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Pathology of the Upper Airways

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During the respiratory cycle, air flows from the nares to the alveoli and back to the atmosphere, through the airways. Although their function would appear simple and straightforward, both upper airways (*i.e.*, nose, paranasal sinuses, pharynx, and larynx) and much of the lower respiratory tract (*i.e.,* trachea, bronchi, and lungs) are endowed with a mucous membrane that humidifies, warms, and purifies the inspired air. Because of this integrated functional role and anatomic contiguity, it should not be surprising that conditions affecting the tracheobronchial tree and lungs are frequently associated with upper airway disease. Examples of the latter association abound and include genetic (see Chap. 9), inhalational (see Chap. 17), infectious (see Chaps. 42, 43, and 45), and neoplastic disorders (see Chaps. 53 and 55).

I will presently focus on a small yet fascinating group of disorders characterized by frequent involvement of both upper airways and lower respiratory tract by the same pathologic process, sometime during their evolution. They include Wegener granulomatosis, lymphomatoid granulomatosis, allergic granulomatosis and angiitis (AGA: *i.e.*, Churg-Strauss syndrome), and relapsing polychondritis (RP). Because the pulmonary involvement in the first three diseases has been discussed in detail in Chapters 68, 55, and 69, respectively, I will stress their upper airway manifestations. Some important causes of upper airway obstruction in children will be briefly reviewed for the sake of completion (Display 72-1).

WEGENER GRANULOMATOSIS

Since its description in 1936, Wegener granulomatosis[1] has been a source of fascination for clinicians and pathologists alike. By definition, Wegener granulomatosis is a disease of an inflammatory nature and unknown etiology.[2,3] Its initial manifestations are usually restricted to one or two anatomic sites; ultimately it may become a systemic disorder with multiorgan involvement. Consequently, the clinical manifestations are dependent on the stage of the disease.[4,5] In its systemic form, the patient has clinical manifestations of malaise, fever, and abnormal laboratory tests, including elevated sedimentation rate and anemia.[6,7] In addition to the lungs, the upper respiratory tract can be the site of dramatic changes (Figs. 72-1 and 72-2). The trachea can also be involved, usually after the lung.[8]

Because the nose is the most surgically accessible area of involvement in Wegener granulomatosis, it is usually biopsied in patients with even mild nasal symptoms.[9] Thus, head and neck pathologists are often the first to see histologic material in cases of suspected Wegener granulomatosis. The pathologist reviewing such cases must be well aware of other lesions included in the differential diagnosis of nasal inflammation, nasal ulceration, and nasal destruction. This is an area of pathology that requires open communication between the attending physician, the surgeon who performs the biopsy, the pathologist, and the microbiology laboratory where cultures are performed. The diagnosis of Wegener granulomatosis, particularly in atypical cases, has been greatly aided by the development of the antineutrophil cytoplasmic antibody (ANCA) test (see Chaps. 62 and 68).[10,11]

Surgeons performing nasal biopsies are usually aware that the most readily available tissue is not ideal to make a histopathologic interpretation. Invariably, the patients will have crusting of the nasal mucous membranes, particularly the nasal septum and nasopharynx. Biopsy specimens taken from a bleeding ulcer bed from which the crust has been removed will often show only granulation tissue. Biopsy from the nonulcerated or more normal-appearing mucosa is often the most rewarding. Cultures should always be obtained during biopsy because some infectious diseases can closely mimic Wegener granulomatosis.

Histopathologically, Wegener granulomatosis is characterized by a necrotizing granulomatous inflammation and vasculitis, the two often occurring in close association. The granulomas are quite different from the small epithelioid, circumscribed granulomas of sarcoidosis. They tend to be larger and have necrotic central zones with an irregular, stellate, or geographic outline

DISPLAY 72-1. UPPER AIRWAY DISEASE ASSOCIATED WITH PULMONARY DISEASE

Wegener granulomatosis
Lymphomatoid granulomatosis
Allergic granulomatosis and angiitis (*i.e.*, Churg-Strauss syndrome)
Relapsing polychondritis
Obstruction of upper airways in the pediatric age group (*e.g.*, hypertrophy of adenoids with pulmonary hypertension, tracheobronchial papillomatosis)

when viewed at low magnification (Figs. 72-3 and 72-4). The periphery of the granuloma contains the usual chronic inflammatory mononuclear cells, palisaded histiocytes, and scattered giant cells.

The pathogenesis of these granulomas has been the subject of much speculation.[12] Giant cells are invariably a part of the inflammatory response in Wegener granulomatosis; in fact, if giant cells are not observed, it is prudent to question the diagnosis of Wegener granulomatosis. Likewise, the presence of discrete sarcoidlike granulomas is distinctly rare and should raise doubt on possible Wegener granulomatosis.

The vasculitis tends to involve small muscular arteries[2]; it consists of an infiltrate of lymphocytes and histiocytes (Figs. 72-5 through 72-7). Occasionally, eosinophils are part of the inflammatory process, including infiltration of the vascular wall. The vasculitis progresses to occlude the lumen of the blood vessel and may be partially responsible for the infarctive type of necrotizing granulomas. Giant cells can also be found in the vasculitis. Fibrinoid necrosis, of the type seen in polyarteritis nodosa, is usually not a prominent feature of Wegener granulomatosis.

In nasal biopsy specimens, the necrotizing granulomas are less than perfectly formed.[13] Often, the granuloma takes the form of zonal necrosis associated with marked chronic inflammation. The zonal necrosis may feature a purulentlike infiltrate in its center and only a vague attempt at a cuff formation by the lymphohistiocytic population. Multinucleate histiocytic giant cells may also occur in this background, and they help in the diagnosis (Fig. 72-8).

FIGURE 72-1. This patient had received treatment for Wegener granulomatosis of 1 year's duration. Notice the deformity of the nasal tip caused by destruction and collapse of the septal cartilage.

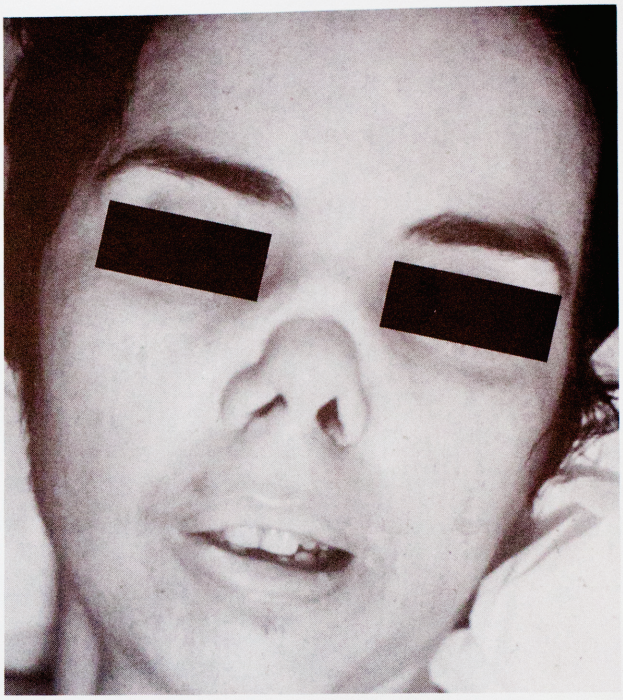

FIGURE 72-2. Advanced nasal septum destruction resulted in saddle-nose deformity in a woman with Wegener granulomatosis at postmortem. (Contributed by the editor.)

Vasculitis in nasal biopsies tends to be even more elusive.[14] This is because the intensity of the inflammation often precludes its recognition. It is important to search for the vasculitis in areas where the background inflammation is less intense, this often being at the edge of the ulceration. It avoids overinterpreting as vasculitis the finding of small blood vessels surrounded by chronic inflammatory cells, frequently a coincidental finding. True vasculitis requires inflammation of the blood vessel wall itself. The pathologist must be willing to search diligently, even in the small blood vessels surrounding the most intense portions of the inflammatory process. By doing so, occasionally small areas of acute capillaritis or venulitis will be the only manifestation of the lesion.

