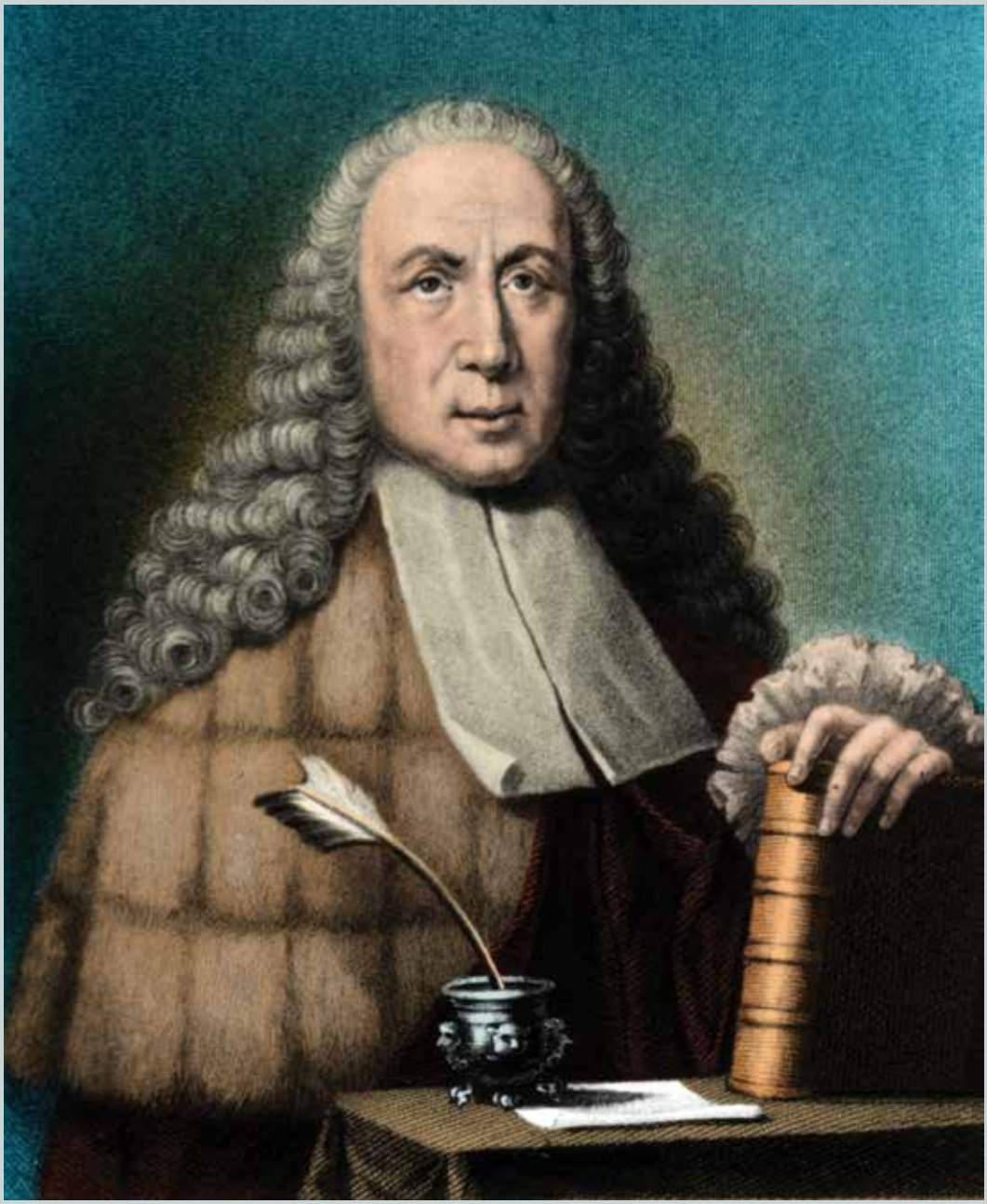

The Antiquity of Rheumatic Diseases as in Giovanni Morgagni's 1761 *De Sedibus Et Causis Morborum Per Anatomen Indagatis*

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Studies of rheumatic diseases, and particularly of their antiquity, have provided insights about their distribution and determinants.[1-7] Gout, osteoarthritis (OA), and spondyloarthropathies (SpA) were documented well before the 1700s,[8-11] while rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and vasculitides were recognized more recently.[1,12-14]

