in Long COVID, which is characterized by the persistence of symptoms which appear during SARS-CoV-2 infection or in individuals who were asymptomatic while infected as well as the appearance of new diseases after infection, and which has posed a significant challenge for patients, physicians and society at large.[23]

Discussion

The results of the investigation of the immunological nature of the pathological effects of SARS-CoV-2 and other pathogens which permits immune mechanisms to protect some individuals from such effects despite high pathogen loads demonstrate that the occurrence of such pathological effects does not depend on a nature that requires immune mechanisms to attack and destroy pathogens in order to protect us but rather on a nature of their causative influence which allows immune mechanisms to protect us without reducing pathogen load by blocking the pathway through which the pathological effects of other causes which exert causative influences of the same nature are brought about. And in the light of these results we see that only when we become able to block this shared pathway will we be able to cure, with precision, those severe manifestations which occur in spite of lower loads of a pathogen that causes only one of the co-

occurring diseases that produce such manifestations and in spite of treatments that achieve the desired result of reducing the load of such a pathogen.

We are therefore able to answer the question, “Do we need to reconsider treatment Protocol?” which was asked by the clinicians who reported recovery in a case of SLE with severe COVID-19 pneumonia which was managed conservatively without specific antivirals or steroids.[20] And the answer is that treatment protocol now needs to do more than reduce pathogen load with specific anti-pathogen treatments if co-occurring diseases that produce severe manifestations despite lower loads of the pathogen that causes one of them from will be prevented from causing death with precision. Such protocol must also block the pathway through which the manifestations of diseases that co-occur with the diseases that the pathogen causes by exposing immune mechanisms to conditions that permit them to attenuate the influence of the pathogen, the nature of which is the same as the influences through which all other diseases in the pathogen’s immunological spectrum are produced.

The surprised clinicians who reported the disappearance of all evidence of hematological malignancy in two patients who presented with acute leukemia concomitantly with COVID-19 pneumonia and had only supportive care until recovery from COVID-19 asked if COVID-19 could induce remission of acute leukemia and demanded investigations to find an explanation for such regression that is associated with infection with the hope that such investigations will lead to an understanding of the immunological mechanisms and consequently to the discovery of a

new therapeutic modality for patients with hematological malignancies.[21] And such investigation which they demanded now furnishes us with the capacity to answer their question.

The manifestations that include those of the disease that SARS-CoV-2 causes, which all appeared to be manifestations of this single disease that is known as COVID-19, do not induce the remission of malignancies that appear concomitantly with them. Such malignancies only disappear because their immunological spectrum, which includes not only those of diseases which our oncologists attempt to cure with cancer treatments but also COVID-19 and other diseases which they do not attempt to cure with such treatments, are all produced through the same pathway and upon the appearance of conditions that permit immune mechanisms to attenuate the influence of the cause of any of these diseases, the shared pathway is blocked and the manifestations of all the diseases in the spectrum disappear. Therefore, such new therapeutic modality that patients with malignancies need is that which will enable oncologists to block the pathway through which the gravity-like unobservable produces all diseases which belong to the same immunological spectrum as such malignancies.

The results of this investigation also throw light on the origin of those multisystem manifestations, such as those of SLE, which we attribute to a pathogen when the different diseases in the immunological spectrum of the pathogens are produced by the gravity-like unobservable in response to the influence of the same nature as the influence of the pathogen which their causes exert on it and which we attribute, in the absence of the pathogen, to a mistaken attack on the body that immune mechanisms make because the pathogen is mimicked

in absentia. In the light of these results, we are able to explain why such multisystem manifestations that are linked with pathogens occur even in the absence of pathogens without resorting to assumption of autoimmunity.

Such multisystem manifestations are only linked with a pathogen because they are brought about by their different causes through influences that have the same immunological nature as the influence of the pathogen so that when the pathway through which the pathogen's pathological effects are produced is unblocked, such multisystem manifestations will appear without the manifestations of the disease the pathogen causes if the pathogen is absent or no longer exerts a causative influence on the gravity-like unobservable at such a time.

On the basis of the assumption that multisystem manifestations, such as SLE, that are temporally linked with pathogens are brought about by such pathogens through the induction of autoimmunity, the notion of vaccine-induced autoimmune response is suggested whenever such manifestations are temporally linked with vaccines.[24,25] But the light that the results presented here has thrown on the origin of the multisystem manifestations, which appeared to be autoimmune in the absence of such results, enables us to see that neither pathogens nor vaccines are the cause of such multisystem manifestations with which they are temporally linked.

The immune mechanisms that protect from the pathological effects of the pathogen do not achieve this desired result by attacking the pathogen and therefore could not bring about pathological manifestations by mistakenly attacking the organism when the pathogen is

mimicked in absentia. Multisystem manifestations are brought about by their causes through their influence on the gravity-like unobservable and the temporal relationship between such multisystem manifestations and the pathogen is a consequence of the concomitant appearance of the pathological effects of the pathogen and those of the different unknown causes of such manifestations upon the disappearance of the conditions that permit immune mechanisms to block the pathway through which pathological effects are produced by this unobservable in response to causative influences of the same nature which the pathogen and such causes exert by reducing the influence of the pathogen or one of such unknown causes with which the pathogen is immunologically linked. The appearance of such multisystem manifestations which we described as autoimmune must therefore occur whenever conditions that permitted the obstruction of this shared pathway disappear and the gravity-like unobservable produces pathological effects in response to their different unknown causes even if the pathogen is absent at the time.

The results presented here, however, do not furnish us with answers to the following important questions. What are the predictors of a state in which conditions permit protective mechanisms to block the pathway through which different diseases with the same immunological nature are produced in response to different causes through the same pathway by reducing the causative influence of the pathogen? And how can we bring about such a state in those individuals who suffer from severe manifestations that are linked with a pathogen despite treatments that reduce pathogen load because diseases of different kinds, which are produced through the same pathway as that which the pathogen causes, continue to exert their causative influence on the gravity-like unobservable?

The answers to these questions call for an investigation of the purpose for which those mechanisms that reduce pathogen load exist, the nature of the gravity-like unobservable which produces different diseases under the influence of different causes as well as the nature of the immune mechanisms which block the pathway through which such diseases are produced and protect organisms from diseases without affecting pathogen loads. And the results of such investigation ought to be presented in another paper in the shortest possible time.

Declaration of Competing Interest

I declare that there are no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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