Another aid in the recognition of vasculitis is the performance of elastic van Gieson stains. This allows the recognition of blood vessels that otherwise are totally obscured by the inflammatory process. Lastly, it should be remembered that the microscopic findings of Wegener granulomatosis are not pathognomonic. An appropriate pathology report would state the presence of necrotizing granulomas with vasculitis and whether or not the stains for microorganisms were negative.

When clinical suspicion of Wegener granulomatosis exists, the pathologist is often called on to confirm or deny the possibility of the diagnosis. Absence of the typical microscopic features of Wegener granulomatosis does not always preclude this possibility; therefore, it is of great help to have ancillary laboratory studies. The ANCA test frequently fills this need[10,11,15]; it can be extremely helpful if the titer is elevated in patients who clinically have a disease consistent with Wegener granulomatosis but in whom the nasal biopsy has failed to disclose the typical microscopic findings.[16] The test can also be useful in separating the glomerulitis of Wegener granulomatosis from other forms of renal disease (see Chaps. 62 and 68).

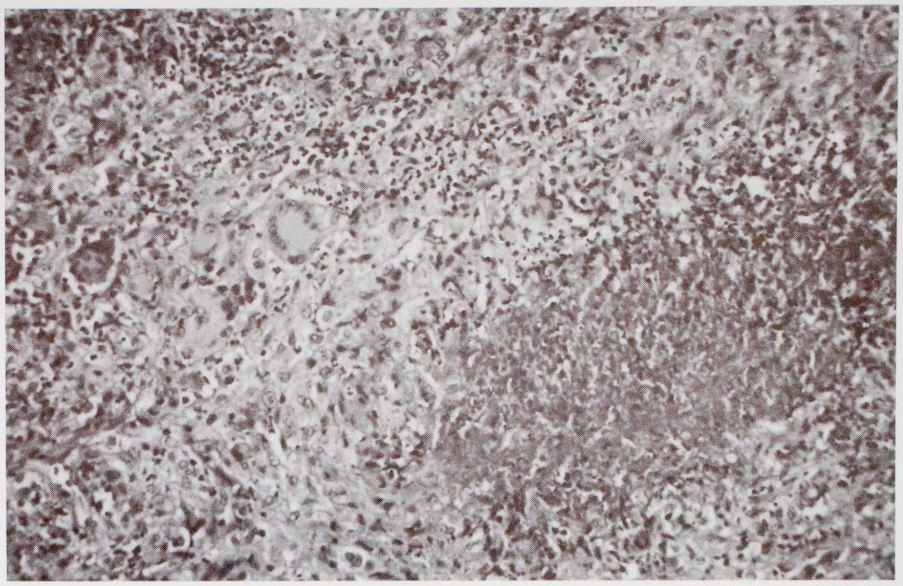

FIGURE 72-3. This photomicrograph of a specimen from a patient with Wegener granulomatosis shows an ill-defined necrotizing granuloma, surrounded by fibroinflammatory tissue containing multinucleate histiocytes. In the upper respiratory tract, granulomas tend to be smaller and not as well defined as those in the lung. (H & E stain; low magnification.)

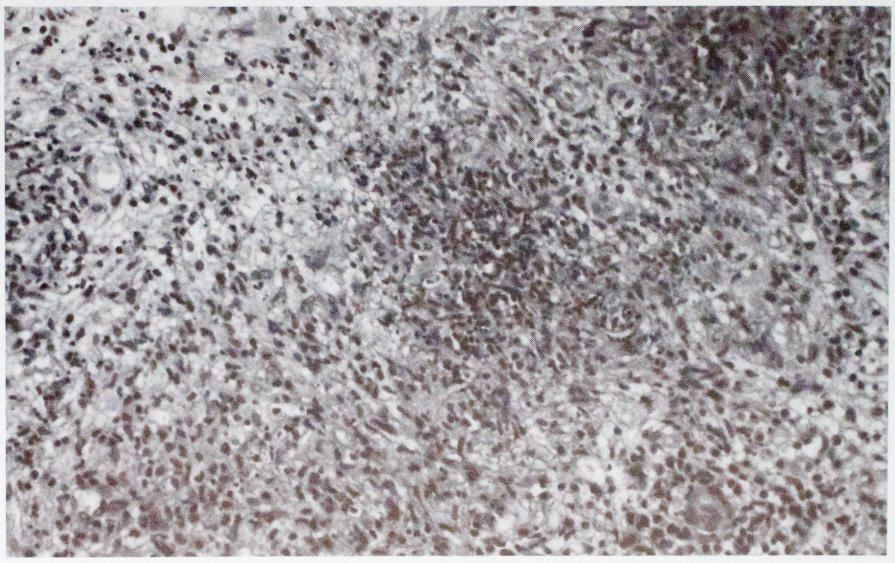

FIGURE 72-4. This nasal biopsy specimen from a patient with Wegener granulomatosis shows necrosis and acute inflammation; frequently, this is the extent of the necrotizing granulomatous inflammation in these specimens. Insistence on the presence of well-formed granulomas for diagnosis will result in undiagnosed cases of Wegener granulomatosis. The inflammatory infiltrate also contains an abundance of lymphocytes and histiocytes. (H & E stain; low magnification.)

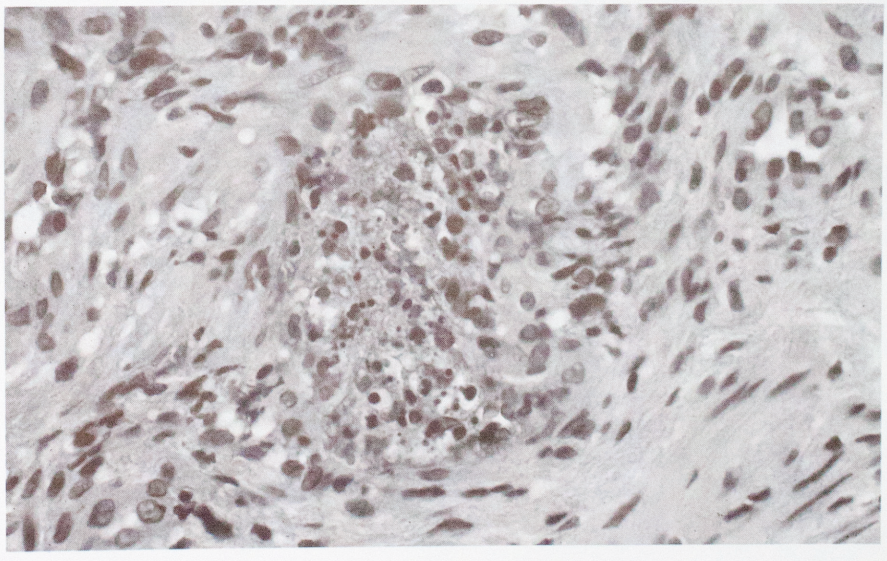

FIGURE 72-5. In this nasal biopsy specimen from a patient with Wegener granulomatosis, the presence of vasculitis is subtle and involves relatively small vessels. In these specimens, the vasculitis is often elusive; therefore, it is necessary to search for such small foci of vasculitis to establish a diagnosis. This applies also to blood vessels of capillary size (*i.e.*, capillaritis). (H & E stain; intermediate magnification.)

