LESIONS OF THE PHARYNX IN ACUTE RHEUMATISM

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Within recent years several observers have noted the presence of rheumatic lesions in the neighbourhood of the tonsils.

Shaw¹, in his examination of the tissues from a girl aged 15 who died of rheumatic fever and chorea, found a few Aschoff nodules in the outer layers of the fibrous capsule of the tonsil. There was no evidence of any damage to the nearby fibres of the superior constrictor muscle of the pharynx.

Graff² has described rheumatic lesions in the peritonsillar tissues of a man aged 22 who died 16 days from the commencement of a first attack of acute polyarthritis. The essential nature of the lesions was degeneration of the collagen fibres and increase of fibroblasts. Lymphocytes and plasma cells played only a slight part and multinucleated cells were very scarce. Polynuclear cells were seldom seen. The lesions were numerous and were found in the tonsillar capsule and in the connective tissue of the superior constrictor muscles. No damage to muscle tissue was observed.

In the capsule of the left tonsil of Graff's case there was an extensive rheumatic infiltration reaching from the margin of the adenoid tissue deep into the musculature of the tonsil bed. Similar smaller lesions, evidently at an earlier stage of their evolution, were found in the neighbourhood of the right tonsil.

Graff, who considers that the lesion in the left tonsil is the primary one (Primärfekt), is of the opinion that rheumatic fever is caused by a specific micro-organism—infection passing from the surface of the tonsil to the deeper tissues by way of the lymph stream.

Klinge³ has confirmed Graff's observations as regards the occurrence of these peritonsillar lesions in the early stages of rheumatic fever, and has also reported their presence in the fibrous tissue at the root of the tongue. Further, Klinge has noticed that the muscle tissue bordering the nodules may show varying degrees of damage, from simple loss of striation to complete necrosis.

Yoshitake⁴, who made a more extended examination of the tissues from Graff's case, found the nodules in the upper part of the oesophagus and in the posterior third of the tongue as well as in the tissues of the pharynx generally. They were especially numerous in the posterior wall of the throat. In a second case Yoshitake observed that the rheumatic nodules were present also in the larynx.

Present investigations.—The present report deals with the histological examination of the pharyngeal tissues and the cervical lymph nodes of four patients who died of rheumatic fever uncomplicated by any other disease.

Case 1.—Female, aged 20. Admitted with acute arthritis and heart disease. History of an attack of rheumatic fever two years previously. Has been troubled a great deal with sore throats and is recovering from a severe attack of tonsillitis which began two weeks before admission and before the present severe illness began. Death occurred ten days after admission.

AUTOPSY PROTOCOL. Moderate dilatation and hypertrophy of the heart. Rheumatic pericarditis, myocarditis, and endocarditis of the mitral and aortic valves. No marked fibrosis of the valve leaflets. A few ounces of blood stained fluid in each pleural cavity. Chronic venous congestion of viscera.

HISTOLOGICAL EXAMINATION (Figs. 1—13). The tonsils are large and swollen, with deep wide crypts full of cellular debris, polynuclears, and bacteria, mostly Gram-positive cocci. The germ centres are not conspicuous, and plasma cells are prominent especially at those points where the surface epithelium is ulcerated. In and just beneath the epithelium there is much polynuclear cell infiltration. There is marked proliferation of the endothelial cells, and some of the smaller vessels show a moderate degree of intimal thickening. In the tonsil capsule on both sides there are numerous lesions of rheumatic type. Some are entirely confined to the capsular tissue, but the large majority are situated at the outer edge where the superior constrictor muscle fibres are attached. Here they may be either pushing the muscle aside or infiltrating into the fibrous tissue between the muscle bundles. There is a marked increase in the number of these lesions in the connective tissue of the muscle immediately surrounding the tonsils, and also in the region of the sinus pyriformis where they can be seen in conspicuous numbers in the submucosa as well as in the deeper layers. Further out from the neighbourhood of the tonsils they are not so frequently found, but they again become very numerous towards the upper end of the œsophagus.

There are two distinct forms of the lesion. A small one situated in the fibrous tissue surrounding small or medium sized arteries and identical with the Aschoff nodules of the myocardium (Fig. 1). A more diffuse one which has not the same definite relationship to the vessels and which corresponds more to the changes found in the region of the joints and tendons of rheumatic subjects (Fig. 2 and 3). The diffuse type is more common. Both show the same histological features.