Morgagni's 1761 text, case histories and autopsies from 604 patients, was a milestone in anatomical pathology and clinical medicine. The hypothesis that he might have described certain rheumatic diseases before they were a recognized diagnosis was tested by reviewing William Cooke's 1824 English translation of Morgagni's work, focusing on the clinical vignettes and corresponding autopsy results that seemed to reflect rheumatic diseases.[15,16]

Giovanni Battista Morgagni

Giovanni Battista Morgagni was an Italian anatomist who lived from 1682 to 1771. He is known for his book *De Sedibus Et Causis Morborum Per Anatomen Indagatis* (On The Seats And Causes Of Diseases Investigated Through Anatomy), published in 1761.[15,16] His work was formative in the field of medicine, as he was the first to provide a link between medical case reports and autopsy findings.

Through clinical vignettes Morgagni investigated the organic causes of disease in his patients and correlated anatomical findings with clinical symptoms. Medical author, humanist, and historian, Sherwin Nuland, wrote that Morgagni innovated an "…entirely new basis…to understand the nature of disease…. The cause of disease would be seen, therefore, as a failure in some part of the machinery."[17]

However, when reading Morgagni's text, it is clear that the cause of the disease in certain cases was not necessarily known, as Nuland observed, "…Morgagni did not speculate about the underlying stimuli which initiate the process of breakdown. This more basic step could not be taken until such disciplines as bacteriology and biochemistry were developed in the nineteenth century."[17]

In some of the enigmatic cases Morgagni presented, the etiology of disease may have been rheumatologic.

Gout

Gout, recognized by the ancient Egyptians, is recounted in the Old Testament (King Asa), and the diagnosis was solidified first by Hippocrates, and later by Galen.[8] In 1679, Antoni van Leeuwenhoek described the uric acid crystals that contribute to gout.[8] By the time Morgagni's book was published, gouty arthritis was well known.

Morgagni referenced three cases of gout, although he admitted that the prevalence of gout may have been underestimated since gout "is a disease which generally attacks the rich, but dissections are usually performed on the bodies of the poor."[16]

One of Morgagni's cases involved a patient who had a presumed diagnosis of gout, with clinical findings of "podagra

CONDITION	CLINICAL PRESENTATION	AUTOPSY FINDINGS
Gout (also features of vasculitis) Cooke, 1824, Vol. II, 40-2.	"The subject of this case was a nobleman of Bologna, sixty-one years of age, who for many years had been afflicted with hemicranial, sometimes with erratic or fixed gout, and at others with renal calculi. He was invaded by an accession of podagra in the right hand…The hand recovered, but the patient then suffered pain in the right kidney…The day previous to his death he vomited…and felt slight pain with pulsation and heat, in the region of the stomach… The pain and pulsation in the region of the stomach continued, and he discharged blood per anum."	"The whole tract of intestines, from the stomach to the termination of the rectum, was horribly inflamed, so that not the least part was free from lesion. They contained bloody matter like that which had been discharged. The stomach and kidneys were in a healthy state. The posterior part of the lungs, especially on the right side, was slightly inflamed, and the pericardium contained a small quantity of fluid."
Gout Cooke, 1824, Vol. II, 280	"A priest, fifty years of age, having been for many years subject to arthritic pains, especially in the fingers, was at length seized with nephritic pains also."	"All the intestines inclined to a livid hue. The stomach was healthy, and there was no trace of the part from which the blood had issued. There were several very small calculi in the kidneys, some of which were black and others white… At the joints of the fingers, a yellowish white colour... in the theca of the tendons."
Gout Cooke, 1824, Vol. II, 545-6	"George Corneli, a cardinal of the Roman church, was subject to pains in the joints, and in the kidneys. Having voided some calculi he lost all symptoms of the kidneys' being affected, but, at times, his arthritic complaints returned…In this state he had scarcely passed his sixty-fourth year, when he lost his appetite, and was attacked with an arthritic paroxysm. His right hand and left knee began to swell."	"Both the kidneys exceeded their natural size, but the right was the largest, and, with the investing fat, it almost equalled the size of a man's head. It contained eleven calculi, and most of them were ramified, and of considerable magnitude. The left contained a solitary branched calculus. In appearance these calculi resembled black coral, and that part of the substance of the kidneys which lay in contact with them was hard and callous."
Osteoarthritis Cooke, 1824, Vol. II, 548.	"[A] woman who died from apoplexy."	"In the knee… that part of the cartilaginous crust of the patella, corresponding with the external condyle of the femur, appeared as if it had been rubbed away, and was marked with slight and small parallel furrows, as if the point of a chisel had been drawn along it. A great number of globules were prominent within the joint…The larger adhered to a cartilaginous crust, or rather to the fibriae of a synovial gland, which closely covered the cartilage in some recesses of the bones; and the smaller were adherent to the capsular ligament. These bodies were white, and had a smooth surface; some of them were bony, and others contained a bony nucleus beneath a cartilaginous crust."
Osteoarthritis Cooke, 1824, Vol. II, 551-552	"A woman, about forty years of age, lame on the left side, had recently received a violent contusion on the lower ribs."	"The os femoris was deprived of its head and neck. The former remained in the acetabulum, though the cartilage with which both these parts were incrusted was ulcerated in places, and the bony substance of the head was not quite healthy."
Osteoarthritis Cooke, 1824, Volume II, 553	"A lame woman, nearly eighty years of age, died from apoplexy…She had been lame on the left side, and the corresponding leg was not only shorter than the right, but was much extenuated."	"On exposing the left hip-joint, we found that the head of the femur, head, instead of being globular as usual, was almost flat, was somewhat enlarged, and was not furnished with any round ligament."
Osteoarthritis Cooke, 1824, Vol. II 554.	"The subject of this case was born with an equality of limbs, but he had been lame nearly the whole of his life."	"The anterior half of the original acetabulum remained, and in its fundus there was a substance of pale reddish color, which seemed morbid, and somewhat resembled glandular textures. The other half was filled with a bony substance."
Rheumatoid Arthritis Cooke, 1824, Vol. XX, 543	"A woman had frequently been affected with sciatic pains in the joint of the right femur."	"The head of the os femoris was not rounded into a globular form, but was depressed; and instead of being covered by a smooth and white cartilage, this substance was of an ash colour. At the posterior part the cartilage was deficient, so that the bone exhibited numerous roundish and protuberant particles."