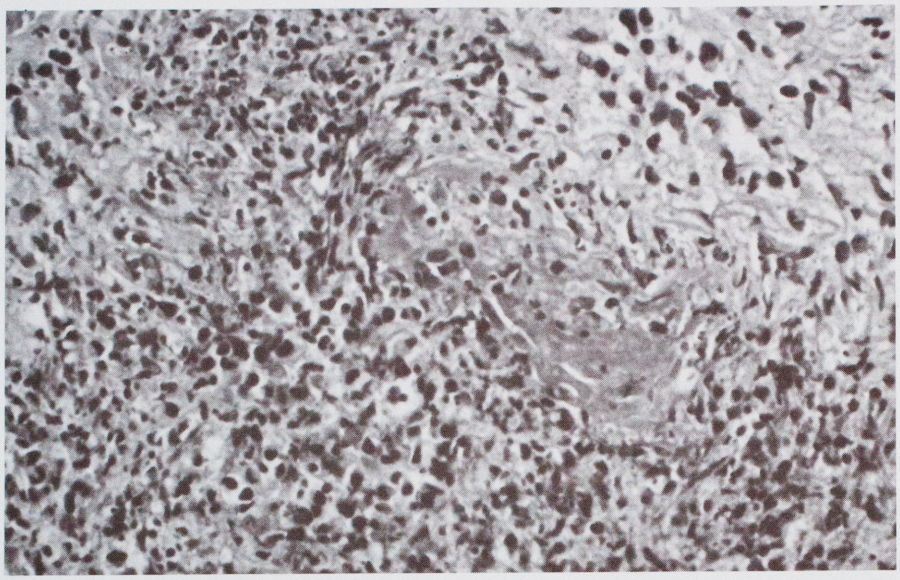

FIGURE 72-6. Biopsy findings in a patient with Wegener granulomatosis shows a small blood vessel with fibrinoid necrosis and extravascular fibrin as a manifestation of vasculitis. Fibrinoid necrosis in Wegener granulomatosis is somewhat unusual, particularly in nasal biopsy specimens. There is an abundance of lymphocytes and histiocytes in the surrounding tissues, and tissue necrosis is beginning. (H & E stain; intermediate magnification.)

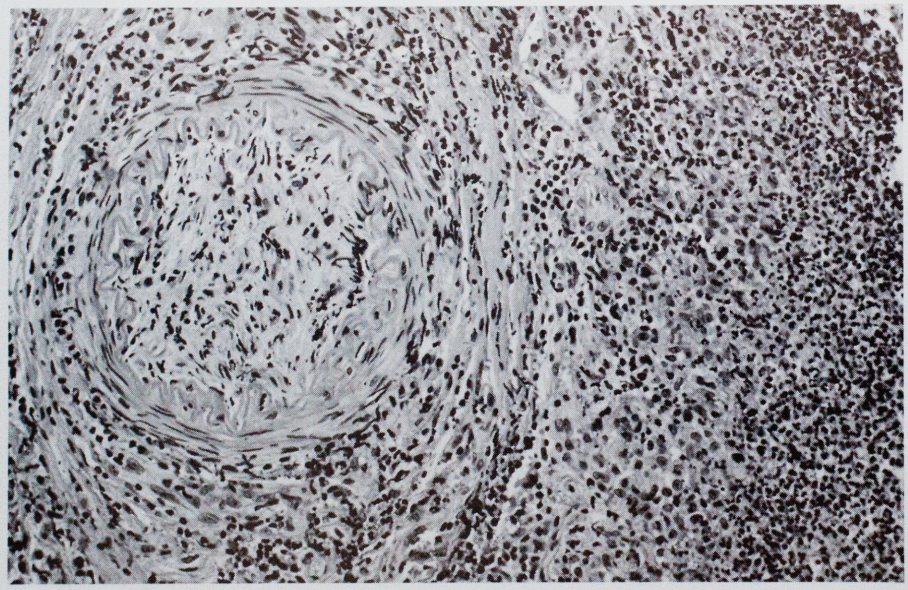

FIGURE 72-7. Wegener granulomatosis vasculitis is often affected by treatment. In this photomicrograph, the small artery is completely obliterated by fibrous tissue. This is a manifestation of healed arteritis. Ulceration and chronic inflammation are present on the mucosal surface. (H & E stain; low magnification.)

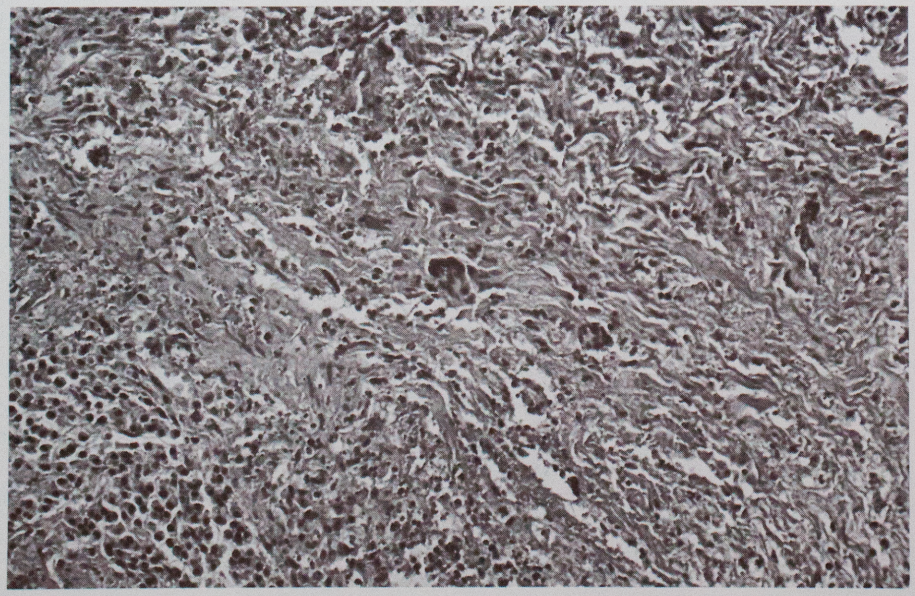

FIGURE 72-8. In this nasal biopsy specimen from a patient with Wegener granulomatosis, there is an abundance of fibrous tissue and less conspicuous chronic inflammation. Multinucleate giant histiocytes are almost invariably present in these specimens; therefore, their presence should always be sought and their absence should suggest the possibility of a different process. (H & E stain; low magnification.)

It is of interest that the microscopic lesion of extrarespiratory Wegener granulomatosis is typically that of vasculitis. Although necrotizing granulomas have been observed, the microscopic findings do not include the granulomatous component. In the kidney, the vasculitis takes the form of glomerulonephritis, usually segmental in nature. However, the renal lesion is not specific, because morphologically identical glomerular lesions can be seen in other conditions.

The paucity of granulomas in extrarespiratory sites and the commonness of the granulomas in the respiratory tract are phenomena that lack explanation. It has been speculated that the vasculitis represents an immune complex disorder.[17] The presence of necrotizing granulomas that bear such a striking resemblance to infectious granulomas suggests that the initial lesions of Wegener granulomatosis may be due to a microbial agent. Further support for this concept is the favorable clinical response of some patients with Wegener granulomatosis to broad-spectrum antibiotics.[13] Although microorganisms have not been identified as a causative agent of Wegener granulomatosis, the possibility of an infectious etiology remains to be elucidated.

LYMPHOMATOID GRANULOMATOSIS

This disease has remarkable similarity to Wegener granulomatosis.[18–20] It has a predilection for the respiratory tract but also can involve other organ systems. It is usually included in the differential diagnosis of Wegener granulomatosis because there is microscopic involvement of blood vessels. However, lymphomatoid granulomatosis is a lymphoproliferative neoplastic disorder and thereby remarkably different from Wegener granulomatosis.[21] For patient management, it is essential that lymphomatoid granulomatosis be distinguished from Wegener granulomatosis.[22]

Terminology for this disease has been confusing and controversial.[23] The terminology includes polymorphic reticulosis for lesions of the upper respiratory tract and lymphomatoid granulomatosis for the lower respiratory tract. Other terms that have been used include lethal midline granuloma, midline reticulosis, granuloma gangraenescens, Stewart syndrome, and various other names. All of these terms are now obsolete and should be abandoned. In particular, lethal midline granuloma has no place in modern terminology, unless it is used as a clinical term in referring to someone with a midfacial destructive problem, lethal or not.