In the earliest stage there is a varying amount of degenerative change of the collagen fibres accompanied by increased proliferation of fibroblasts. The collagen becomes swollen and disintegrated and looks and stains like fibrinous material. Occasionally this collagen necrosis is the predominating feature so that in comparison the fibroblastic proliferation is slight (Fig. 4). At a later stage of development there are numerous basophil giant cells which appear to be replacing the fibroblasts or to be themselves altered fibroblasts. A few of these basophil cells are multinucleated. Degenerated collagen may be great in amount or scanty. Plasma cells, polynuclears, or lymphocytes are seldom seen. In the more advanced stages there may be a fair number of plasma cells scattered about among the basophil giant cells. There is also an increase in the number of multinucleated cells, and necrotic collagen is represented by small masses here and there (Fig. 5 and 6). Towards the periphery there may be numerous capillaries and much polynuclear cell infiltration. Lymphocytes as a rule are scanty and eosinophils are seldom seen.

Damage to the muscle in the neighbourhood of these rheumatic nodules varies greatly and muscle necrosis is seen only where the nodule cells are infiltrating the connective tissue between the muscle bundles (Fig. 7). Muscle giant cells are rarely found. Elastic tissue fibres within the nodes are widely separated, but seldom is there any break in their continuity.

Tongue. In the anterior and middle third of the tongue there are no nodules, but they are present in the posterior third and become very numerous towards the root. None can be seen in the submucosa. They are more common in the deeper layers lying in the fibrous tissue between the muscle bundles and around the small vessels. They are equally numerous on either side but appear to be more frequent near the mid-line. Damage to muscle is seldom seen to any great extent since the larger expanses of fibrous tissue in this region allow for a considerable spread of the lesion before the muscle tissue is reached (Fig. 8 and 9),

FIG. 1. Case 1. Aschoff nodule in the adventitial tissue of a small artery in the capsule of the tonsil ($\times 315$).

FIG. 2. Case 1. Diffuse rheumatic lesion in the tonsillar capsule ($\times 90$).

FIG. 3. Case 1. High power view of Fig. 2, showing basophil giant cells ($\times 315$).

FIG. 4. Case 1. Lesion in the tonsillar capsule compressing the fibres of the superior constrictor muscle. There is marked collagen fibre degeneration ($\times 90$).

FIG. 5. Case 1. Extensive rheumatic lesion in the pharyngeal wall near the oesophagus ($\times 90$).

FIG. 6. Case 1. High power view of Fig. 5 to show basophil giant and multinucleated cells and plasma cells ($\times 315$).

FIG. 7. Case 1. Rheumatic lesion in the wall of the pharynx near oesophageal entrance, showing marked destruction of the muscle tissue ($\times 90$).

FIG. 8. Case 1. Composite rheumatic nodule in the root of the tongue ($\times 90$).

Œsophagus. The upper third only was available for examination. Rheumatic nodules are numerous in the wall of the upper half, but are scanty in the lower part. An occasional one can be seen in the submucosa, but the majority are situated in the muscle connective tissue and peri-œsophageal fascia.

Larynx. There are many nodules in the fibrous tissue around the thyroid cartilage and in the connective tissue of all the intrinsic muscles of the larynx. They are most numerous in the thyro-arytænoid muscles where they are mostly at the advanced stage and have caused much muscle destruction. In the submucosa just above the false vocal cord on either side there are a few small nodules. There are none in the wall of the trachea below the cricoid cartilage, but a few can be seen in the connective tissues between the trachea and the thyroid gland. In all of the regions examined evidence of the existence of previous active lesions is commonly seen in the shape of nodular areas of dense fibrous tissue, sometimes in very close proximity to the active lesions. These scars are very obvious in the constrictor muscles of the pharynx and intrinsic muscles of the larynx.