CONDITION	CLINICAL PRESENTATION	AUTOPSY FINDINGS
SLE Cooke, 1824, Vol. I, 264	A young man who had previously laboured under chronic fever, was seized with an acute febrile affection, united with pain of the thorax, difficulty of respiration, cough, and occasional expectoration of matter which was tinged with blood."	"The magnitude of the spleen was augmented in at least a three-fold degree. The left lung was extremely turgid; it was also universally inflamed and indurated, and adherent to the costal pleura; and this membrane was slightly red. The pericardium was distended by a fluid resembling whey; and there were some concretions scattered on the surface of the heart."
Vasculitis Cooke, 1824, Vol. I, 360–1	"A washer-woman apparently about forty years of age...was repeatedly brought into the hospital within the last six years of her life on account of a difficulty of breathing... during the continuance of the paroxysms no pulsation could be perceived at the wrists."	"The pericardium...was thickened, and appeared of a tendinous structure; and the heart was enlarged. Its parietes [sic] were thicker than ordinary, but the interior structure of this organ was natural, with the exception that the sinus of the left auricle was more capacious than usual... The corpuscula Arantii of the aortic valves were thickened, and indurated; and internally they were, in many places, of a yellow colour."
Vasculitis Cooke, 1824, Vol. I, 386–8	"The wife of a painter at Padua forty years of age... began to be afflicted with palpitation of the heart... In addition to palpitations of the heart, she had a sense of erosion in the thorax"	"Both cavities of the thorax contained a considerable quantity of serous fluid...the pleurae were adherent at the lower and back part of the left lung... The aorta seemed to be a little contracted, and the heart was somewhat enlarged...In the vicinity of the emulgent arteries, the internal lamella of the aorta could be easily rubbed off by lightly applying the nail to it; and a little above the semilunar valves there was a narrow ulcer, where the fibres were displayed in a divided state."
Vasculitis Cooke, 1824, Vol. I, 379–80	"A knight sixty-five years of age...who, during some years had suffered from obstinate ulceration of the legs...At length... was affected with rheumatic pains, but they were so slight as not to prevent him from going out...he was attacked with violent pain beneath the sternum and in the arms, with some confusion of mind."	"The pericardium was distended with blood of a black colour, which had been effused from the left ventricle of the heart through a fissure half an inch in length, and in the longitudinal direction of the ventricle. The fibres in the circumference of the rent were destroyed by ulceration."
Spondyloarthropathy Cooke, 1824, Vol. II, 547–8	"A young man... had violent pain in his right lumbar region...A year having elapsed, the pain, began to attack the left side also, and he experienced some pain in his neck which seemed to be rheumatic. An inability to move his legs followed, the abdomen became tympanitic."	"We were only permitted to examine those parts in the loins which had been the seat of the obstinate and violent pain... When the tendon of the latissimus dorsi was removed, we observed that the thick fleshy mass which affords a common origin to the sacro lumbalis and longissimus dorsi muscles was greatly discoloured... This appearance was observable also in the subjacent sacro-lumbalis, and in the quatratus lumborum muscles. The fibres within this space were astonishingly flabby, and were disjoined by numerous coagula of blood."
Sarcoidosis Cooke, 1824, Vol. II, 17–9	"A lady of rank in Padua... in her thirty-fourth year, began, whist lying-in, to be annoyed with frequent vomiting... the vomiting continued to the time of her death, which event did not happen till after the lapse of twenty-four years... When the hour of dissolution approached, she gave direction for her body to be examined after death, hoping, that if the cause of her protracted illness should be apparent, the discovery of it might be rendered of advantage to her children, with respect to an hereditary disease. For her mother, who had been dead many years, laboured under vomiting; and her daughter began to be affected with it."	"The abdomen contained a considerable quantity of yellowish serum, and the omentum adhered to the peritoneum on the left side. The stomach was contracted, and near the antrum pylori the contraction was so much greater than in other parts, that the viscus appeared as it if had been divided into two cavities; and the mucous coat was of a red colour, as if from inflammation...The pancreas was white and indurated...The whole of the spleen was of a pale colour, and also part of the surface of the liver. The parietes [sic] of the gall-bladder were thickened to a degree which exceeded any thing of the kind I had previously observed... All the intestines were greatly contracted, but especially the small intestines... Both cavities of the thorax contained a considerable quantity of bloody serum; and the pleurae were connected together by thick and rather long membranous filaments. The pericardium adhered closely to the whole surface of the ventricles of the right auricle, and also to the surface of the large vessels pertaining to the heart: and the extreme border of the aortic valves was greatly thickened, and was of cartilaginous hardness."