Polymorphic reticulosis and lymphomatoid granulomatosis have become somewhat ingrained in the literature, but even they can be abandoned. As will be discussed later, all of these terms should be replaced by the more current terminology of malignant lymphomas. A historical review of the divergent diagnostic terminology explains much of the confusion that has existed.[23] Modern laboratory technology with immunophenotyping studies and gene rearrangement techniques has remarkably clarified the nature of this disease and placed it in the neoplastic category.[24,25]

It is also important to appreciate that lymphomatoid granulomatosis exhibits a remarkable spectrum of clinical behavior, from extremely aggressive lymphoproliferative lesions to indolent cases. This concept encompasses the diseases known as angiocentric large cell pulmonary lymphoma,[26,27] lymphomatoid granulomatosis,[25,28,29] and benign lymphocytic angiitis and granulomatosis.[30–34] Of these three expressions of lymphoproliferative disease, malignant lymphomas and lymphomatoid granulomatosis are fairly well recognized in the upper respiratory tract. Lymphomatoid granulomatosis is considered the prototype of this spectrum of lymphoproliferative diseases.

Clinically, lymphomatoid granulomatosis has a remarkable tendency to involve the lungs and upper respiratory tract; but as with Wegener granulomatosis, multiple other organ systems can be involved.[22] These include kidney, gastrointestinal tract, brain, skin and subcutis, liver, adrenal glands, and other organs.[35] In the upper respiratory tract, there are some clinical differences that can provide a clue to the correct diagnosis. Whereas Wegener granulomatosis tends to involve the nasal mucous membranes with a more diffuse granularity and ulceration, lymphomatoid granulomatosis tends to be more tumefactive in its presentation.[9] The lesions are slightly more localized than the lesions of Wegener granulomatosis.

Occasionally the destruction is overwhelming, with extensive loss of tissue through ulceration (Fig. 72-9). The differential diagnosis of any midfacial destructive lesion includes specific processes (*e.g.*, leishmaniasis, syphilis, leprosy, Wegener granulomatosis, lymphomatoid granulomatosis, malignant neoplasms). Fortunately, with a thorough evaluation, most lesions can be categorized in the previously described scheme. Only a rare case will fail to fit into one of the specific categories, and such cases will be considered idiopathic.

As in Wegener granulomatosis, it is important to obtain adequate tissue cultures and special stains for microorganisms. If a diagnosis of lymphoproliferative disease is suspected, the laboratory is expected to obtain the tissue samples and perform the appropriate studies for malignant lymphoma. In addition to tissue

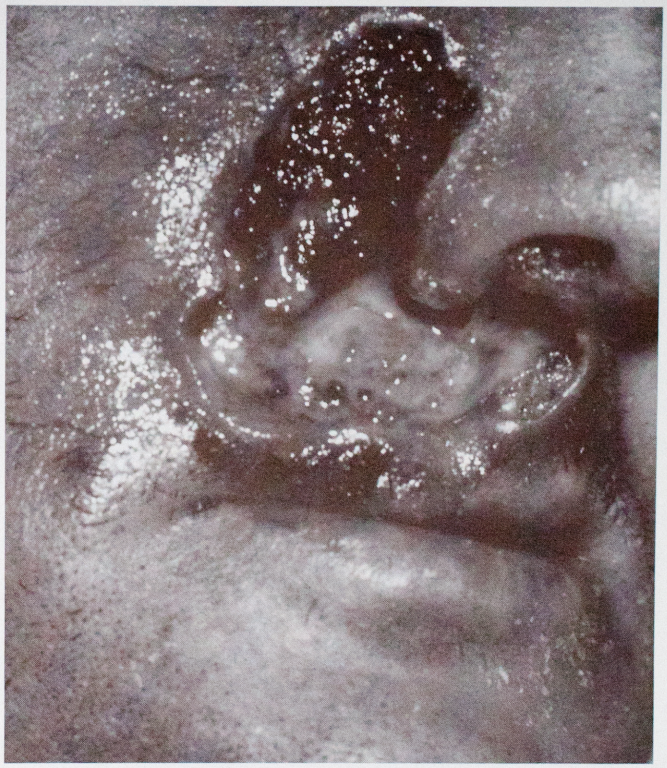

FIGURE 72-9. Lymphomatoid granulomatosis producing extreme destruction of the right upper lip and nose. Although this lesion has the gross appearance of a rodent ulcer, microscopic examination revealed the atypical lymphoid infiltrate characteristic of lymphomatoid granulomatosis.

FIGURE 72-10. In this nasal biopsy specimen from a patient with lymphomatoid granulomatosis, there is an intense lymphoid infiltrate and partial necrosis. Notice the absence of germinal centers and the compactness of the cellularity. Note also the absence of granulomas. (H & E stain; low magnification.)

for diagnostic light microscopy, it is imperative to obtain touch preparations, to freeze some of the tissue for further immunologic and gene rearrangement studies, and to obtain appropriate cultures.[36] If these procedures are observed, a correct diagnosis can almost invariably be rendered.

Pathologically, lymphomatoid granulomatosis is most challenging to pathologists unfamiliar with its microscopic findings. In general, the latter includes an intense proliferation of mixed lymphoid cells; the most impressive cells are relatively large and often somewhat atypical. These atypical cells lead to the designations "reticulosis" and "polymorphic reticulosis."[23] They may be few or abundant in number; when they are abundant, the neoplastic nature of the lesion is apparent, and often such cases are designated malignant lymphoma from the outset (Figs. 72-10 through 72-12). Admixed with these reticular cells are lymphocytes in various stages of maturation and differentiation. Some are plasmacytoid, some are mature, and some appear lymphoblastic. Eosinophils can be present in abundance or only as an occasional contributor to the picture.

Lymphomatoid granulomatosis has an infiltrative pattern and frequently involves nerves and minor salivary glands in nasal biopsies. Of greater importance is the propensity to infiltrate blood vessels and thereby mimic Wegener granulomatosis (Figs. 72-13 and 72-14). However, whereas Wegener granulomatosis features lymphocytes and histiocytes in its vascular infiltration, the predominant angioinfiltrative cell in lymphomatoid granulomatosis is an atypical lymphocyte or reticular cell. Thus, the resemblance of the vascular lesion in Wegener granulomatosis to the vascular lesion in lymphomatoid granulomatosis is superficial at best.

Necrosis is relatively common in lymphomatoid granulomatosis (see Fig. 72-10); however, in contrast to the necrotizing granulomas of Wegener granulomatosis, it seems to be tumor necrosis. Granulomas, by the most common definition, are rare or nonexistent in lymphomatoid granulomatosis. To pathologists with abundant experience, the overall picture of Wegener granulomatosis is one of an inflammatory reaction, whereas the picture of lymphomatoid granulomatosis is one of a neoplastic lympho-

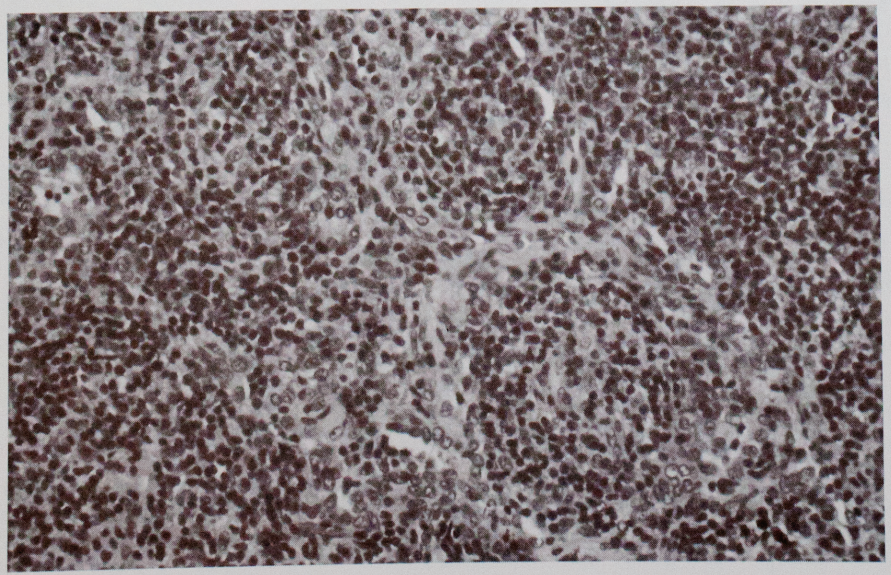

FIGURE 72-11. Notice the intensity of the lymphocytic infiltrate in this nasal biopsy specimen from a patient with lymphomatoid granulomatosis. Small blood vessels, infiltrated and surrounded by the lymphocytes, can be seen. Notice the absence of granulomas. (H & E stain; low magnification.)

