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Tietze's Syndrome

A Review of the Literature

HAROLD L. KAYSER, M.D.
Philadelphia, Pennsylvania

In 1921 Tietze1 published a report of four unusual case histories and summarized the clinical picture as follows: "We are dealing with the appearance of painful swellings in the region of the upper costal cartilages ... that have developed in a matter of several weeks to months and have shown variations and remissions in their course." These swellings appeared neither inflammatory, granulomatous nor neoplastic in nature. Tietze referred to the lesions as a dystrophy of the costal cartilage. They have since been called "Tietze's disease," "Tietze's syndrome" and "costal chondritis." In 1952 fourteen cases apparently identical with this condition were reported by Chantraine,2 who suggested the term "chondropathia tuberosa." Düben3 believed that this designation was superfluous. Since the etiologic and pathologic identities of this condition remain obscure, I prefer the term Tietze's syndrome to Tietze's disease or costal chondritis.

As more than 155 cases have been reported since Tietze's article it seems that a critical review of the world literature is in order. This will be preceded by the description of a typical case which I have observed:

CASE REPORT

A sixteen year old girl was first seen in the Outpatient Department of the Hospital of the University of Pennsylvania on January 12, 1953. She complained of "gas pains" and a "lump on the chest." She had been well until December 24, 1952, on which date she began to have sharp, intermittent pains over the upper sternum, radiating occasionally toward the right shoulder. Pain was exacerbated by coughing and deep inspiration. On self-examination the patient had found a tender swelling, the size of an egg yolk, on her chest. The swelling had not been noticed previously and there was no history of trauma to the area. Tenderness to pressure had disappeared a few days after onset and had never recurred.

Systemic review was non-contributory. There were no symptoms pertaining to the respiratory tract. Past medical history and family history were essentially negative.

Physical examination revealed a well developed, apparently well nourished sixteen year old Negro girl. She was apathetic and showed moderate retardation of thought. Temperature, pulse and respirations were normal. The blood pressure was 120/75. There was a soft, blowing pulmonic systolic murmur. Examination of other systems was entirely normal except for the following: Over the right second costal cartilage was a hard, fixed, non-tender, fusiform swelling which measured approximately 3 by 5 cm. There was no local heat or erythema. The overlying skin was freely movable and was neither ulcerated nor edematous. (Fig. 1A and B.)

The patient was examined on several occasions during the next nine months. Spontaneous pains had gradually subsided by June 1, 1953. The swelling remained essentially unchanged. No treatment was given.

Roentgenograms of the chest, including tomograms, were negative. All costal cartilages were normally radiolucent and showed no calcification. An electrocardiogram was within normal limits. In June, 1953, the hemoglobin was 12.0 gm. per 100 ml., the leukocyte count was 5,200 and a peripheral blood smear was normal. Erythrocyte sedimentation rate and repeated urinalyses were normal. Serum Kolmer and Kline tests were non-reactive. Intradermal tests with old tuberculin were negative in the 0.01 mg. and 0.1 mg. strengths.

On October 15th a biopsy of the right second costal cartilage was performed. At operation there was no evidence of inflammation or adhesions in the tissues overlying the cartilage. A moderate degree of anterior angulation of the cartilage was noted, especially at the costochondral junction. The perichondrium was smooth and not grossly thickened; the cartilage appeared normal upon section. A small wedge of

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tissue was excised, including cartilage, costochondral junction and rib. Microscopically the specimen appeared to be normal cartilage, showing no evidence of tumor or inflammation. The fragment of bone included in the specimen showed “numerous cement lines, suggesting waves of bone formation.”

The operative wound healed normally. The swelling increased slightly in size during the first few months following biopsy. The patient was last examined in May, 1954, at which time the swelling was slightly more prominent than it had been when the patient was photographed. There has been no recurrence of pain since the biopsy was performed.

REVIEW OF THE LITERATURE

A search of the world literature through May, 1954, has disclosed 159 cases which are compatible with the clinical picture of Tietze's syndrome. Since some of these case reports are substantiated by only scant clinical data, this series might well include cases of undiagnosed neoplasms, infections, etc., of the costal cartilage. The diagnosis of Tietze's syndrome, I believe, can be proved only by biopsy. Therefore all biopsied cases have been studied in more detail. In Table 1 the roentgenologic and pathologic findings of all biopsied cases have been copied or paraphrased essentially in toto from the original articles or translations thereof.