Lymph nodes. Changes are present in all of the cervical lymph nodes of both sides, but are most conspicuous in the upper deep cervical group. There is no obvious enlargement but the nodes appear swollen. There is very marked proliferation of the endothelial cells and the adenoid tissue is scanty and germ centres are not prominent. Plasma cells are numerous, but eosinophil cells are seldom seen. The sinuses are full of proliferated endothelial cells with a good admixture of polynuclears. Some of the endothelial cells contain two or three nuclei. The fibrous stroma of these nodes is much infiltrated by endothelial, plasma, and polynuclear cells, which are frequently seen in small groups in the vicinity of blood vessels showing intimal proliferation. Specific rheumatic lesions are also present in some of these deep cervical lymph nodes. They are found in the capsule (Fig. 10 and 11) and in the fibrous stroma, particularly in the region of the hilum. In every instance these rheumatic nodules are situated in the connective tissues around the vessels. In the case of the smaller vessels there is sometimes pronounced proliferation of the lining endothelial cells accompanied occasionally by marked destruction of the outer layers of the wall which are within the area of the nodule. The nodules are of the discrete type, corresponding in every way to the typical Aschoff nodule. There is a central area of collagen fibre necrosis surrounded by basophil giant cells—some of which are multinucleated. Some plasma cells may be seen, but polynuclears, lymphocytes, and eosinophils are uncommon. In the fibrous framework of the lymph node the rheumatic nodules are more difficult to demonstrate because of the marked cellular infiltration of the stroma and the close proximity of the lymphoid follicles and crowded sinuses. Where they are situated in the connective tissue surrounding a medium sized vessel however, their true nature can be detected (Fig. 12 and 13). They are then seen to be more cellular than those in the capsule. The basophil giant cells are more numerous and there may be a great many plasma cells. The amount of necrotic collagen present is usually not great.

The above case may therefore be summarized as an example of recurrent rheumatic fever showing rheumatic nodules and scars of previous lesions in the wall of the pharynx, and in the tongue, larynx, and œsophagus. The nodules are particularly numerous in the neighbourhood of the pharyngeal tonsils, the lingual tonsil, and the laryngeal tonsil. A conspicuous number of lesions in their earlier stages of development can be seen in the capsule of both the right and left tonsil. The cervical lymph nodes generally show marked proliferation of the endothelial cells of the sinuses, blood vessels, and reticulum accompanied by much plasma and polynuclear cell infiltration of the stroma. Specific rheumatic lesions are present in some of the upper deep cervical nodes of both sides.

Case 2.—Female, aged 8 years. Admitted as a possible case of miliary tuberculosis. No previous history of rheumatic fever. Died six days after admission.

AUTOPSY PROTOCOL. Moderate hypertrophy and dilatation of the heart. Rheumatic pericarditis, myocarditis, and endocarditis of the mitral and aortic valves. No obvious fibrosis of the valves. Chronic venous congestion of the viscera.

HISTOLOGICAL EXAMINATION (Figures 14 and 15). The tonsils are much enlarged. The crypts are not dilated but contain many pus cells and gram-positive cocci. Frequently these pus cells and cocci extend into the subepithelial tissue, the epithelial layer having been ulcerated. Sometimes in these ulcerated spots there may be many plasma cells. Throughout the adenoid tissue plasma cells are numerous, but eosinophils are not seen. There are also areas where endothelial cell proliferation is marked but this is not a very prominent feature. There are numerous rheumatic nodules in the tonsillar capsule on both sides, and in the connective tissue of the superior constrictor muscles at the base of the tonsils they are even more numerous (Fig. 14 and 15). In the pharyngeal wall outside of this region there are no nodules. The tongue, larynx, and upper part of the oesophagus are likewise free from lesions.

Lymph nodes. Those of the upper deep cervical group which were the only ones examined show marked proliferation of the lymphoid cells and germ centres are small and not easily seen. Plasma cells are numerous but there is no evidence of increased proliferation of the endothelial cells. The small blood vessels appear normal and there are no specific rheumatic nodules.

In Case 2, an example of rheumatic fever with a history of recent onset, there are found specific nodules in the capsule and the muscle bed of the right and left tonsil. The regional lymph nodes show a marked proliferation of the lymphoid cells, but there are no other conspicuous changes.

Case 3.—Female, aged 8 years. Admitted with joint pains and heart disease. History of rheumatism since the age of four. The chief complaint has always been of pain in the muscles and joints of the arms and legs, but in the last six months there have been frequent attacks of severe abdominal pain. No history of throat trouble. There is a brother of six with rheumatic heart disease. Death took place six weeks after admission.

AUTOPSY PROTOCOL. Hypertrophy and dilatation of the heart, with marked fatty degeneration of the myocardium. Rheumatic pericarditis, myocarditis, and endocarditis of the mitral, tricuspid and aortic valves. A fair amount of yellow fluid in the peritoneal and pleural cavities. Chronic venous congestion of viscera. Moderate fibrosis of all valve leaflets.

Case 4.—Female, aged 7 years. Admitted with pericarditis. The illness began with pain in the muscles and joints fourteen days previously. Died five days after admission.

AUTOPSY PROTOCOL. Slight hypertrophy and dilatation of the heart with rheumatic pericarditis, myocarditis, and endocarditis of the mitral and aortic valves. No obvious fibrosis of the valve leaflets. Chronic venous congestion of viscera.