in the right hand," and right kidney pain.[16] In the autopsy, Morgagni focused on the gastrointestinal and pulmonary inflammation. Had he dissected the joint, it is possible that he would have found tophi characteristic of gout.

In an autopsy (performed by Morgagni's mentor, Valsalva) of a patient who presented with "arthritic pains, especially in the fingers…[and was] at length seized with a nephritic pain,"[16] Morgagni described "several very small calculi in the kidneys" and "[at the] joints of the fingers, a yellowish white colour...in the theca of the tendons."[16]

Renal calculi that "resembled black coral" were noted by Morgagni in autopsy findings of a cardinal who "was subject to pains in the joints, and in the kidneys," pointing to a diagnosis of gouty arthritis with renal involvement.[16] It should be noted, however, that the black color of the stones would be atypical for gout, where the stones would be an orange or red color.

Modern population-based epidemiological studies estimate the prevalence of gout at one to four percent, but it may be as high as 10 percent in some regions;[18] in Morgagni's series it was less than one percent of the population, likely for reasons previously discussed.

Osteoarthritis

Morgagni described four cases of possible OA. He commented on the classic joint findings in one patient that included a "rubbed away" appearance of the patella, and "slight and small parallel furrows" in the joint.[16]

He reported other instances of likely post-traumatic OA. One patient had clinical features of "[an] os femoris [that] was deprived of its head and neck."[16] Another had a femur that "was almost flat, [and] was somewhat enlarged."[16] Yet, another patient was found to have only the "anterior half of the original acetabulum [that] remained, and in its fundus there was a substance of pale reddish color."[16]

It is likely that the prevalence of OA was actually higher than the four cases Morgagni described among the 604 autopsies. The dissections focused on the areas of the body that corresponded with the patient's chief complaint and cause of death. Morgagni related several cases of infections such as gonorrhea and syphilis in his text, but the autopsies were mostly performed in the genitourinary region, thus missing potential examples of reactive arthritis.