Incidence. The fact that only 159 cases were found in the literature over a twenty-three-year period would indicate that Tietze's syndrome is a rare entity. Of these cases only seven have appeared in North American journals. Since many physicians may not be aware of this syndrome, many cases probably are either unrecognized or unreported; therefore the rarity of the syndrome may be more apparent than real.

For example, Geddes could report on twenty-two patients during a three-year period and mentions eight others whose records were lost. An orthopedic surgeon has, within the past four years, seen at least three cases of unexplained, painful swelling of the costal cartilage among student nurses at a Philadelphia hospital of modest size. The literature contains occasional reports of undiagnosed costal cartilage swellings, some of which may have been Tietze's syndrome.

Etiology. Predisposing factors: The patient's age was given in eighty-three cases. The mean age is 32.3 years; the median, twenty-eight years. The range is from eleven to seventy-nine years. Thirty patients were in the third decade of life. (Fig. 2.) Of the biopsied cases, the age was stated in fourteen. The mean age is 28.8 years, with a range from eleven to fifty-seven years. The sex of the patient was stated in 119 cases; there were fifty-nine males and sixty females. As to race, the syndrome has been seen largely in Western European and in Japanese subjects; the patient reported on herein is an American Negro. Tietze's syndrome appears to have no occupational preference. Patients with many diverse occupations have been seen.
Although nutritional deficiencies were implicated etiologically in earlier reports, the data now available do not support this viewpoint. A statement as to clinical nutritional status was found in sixty cases. Forty-eight of these patients were said to have a normal nutritional status; twelve were malnourished. Among six biopsied cases in which data were given, five patients were considered adequately nourished. Evans and Eames believed that the syndrome was a local manifestation of vitamin B and C deficiencies. Guarner suggested the possibility of deficiency in certain amino acids.

That Tietze's syndrome may have some relationship with pulmonary tuberculosis has been considered but is substantially ruled out. In the cases reviewed herein no patient was reported as having active tuberculosis; in several of the cases tuberculin skin tests were negative.

Premature calcification or ossification of the costal cartilages was thought to be associated with Tietze's syndrome by Hartung. Although eight reported cases have shown calcified costal cartilages, at least twenty-one have not. Sufficient data are not available to compare the incidence of cartilage calcification in Tietze's syndrome with that in the general population. It is, however, apparent that calcification is not a sine qua non for the occurrence of this syndrome.

In four reported cases there was an associated rheumatic or arthritic condition. This association would appear coincidental. Although involvement of the manubriosternal and chondrosternal articulations may be seen in rheumatoid spondylitis, Tietze's syndrome does not primarily involve these joints. Congenitally bined ribs have been reported in two cases of Tietze's syndrome. Their significance is unknown.

Precipitating factors: Hormonal factors have been suspected but have not been proved to have etiologic import. External trauma has been mentioned as a precipitating factor by some clinicians. Trauma to the chest appears, for example, in the histories of three of Geddes' twenty-two cases, in two of Guarner's three cases, and in four of Chantraine's fourteen cases. Gukelberger thought that "unaccustomed mechanical stress" on the cartilage was a precipitating factor in eight of his ten cases. In none of the cases verified by biopsy was a history of trauma given. The trauma of coughing has received considerable attention in the literature on this syndrome. Rib fractures due to coughing are reported from time to time, and violent coughing can inflict considerable stress on the costal cartilages and costochondral junctions. However, in the majority of reported cases a history of cough was not given.

In a handful of cases an association with a distant focus of infection has been described. Acute viral and bacterial infections of the respiratory tract are sometimes associated with Tietze's syndrome. All of Geddes' twenty-two patients had a respiratory infection from one month before to two days after the onset of pain in the chest due to Tietze's syndrome. In the majority of cases the symptoms were those of the common cold. On the other hand, all of Dübener's ten patients were said to be free of disease of the respiratory tract. A statement as to the presence or absence of respiratory infections was found in sixty-five cases. Of these, fifty-one patients had either a cough or a respiratory infection; fourteen patients did not. Common colds, bronchitis and pneumonia were mentioned most frequently. This association appears to be significant but is not invariable; whether it is due to toxic factors, to the trauma of coughing or both is unknown.