HISTOLOGICAL EXAMINATION (Cases 3 and 4; Figures 16 and 17). Cases 3 and 4 show similar changes. The tonsils are only moderately hypertrophied and they show the same histological features as Case 2. There are a few rheumatic nodules in the tonsil capsule with a still fewer number in the tonsillar bed tissues (Fig. 16 and 17). In each case the picture is the same on both sides. The rheumatic lesions are all at an early stage of their evolution and there is practically no destruction of muscle. There are no lesions in the rest of the pharyngeal wall, nor in the tongue, larynx, or upper part of the oesophagus.

Lymph nodes. In both cases the upper deep cervical group of lymph nodes show the same lymphoid cell hyperplasia observed in those of Case 2.

FIG. 9. Case 1. High power view of an area in Fig. 8 ($\times 315$).

FIG. 10. Case 1. Rheumatic lesion surrounding a small vessel in the capsule of a regional lymph node ($\times 90$).

FIG. 11. Case 1. High power view of Fig. 10. Note the collagen necrosis, the basophil giant and multinucleated cells and the proliferation of the vascular endothelium. Part of the vessel wall is necrotic ($\times 315$).

FIG. 12. Case 1. Rheumatic nodule in the neighbourhood of a small vessel in the fibrous stroma of a deep cervical lymph node ($\times 90$).

FIG. 13. Case 1. High power view of Fig. 12, showing basophil giant and multinucleated cells and plasma cells. The amount of collagen degeneration is slight ($\times 315$).

FIG. 14. Case 2. Section through the bed of the tonsil to show the nodules in the connective tissue of the muscle ($\times 90$).

FIG. 15. Case 2. High power view of one of the nodules in Fig. 14, showing collagen degeneration and proliferation of fibroblasts ($\times 315$).

FIG. 16. Case 3. Section through the base and muscle bed of the tonsil, showing rheumatic lesions of the capsule and muscle connective tissue ($\times 90$).

Cases 3 and 4 are both examples of rheumatic infection, one a recurrent case and the other of recent duration. Both show early stage rheumatic nodules in the tonsil capsules and in the immediately surrounding tissues of the tonsillar bed. There is marked lymphoid cell hyperplasia in the upper deep group of cervical lymph nodes, but no rheumatic nodules can be seen.

Discussion.

The pharyngeal lesions described above provide a specific histological basis for the sore throat so frequently associated with rheumatic infection. Their symmetrical distribution round the adenoid tissue of the throat suggests

FIG. 17. Case 3. High power view of the capsular lesion in Fig. 16, showing degeneration of collagen and basophil fibroblastic proliferation ($\times 315$).

that the tonsils, and less frequently the other adenoid collections, are the portal of entry of the infection. That there may be no clinical evidence of the presence of such lesions round the tonsils is shown by the three cases with no symptoms or complaint of throat trouble.

The first case throws considerable light on Schlesinger's⁵ clinical observation in regard to the association between sore throat and recurrence of rheumatic fever symptoms. Schlesinger has shown that in convalescent rheumatic cases a definite time interval, approximately 10 to 21 days, intervenes between the onset of a throat infection and the reappearance of rheumatic symptoms. The pathogenesis of Schlesinger's clinical picture is well represented by the histological findings in Case 1. Here we have a recrudescence of acute rheumatic symptoms 14 days or so after a severe

throat attack. There are rheumatic lesions in the neighbourhood of the tonsils and also of the other adenoid tissues of the throat. A generalized simple cervical adenitis is present and there are rheumatic nodules in some of the lymph nodes in the upper deep cervical groups.

The presence of the Aschoff nodules in the lymph nodes draining areas where there are extensive rheumatic lesions is evidence of a specific virus spreading via the lymph stream.

Summary.

Rheumatic nodules have been found in the pharyngeal tissues of two recurrent and two early cases of rheumatic fever. The nodules were more commonly seen in the neighbourhood of the tonsils, radiating out from the tonsillar capsule into the connective tissue of the muscles of the pharynx.

Similar lesions were present in the region of the lingual and laryngeal tonsils in one of the recurrent cases. In this case also there were significant changes in the regional lymph nodes. These changes consisted of marked endothelial hyperplasia with much polynuclear and plasma cell infiltration.

Aschoff nodules were found in the connective tissue surrounding the vessels in the capsule and fibrous stroma of some of the nodes in the upper deep cervical group on both sides.

I have to thank my colleagues on the Staff of the Bristol Royal Infirmary for their kindness in allowing me access to the clinical notes of their cases.

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