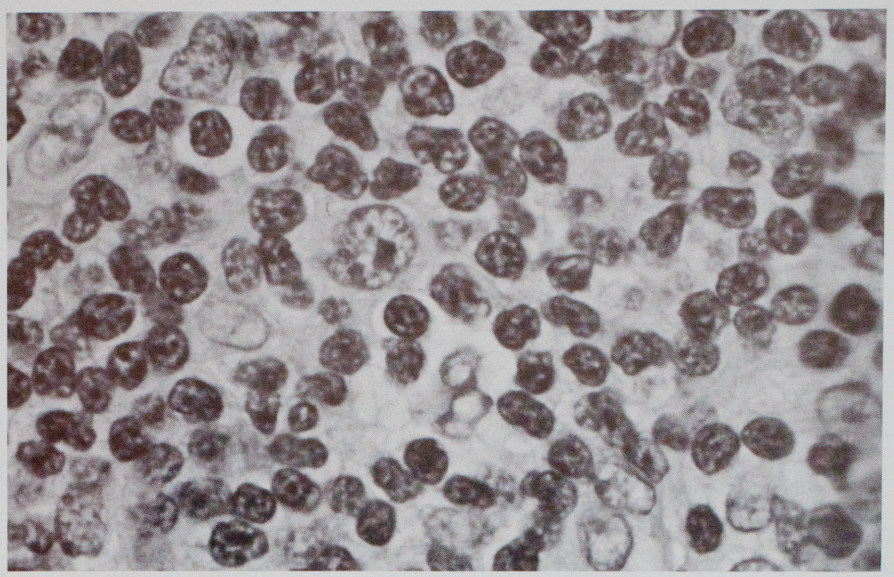

FIGURE 72-12. High magnification of a specimen from a patient with lymphomatoid granulomatosis shows a mixture of lymphocytes, plasma cells, and larger cells with prominent nucleoli. These larger cells, formerly referred to as "atypical reticular cells," bear a superficial resemblance to Reed-Sternberg cells. (H & E stain; high magnification.)

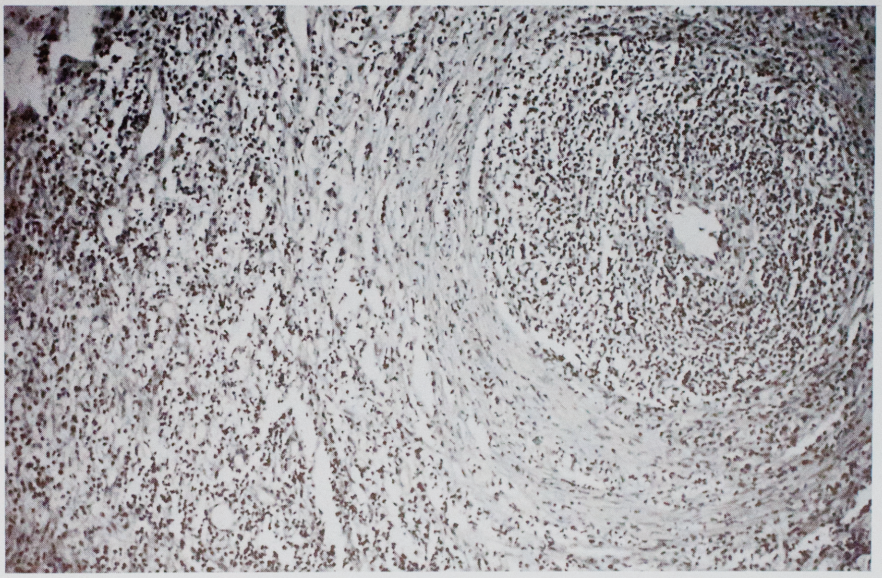

FIGURE 72-13. Notice the intense lymphoid infiltrate in a small muscular artery with resulting near-total compromise of the lumen. Such angiocentricity and angioinvasiveness are typical of lymphomatoid granulomatosis or polymorphic reticulosis, a form of angiocentric T-cell lymphoma. This condition has only a superficial resemblance to the vasculitis of Wegener granulomatosis. (H & E stain; low magnification.)

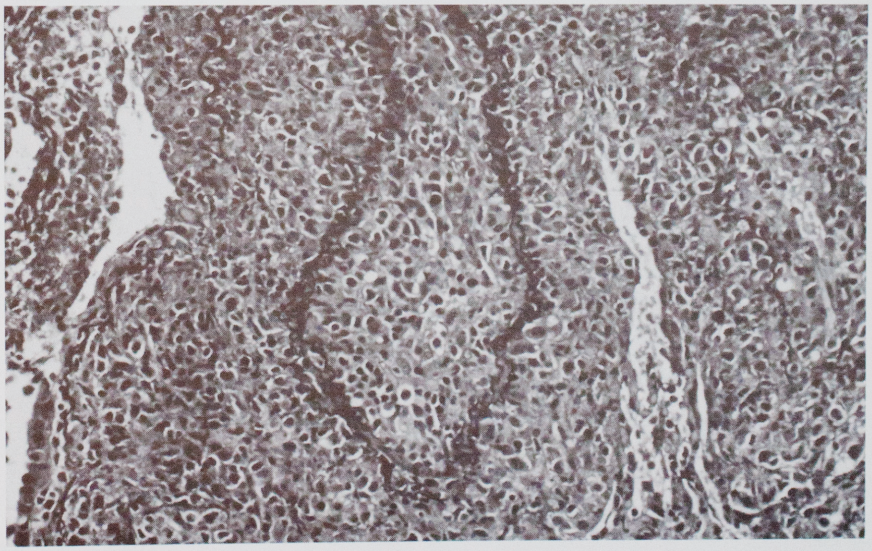

FIGURE 72-14. Angiocentricity of lymphomatoid granulomatosis can sometimes be best appreciated with elastic stains that outline blood vessels. In this specimen, the elastic fibers of a vein are readily demonstrated. Routine hematoxylin-eosin sections failed to disclose a blood vessel and showed only the intense lymphoid infiltrate. (Elastic-van Gieson stain; low magnification.)