Modern epidemiological studies report much higher rates of OA than in Morgagni's series. OA, particularly of the knee, is the most common joint disease today, with an estimated prevalence of 10 percent to 13 percent in the United States.[19]

Autopsy studies like that of Morgagni's cannot provide valid estimates of disease prevalence, but the high prevalence of osteoarthritis today may be the result of more awareness of the condition, longer life expectancies, and environmental factors such as obesity.[19]

Rheumatoid arthritis

Other rheumatologic diseases such as lupus, RA, and vasculitides were not well described or even recognized at the time of Morgagni's publication.[1,12,-14] It is generally considered that RA was exceedingly uncommon if not non-existent prior to 1800.[1]

After the fall of the Roman Empire, some physicians such as Paulus Aegineta, distinguished gout from other rheumatic disorders. In 1642, in his posthumous edition of *Liber de Rheumatisme et Pleuritide Dorsali*, Guillaume de Baillou differentiated between gout as affecting a single joint and rheumatism as a condition that affected the whole body. It was not until 1858 that Sir Alfred Baring Garrod first used the term rheumatoid arthritis.[12]

The renowned paleopathologist Dr. Juliet Rogers investigated the occurrence of rheumatologic diseases in ancient human skeletons in England, and found that RA was less common than gout and seronegative spondyloarthritis.[14] Many authors regard environmental factors as important in the causation of RA along with post-industrial revolution exposures. Periodontal disease[1,20] and air pollutants[14] may account for why it has emerged as a more common disease in the modern era.[1] Morgagni's cases may be the first reports of RA.

Morgagni wrote of a "woman [who] had frequently been affected with sciatic pains in the joint of the right femur" and found that "the posterior part the cartilage was deficient, so that the bone exhibited numerous roundish and protuberant particles."[16] In his discussion, Morgagni reflected "Here there was no disease or deposition of calcareous matter around the joint, but the whole disease was situated within it. Fernelius believed that the arthritic humour never, or, at least, very seldom penetrated the cavity of the joints, but affected the surrounding ligaments, membranes, and tendons."[16]

Although the location of disease activity was less consistent with RA, and the dissection was limited to the femur, there were features suggesting RA, including synovial membrane thickening and erosions at the os femoris. RA in the hip often results in joint space narrowing and erosive changes that include femoral head collapse and resorption leading to *protrusio acetabula*.[20,21] The patient, and Morgagni's reflections, suggest RA.

The modern estimated prevalence of RA in the United

States is about 0.6 percent,[13] in contrast to the prevalence of RA among Morgagni's cases of 0.17 percent.

Systemic Lupus Erythematosus

Lupus is also a relatively new disease, although Hippocrates first wrote about the skin findings of lupus. Lupus translates to "wolf," in Latin, and the term was first used in medieval times to describe the skin ulcerations often seen with lupus.[22,23]

Understanding lupus and its dermatologic manifestations increased in Europe in the 19th century when Cazenave first used the term "lupus erythematosus." The Viennese physician Kaposi was the first to describe the systemic signs and symptoms of lupus in 1872.[22]

Morgagni discussed a young man whose dissection was performed by Valsalva and was notable for the descriptions of pleurisy and serositis. At his autopsy, he was found to have a "pericardium [that] was distended by a fluid resembling whey," a "left lung [that] was extremely turgid [and] universally inflamed and indurated," and a "spleen [that] was augmented in at least a three-fold degree."[15] These autopsy findings, with inflammation noted in the lungs, pericardium, and spleen, can be found in lupus.[24-26] Massive serositis can also be a presenting symptom of lupus.[25]

Diffuse alveolar hemorrhage is estimated to occur in less than two percent of patients with lupus, and although it is rare it may be the initial presenting symptom.[24] Respiratory findings can also be found at autopsies and include bronchopneumonia, lobar pneumonia, and atypical interstitial pneumonia.[26] Splenomegaly occurs in lupus,[24,26]and autopsy findings may include alterations in the collagen of the spleen.[26]

Worldwide, the prevalence of SLE appears to be highest in North America, at 241 per 100,000 persons.[27] In Italy, the setting of Morgagni's case reports, the prevalence is estimated to be 71 per 100,000 persons.[28] The prevalence was 0.17 percent in Morgagni's series.