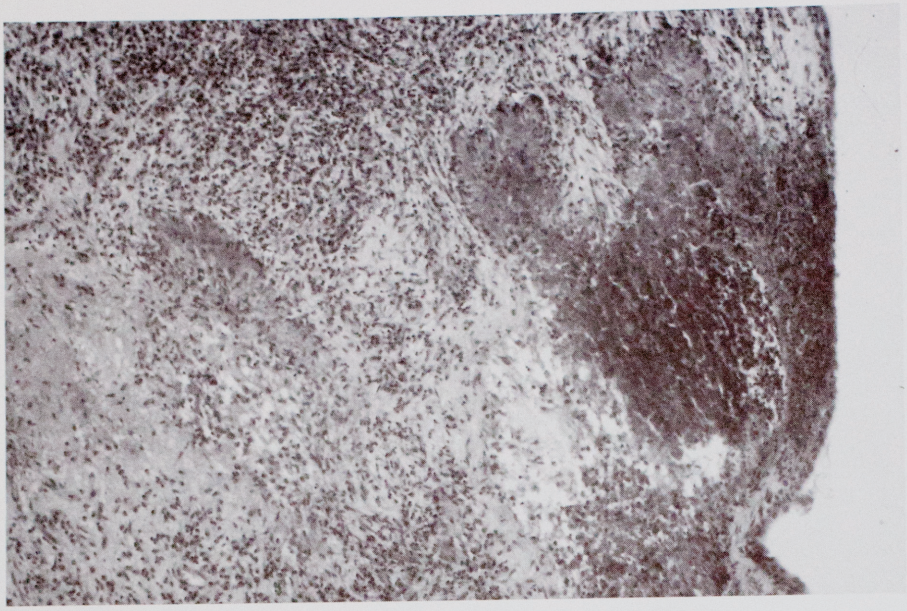

FIGURE 72-15. This nasal biopsy specimen from a patient with allergic granulomatosis and angiitis (*i.e.*, Churg-Strauss syndrome) shows an intense inflammatory infiltrate of the nasal mucosa, highlighted by the presence of an irregular superficial granuloma. The centers of these granulomas are hypocellular and eosinophilic. Tissue eosinophils are prominent in the surrounding tissues. (H & E stain; low magnification.)

proliferative disorder. Admittedly, this is a subjective assessment, and proof that the latter represents a lymphoma requires sophisticated laboratory techniques.

Although many pathologists suspected that lymphomatoid granulomatosis or polymorphic reticulosis was a malignant disorder, it was not until studies defining peripheral T-cell lymphomas were published that a satisfactory explanation was forthcoming. Initially, it was noted that there was a similarity between lymphomatoid granulomatosis and peripheral T-cell lymphomas.[37] Moreover, it was noted that many nasal lymphomas were of a T-cell phenotype.[38] It became apparent that nasal lymphomas can imitate a midfacial destructive lesion or lethal midline granuloma.[39,40]

Studies identifying the angiocentric nature of malignant lymphomas, particularly those of T-cell phenotype and pulmonary tropism, have done much to clarify the previous confusion.[41] The most acceptable concept is that lymphomatoid granulomatosis and polymorphic reticulosis are lymphoproliferative disorders of T-cell phenotype, usually with a striking angiocentricity.[42] The clinical expression of this lymphoproliferative disorder is variable and extends from the aggressive lesion that is usually classified as an angiocentric large cell lymphoma, to benign lymphocytic angiitis and granulomatosis at the other end of the spectrum, with lymphomatoid granulomatosis falling in between.

The malignant nature of benign lymphocytic angiitis is questionable and depends on proving monoclonality of immunoglobulin expression and on gene rearrangement studies.[42a] Of recent interest is the finding of Epstein-Barr viral genomes localized in high-grade angiocentric immunoproliferative lesions.[43] The viral genome was identified in numerous cells. Morphologically, these cells were larger than normal lymphocytes, and with double labeling immunohistochemistry and *in situ* hybridization, the majority of the cells harboring the viral genome were consistent with T-cell lineage. Of significance, low-grade angiocentric immunoproliferative lesions with less microscopic evidence of malignancy only had rare viral genome–positive cells. The authors concluded that Epstein-Barr virus is frequently associated with high-grade angiocentric immunoproliferative lesions. Furthermore, because Epstein-Barr virus is not commonly present in low-grade angiocentric immunoproliferative lesions, it is possible that the virus is responsible for the transformation of low-grade to high-grade lesions.[43]

Because all of the previously discussed lesions are now consid-

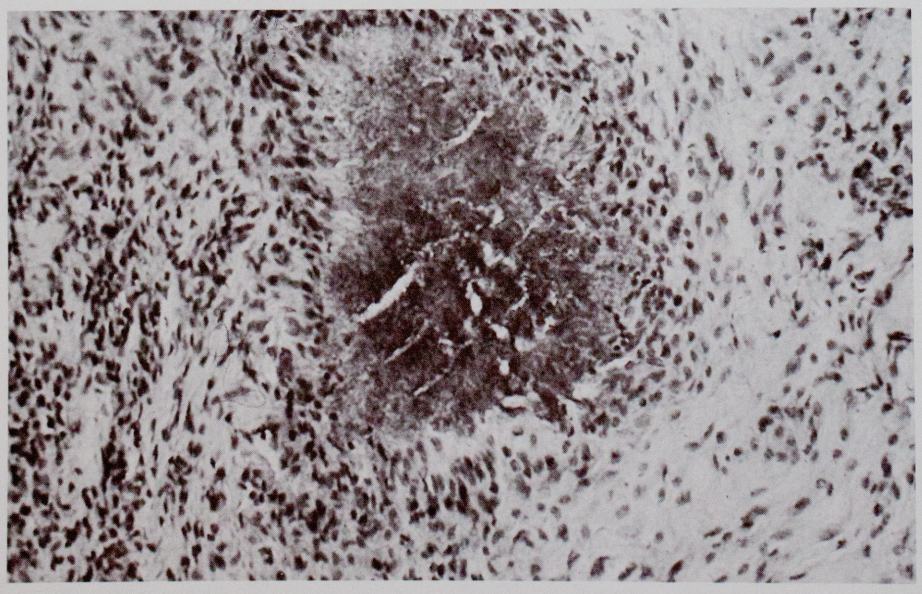

FIGURE 72-16. Allergic granulomatosis and angiitis (*i.e.*, Churg-Strauss syndrome). Higher magnification of an allergic granuloma shows the irregular border of palisading histiocytes surrounding a central area of hypocellular and amorphous eosinophilic debris. Fibrosis and infiltrative inflammatory cells, many of which are eosinophils, surround the granuloma. (H & E stain; low magnification.)

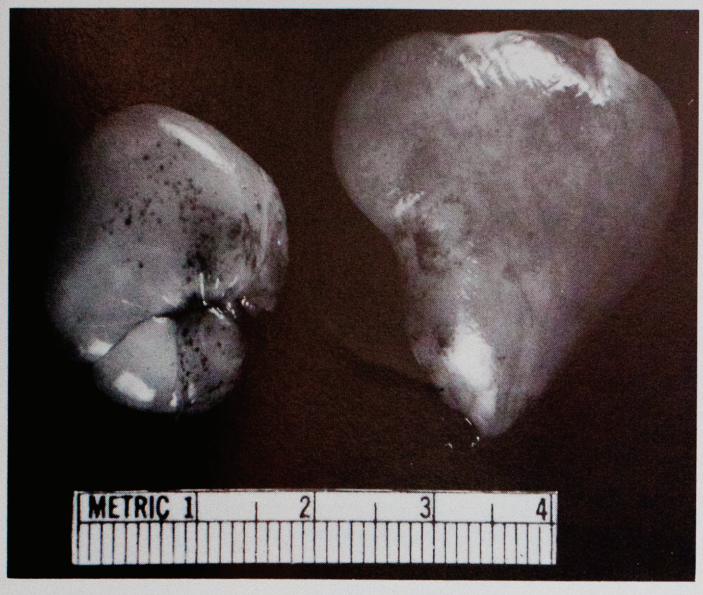

FIGURE 72-17. Myxoid nasal polyps, a manifestation of long-standing allergic rhinitis, are common in allergic granulomatosis and angiitis (*i.e.*, Churg-Strauss syndrome). This patient had both skin and pulmonary involvement with allergic granulomas, although they were absent in the nasal polyps.

ered to be lymphoproliferative disorders, treatment, in principle, is based on this interpretation. Therefore, all of these patients should receive consideration for antineoplastic (*i.e.*, antilymphomatous) management.[44] Finally, separating these lesions from Wegener granulomatosis, which requires different treatment, is mandatory (see Chap. 55).

ALLERGIC GRANULOMATOSIS AND ANGIITIS

AGA (*i.e.*, Churg-Strauss syndrome) was first described in 1951.[45] It consists of necrotizing vasculitis that is often systemic and accompanied by allergic granulomas.[46,47] Clinically, the patients have severe asthma, fever, and peripheral eosinophilia; the symptoms are produced by both the allergy and the vasculitis.[48,49] In addition to the lower and upper respiratory tract, other involved organs include skin, serosal surfaces, heart, kidneys, brain, and visceral organs, particularly the gastrointestinal tract. Nearly all of the patients have relatively severe asthma. A few cases have been reported in which asthma was not a clinical feature. These cases have been interpreted as overlap syndromes with Wegener granulomatosis.[50]

Because AGA tends to be systemic, symptoms include malaise, night sweats, fever, weight loss, and myalgias. Of interest is the observation that the asthmatic symptoms occasionally regress when the vasculitis and systemic disease emerge.

The classic microscopic lesion of AGA includes a palisading granuloma with a central portion that is deeply eosinophilic (Figs. 72-15 and 72-16).[51] The palisaded outer rim is histiocytic, with eosinophils as a prominent feature. Charcot-Leyden crystals, the result of breakdown of the numerous eosinophils, are occasionally present. The granulomas frequently occur in association with the necrotizing vasculitis; although fibrinoid necrosis may occur as part of the vasculitis, it is rarely as striking as that seen in periarteritis nodosa.

Classic AGA rarely affects the nasal passages. More commonly, it involves the skin and subcutaneous tissues of the head and neck. When AGA produces nasal lesions, the microscopic findings are usually nonspecific and include nasal polyps (Fig. 72-17), rhinitis, sinusitis, and occasionally inflammatory nasal perforations; all of these lesions, however, are striking in their eosinophil content (Fig. 72-18). Eosinophilia tends to diffusely involve the tissues and to form eosinophilic microabscesses. Vasculitis is usually not present in the nasal lesions of AGA.

Few asthmatic patients develop AGA; however, patients with bronchial asthma are known to develop allergic rhinitis.[52] The latter is a common upper respiratory problem. Both conditions have tissue eosinophilia as a microscopic manifestation of the allergic state. A small but definite number of patients with allergic rhinitis will ultimately develop bronchial asthma, or both conditions may develop simultaneously.

Although AGA has clinical and pathologic similarities to other granulomatous diseases, attention to the clinical history, pathologic findings, and laboratory evaluations effectively separates this disease from polyarteritis nodosa, Wegener granulomatosis, and other granulomatous diseases. It is not only possible but necessary to separate these diseases for the purposes of prognosis and treatment (see Chap. 69).[51]

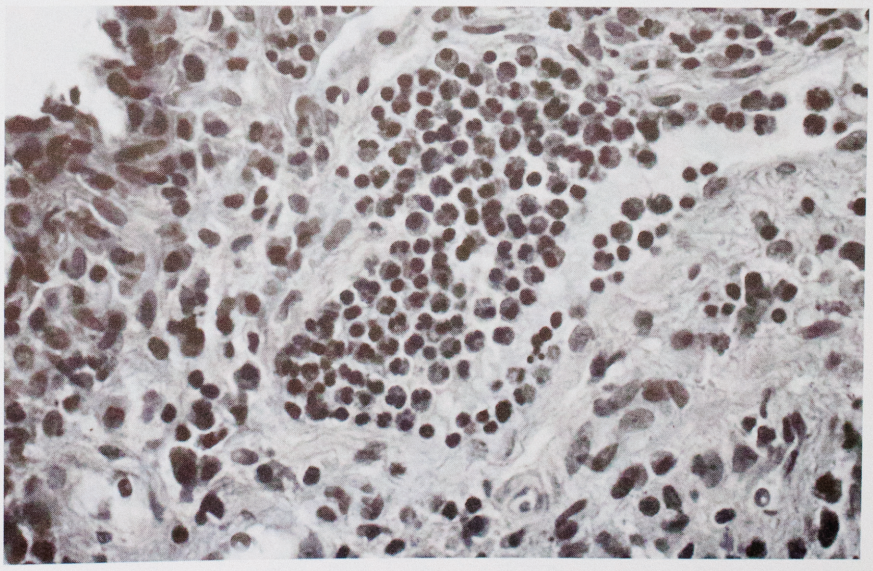

FIGURE 72-18. This photomicrograph of a nasal biopsy specimen from a patient with allergic granulomatosis and angiitis (*i.e.*, Churg-Strauss syndrome) shows a large collection of eosinophils within a blood vessel. (H & E stain; intermediate magnification.)

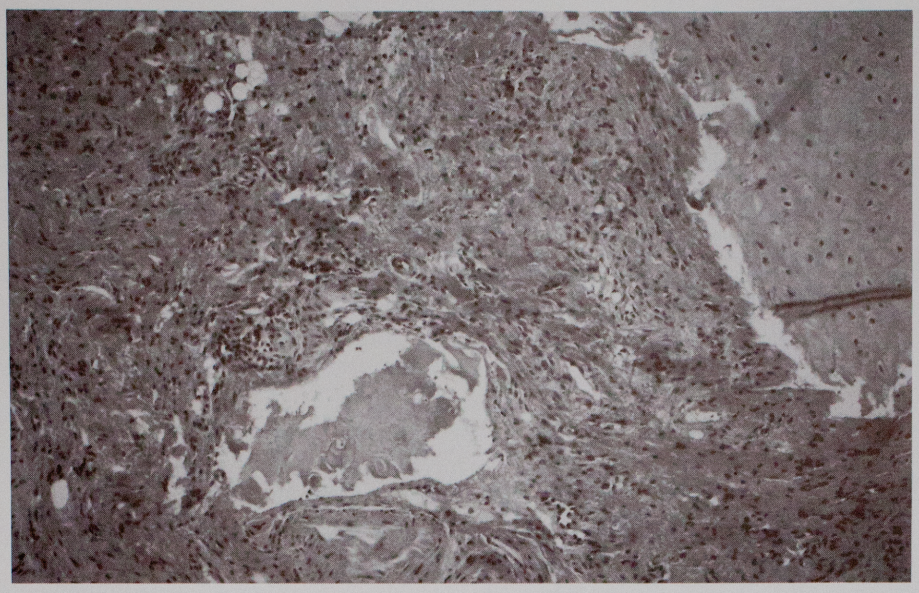

FIGURE 72-19. Low magnification view of relapsing polychondritis shows fragmentation of cartilaginous tissue, chronic inflammation, and fibrosis of the adjacent tissues. (H & E stain.)

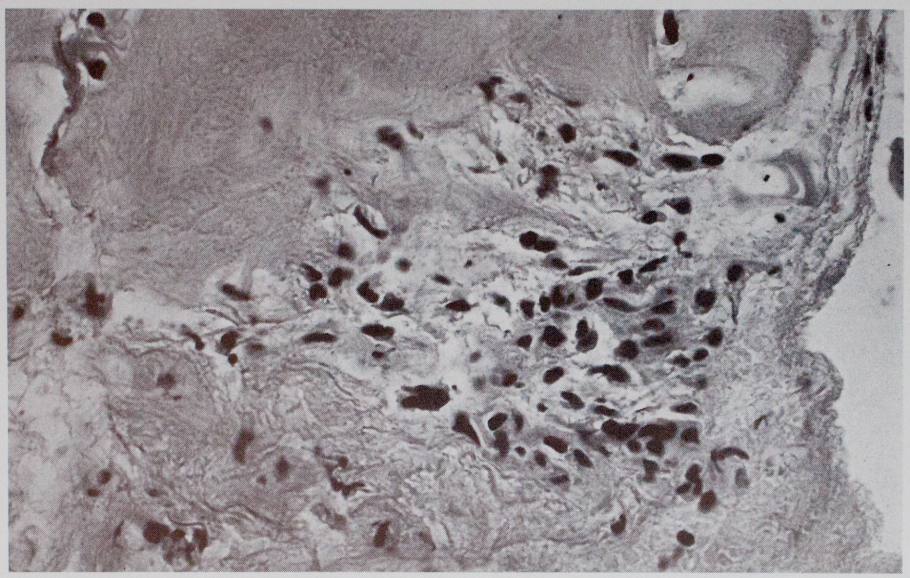

FIGURE 72-20. The hypocellular chronic inflammatory process is composed predominantly of lymphocytes in relapsing polychondritis. The fibroinflammatory process is eroding and fragmenting the adjacent cartilage. The cartilage has lost its normal tinctorial qualities. (H & E stain; low magnification.)