If lupus is a more modern disease, it is possible that environmental factors such as certain microbes or pathogens, smoking, and occupational exposures (i.e., silica) may have contributed to its rise, although this remains speculative.[20,29]

Vasculitis

Case reports of vasculitides began to appear in the 19th century. In their 1866 publication in the *German Archive for Clinical Medicine*, Adolf Kussmaul and Rudolf Meier first described clinical and autopsy findings in polyarteritis nodosa.[2] Granulomatosis with polyangiitis (GPA) was characterized as a disease entity in the 1930s.[3]

Systemic vasculitis seems to have been recognized relatively recently with occupational triggers such as solvents, silica, and allergens as potential contributors.[30] The contemporary estimated incidence of systemic vasculitis varies by type and region, and data regarding its prevalence is still limited.

Di Giacomo (1984) commented on a patient in Morgagni's text that resembled Takayasu's arteritis.[31] The patient was a "…washer-woman apparently about 40 years of age" who at the time of death had "no pulsation [that] could be perceived at the wrists." Her "…pericardium…was thickened, and appeared of a tendinous structure; and the heart was enlarged. Its parietes [*sic*] were thicker than ordinary."[15] In Di Giacomo's assessment, the clinical and anatomic features that were consistent with Takayasu's arteritis were the absence of a radial pulse due to alterations in the subclavian artery, as well as thickening of the aorta. These findings alluded to the cause of heart failure and death in the young woman. This appeared to be one of the earliest documented reports of aorto-arteritis.

Vasculitides of different types might also explain the diffuse inflammation that Morgagni observed in several of his patients. He described a young woman who developed inflammation of the aorta, with enlargement of the heart. On autopsy, "Both cavities of the thorax contained a considerable quantity of serous fluid...the pleurae were adherent at the lower and back part of the left lung... the internal lamella of the aorta could be easily rubbed off by lightly applying the nail to it; and a little above the semilunar valves there was a narrow ulcer."[15] The differential diagnosis for the aortic inflammation, especially in a young woman, includes several inflammatory conditions such as Takayasu arteritis, GPA, and polyarteritis nodosa.[32]

Morgagni then related the cardiac findings in a man who had ventricular rupture and lower extremity ulceration writing, "The pericardium was distended with blood of a black colour, which had been effused from the left ventricle of the heart through a fissure half an inch in length, and in the longitudinal direction of the ventricle. The fibres in the circumference of the rent were destroyed by ulceration."[15] While such ulcerations could certainly be seen in ischemic necrosis following a myocardial infarction, cardiac manifestations can also be seen in vasculitis, and this patient also displayed ulceration of the legs and rheumatic pain that may reflect small vessel vasculitis.

In GPA, cardiac findings include pericarditis, cardiomyopathy, coronary artery disease, and valvular disease.[33] A recent report[34] with an autopsy result significant for GPA

showed cardiomyopathy as well as myocyte necrosis, which is similar to the autopsy findings in Morgagni's patient.

Morgagni also noted intestinal findings (in a dissection by Valsalva) of a patient with gout that are consistent with vasculitis. He wrote, "…he discharged blood per anum.... The whole tract of intestines, from the stomach to the termination of the rectum, was horribly inflamed, so that not the least part was free from lesion.... The posterior part of the lungs, especially on the right side, was slightly inflamed."[16] The findings in the gastrointestinal tract of this case are reminiscent of ulcerative colitis, which could also explain the patient's joint pain; however, small bowel involvement with ulcerative colitis is very rare. The lung and pericardial involvement on autopsy point to a more systemic cause which may include vasculitis. Vasculitides that can affect the gastrointestinal tract and the lungs include polyarteritis nodosa, GPA, eosinophilic granulomatosis with polyangiitis, and microscopic polyangiitis.[35]

In four studies conducted in Europe, the pooled analysis estimated the annual incidence of primary systemic vasculitis to be 0.002 percent.[36] In Europe, the estimated prevalence of GPA, the most common vasculitis, ranges from 0.0024 to 0.0157 percent.[21] Among Morgagni's cases the prevalence of vasculitis was 0.66 percent.

Spondyloarthopathy

Spondyloarthritis may have been described in antiquity and in the *Bible*. Archaeological evidence suggested that ankylosing spondylitis may have existed as early as 2000 BC.[37] Moses and Pharoah[9] may have had this, although subsequent reports considered that they most likely had diffuse idiopathic skeletal hyperostosis.[10]

Morgagni analyzed the case of a young man with severe lumbar pain. "We were only permitted to examine those parts in the loins which had been the seat of the obstinate and violent pain.... When the tendon of the latissimus dorsi was removed, we observed that the thick fleshy mass which affords a common origin to the sacro lumbalis and longissimus dorsi muscles was greatly discoloured... This appearance was observable also in the subjacent sacro-lumbalis, and in the quatratus lumborum muscles. The fibres within this space were astonishingly flabby, and were disjoined by numerous coagula of blood."[16]

The musculoskeletal symptoms and findings in this case are reminiscent of sacroiliitis with an underlying diagnosis that includes ankylosing spondylitis, reactive arthritis, or inflammatory bowel disease. The autopsy in this case was limited to the muscles surrounding the spine, and muscle degeneration was observed. Paravertebral muscle atrophy and fatty degeneration can be seen in ankylosing spondylitis.[38] Fatty metaplasia of the bone marrow is a demonstrated feature of ankylosing spondylitis, with fatty infiltration in the sacrum and ilium.[21] It is possible that had Morgagni been able to dissect the spine, he would have discovered these findings.

A systematic review of the prevalence of AS worldwide found the highest prevalence was in North America (31.9 per 10,000), the lowest in Africa (7.4 per 10,000), and in Europe 23.8 per 10,000.[39]

Sarcoidosis

Sarcoidosis was first described in 1869 by Jonathan Hutchinson.[40] Like lupus, it was initially regarded as a dermatologic condition before the systemic findings of respiratory symptoms became more widely documented. There was one patient in Morgagni's series with possible sarcoidosis.

Morgagni chronicled the long and progressive course of illness, writing "A lady of rank in Padua... in her thirty-fourth year, began, whist lying-in, to be annoyed with frequent vomiting...the vomiting continued to the time of her death, which event did not happen till after the lapse of twenty-four years.... The abdomen contained a considerable quantity of yellowish serum, and the omentum adhered to the peritoneum on the left side. The stomach was contracted…and the mucous coat was of a red colour, as if from inflammation.... The pancreas was white and indurated.... The whole of the spleen was of a pale colour, and also part of the surface of the liver."[16]

These symptoms and autopsy findings are consistent with systemic sarcoidosis in a young woman. The prolonged disease course suggests that it is unlikely that she had a malignancy. The gastrointestinal symptoms described can occur in sarcoidosis, and may even mimic peritoneal carcinomatosis.[41,42] The spleen is more commonly involved in sarcoidosis than other abdominal organs, and intestinal sarcoidosis is more rare.[43]

A recent case report of a patient with sarcoidosis found ascites, generalized lymphadenopathy, enlarged liver and spleen, terminal pneumonitis, bilateral hydrothorax, and mitral valve endocarditis.[44]

Sweden has among the highest rates of sarcoidosis with an estimated incidence of 11.5 per 100,000 per year.[45]

Implications of Morgagni's research

Morgagni's work presaged a clinicopathologic framework for modern medicine. Among his cases, were patients

with likely OA, gout, and SpA, and possible cases of RA, SLE, vasculitis, and sarcoidosis. These latter cases were documented before these were generally known diagnoses. These observations would suggest that many autoimmune conditions may have existed prior to the industrial age, which would challenge the notion that these are relatively modern afflictions.

Since autopsy data are not comparable to population-based disease occurrence estimates, this likely accounts for the relatively low frequencies of these diseases in Morgagni's series and confounds attempts to compare disease frequency to the modern era. For example, there appears to have been a stark increase in the prevalence in lupus since the 1970s. This increase in prevalence may be due to greater detection through anti-nuclear antibody testing.[46]

With each case that Morgagni presented, he created a scientific narrative of clinical symptoms that led to tangible anatomical changes. As the causes of most of the diseases he examined were not apparent, he often did not know what he was observing. The absence of other supporting evidence, such as detailed histories, anatomical drawings, diagnostic studies, imaging studies, serologies, and histology, makes reaching certain diagnoses challenging. One cannot be certain that these interpretations of Morgagni's studies are correct, but they are plausible and persuasive.

Presentations of rheumatic/autoimmune disorders vary and patients may not necessarily have serologic or tissue evidence of disease. Thus, physical examination remains essential for establishing a diagnosis. Morgagni's detailed clinical vignettes and autopsy findings provide an interesting and reasonable framework for speculating about retrospective diagnosis.

While the interpretation of historical case descriptions and autopsy findings through a modern lens is fraught, at least some of the cases related by Morgagni may represent systemic autoimmune and/or rheumatic diseases. Morgagni's publication represents an important landmark in the description of diseases. With new advances in medical knowledge, readers from subsequent generations can benefit from his insights into disease.

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