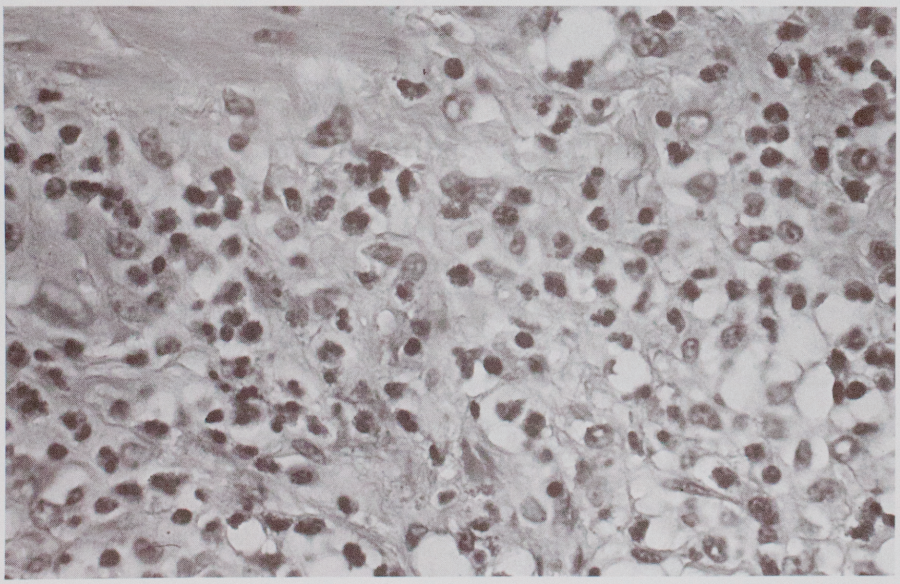

FIGURE 72-21. This specimen from a patient with relapsing polychrondritis shows the interface between granulation tissue and the degenerating cartilage. There is an abundance of eosinophils and other inflammatory cells, including histiocytes and lymphocytes. (H & E stain; intermediate magnification.)

RELAPSING POLYCHONDRITIS

RP is an unusual disease of cartilaginous tissue, particularly of the ears, nose, and large-diameter airways[53]; tissues of noncartilaginous type can also be affected. The etiology of this inflammatory disease of cartilage is unknown, but the possibility of an immunologic disturbance phenomenon is suggested from the small percentage of cases having associated autoimmune diseases.[54] However, circulating antibodies to the inflamed cartilage have not been convincingly demonstrated.

Most microscopic studies of RP are derived from biopsies of the external ear, an anatomic site that allows convenient biopsies. With time, however, other organs become involved, and approximately one half of the patients will develop chondritis of the larynx and trachea. The autoimmune disease, particularly migratory arthritis, frequently precedes the onset of the cartilaginous inflammation.[55]

The most serious consequence of RP is collapse of the major airways at the tracheal level, resulting in suffocation. However, the lesions of the ear and nose are also of concern, but of a less life-threatening nature. The ear lesions tend to be painful; the nasal lesions lead to collapse of the septum cartilage, with resulting saddle-nose deformity, as in Wegener granulomatosis.

Microscopically, RP is characterized by degeneration of the cartilage, usually preceded by an inflammatory reaction that begins in the perichondrium and extends to involve the cartilage proper (Figs. 72-19 and 72-20). As the disease progresses, the cartilage loses its normal tinctorial qualities on microscopic evaluation and becomes infiltrated by inflammatory cells (Fig. 72-21). Ultimately, the cartilage fragments into smaller pieces and is literally dissolved by the inflammatory process resulting in collapse of the nasal septum (see Chap. 73).

OBSTRUCTIVE LESIONS OF THE UPPER AIRWAYS IN CHILDREN

Obstructive lesions of the upper respiratory tract can have profound effects on the cardiorespiratory system.[56,57] One such obstructive phenomenon is hypertrophy of the adenoids and tonsils causing pulmonary hypertension and heart failure (Figs. 72-22 and 72-23).[58,59] Invariably, the alterations in cardiorespiratory function are corrected by removal of the hypertrophic lymphoid tissue. It is a clinical condition not well recognized by pediatricians and other physicians. Physiologic findings of upper respiratory airway obstruction include hypoxia, hypercapnia, and acidosis, resulting in profound secondary effects on the cardiorespiratory system. In children, the findings of congestive heart failure, pulmonary hypertension, and cor pulmonale should alert pediatricians to the possibility of upper airway obstruction. Although tonsillar and adenoidal hypertrophy and airway obstruction are relatively common findings in children, the development of pulmonary hypertension and cor pulmonale is decidedly rare. The explanation for why this condition develops so selectively and in so few patients remains unknown.

Theoretically, other obstructive lesions are capable of causing a similar clinical picture.[60] However, except for tracheobronchial

FIGURE 72-22. Obstructive tonsillar hypertrophy in a child who suffered from pulmonary hypertension and cor pulmonale. This is an unusual condition that affects young children; cor pulmonale secondary to upper respiratory obstruction is rare in adults. The proposed physiologic mechanism for the cor pulmonale is thought to be chronic hypoxia.

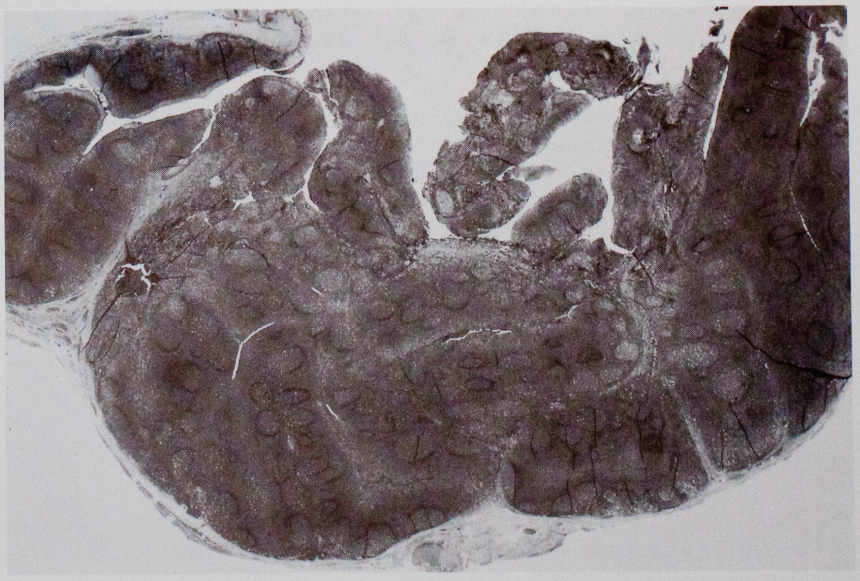

FIGURE 72-23. Hypertrophied tonsils associated with cor pulmonale. This is a photomicrograph of the tonsils shown in Figure 72-22. The tonsils are hypertrophied secondary to marked follicular hyperplasia. Such hyperplasia and hypertrophy are common in children; however, the development of secondary cor pulmonale is very rare. (H & E stain; panoramic view.)

papillomatosis, obstructive lesions of the airways are relatively rare in children. Occasionally, tracheobronchial papillomatosis can involve the larynx, trachea, and bronchi to the point of asphyxia (see Chap. 53).[61]

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