The most recent etiologic theories have been proposed by American observers. Motulsky and Rohn state that the anatomic location of an inconstant structure, the interarticular sternocostal ligament, parallels the incidence of involvement of the various cartilages in Tietze's
syndrome. They suggest that "microtrauma" or disease of this ligament may be a causative factor. Beck and Berkheiser\(^6\) have proposed that the pathologic process consists of a contracture of the ligament lying subjacent to the second costal cartilage, causing the cartilage to buckle forward.

The possibility of multiple etiology is mentioned by Raffel,\(^7\) who believes that such factors as malnutrition, infection of the respiratory tract and local congenital anomalies could all be operative in the same individual. He believed the essential factor to be an "unusual distribution of local stresses and strains" on the cartilages.

**Epidemiology.** All cases reported have been isolated with the possible exception of Geddes\(^6\) series. Although he reported four patients from one regiment, three from one reinforcement unit and two from one transport unit, he does not imply that contagion was involved.

The season of onset was given in eight of the biopsied cases. Of these, five cases appeared in winter,\(^{21,22,23,24}\) one in "fall or winter"\(^6\) and two in summer.\(^{16,20}\) As to geographic distribution, biopsied cases have been reported from six Western European countries, Japan and the Eastern United States.

**Pathology.** The site of the lesion was stated in ninety-six cases. Of these, sixty-six patients (68.75 per cent) had single swellings; thirty patients (31.25 per cent) had multiple swellings. Of the sixty-six swellings, equal numbers were right- and left-sided. The single lesions were localized as follows: first costal cartilage, five; second, forty-six; third, six; fourth, six; seventh, two; tenth, one. When the swellings were multiple, neighboring cartilages on the same side were most often involved. Only two patients\(^{6,13}\) had bilateral lesions. Thirteen patients presented two lesions; twelve patients, three lesions; and three patients, four lesions. One case each of five and six swellings is reported.

Of the cases in which biopsy specimens were taken, the site of the lesion was stated in thirteen. Nine patients presented single swellings; in four they were multiple. The locus of swellings in these thirteen cases is diagrammed in Figure 3.

Gross findings at operation have been difficult to interpret. (Table 1.) Some observers have noted swelling or edema of the perichondrium and soft tissues; others have not. The adjoining ribs have appeared normal except in three cases.\(^{21}\) To most authors the cartilage itself appears abnormally prominent. It is not clear whether this represents an actual increase in the mass of the cartilage or simply a forward angulation. Beck and Berkheiser\(^6\) take the latter view.

No specific histologic changes have been found in Tietze's syndrome. (Table 1.) Typically, the report is of essentially normal cartilage. No signs of tumor or inflammation were found except in one case,\(^{35}\) in which the findings were compatible with a granuloma.

**Clinical Manifestations.** The chief complaint in the vast majority of reported cases was pain, although an occasional patient noted a swelling before the onset of pain. Pain is generally localized to the affected cartilage, but radiation laterally and even into the arm has been described.\(^5,44\) Onset is sometimes sudden\(^6\) and sometimes gradual. Intensity ranges from mild to severe. Patients have described the pain variously as aching, gripping, neuralgic, sharp, dull, and even as "gas pains." Exacerbation with coughing or deep breathing has been reported.\(^1,34\)

On physical examination the finding of a firm, fusiform or spindle-shaped swelling confined to one or more of the upper four costal cartilages is characteristic. Heat and erythema are absent. Tenderness is usually although not always present initially; when present it seems to be the first finding to disappear. Almost all investigators have found the tenderness to disappear in ten days to eight or nine weeks.
### Tietze's Syndrome—Kayser

#### TABLE 1

<table>
<thead>
<tr>
<th>Author</th>
<th>No. of Cases</th>
<th>Age (yr.) and Sex</th>
<th>X-ray Findings</th>
<th>Pathologic Findings</th>
<th>Gross</th>
<th>Microscopic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tietze</td>
<td>1</td>
<td>18, M</td>
<td>No data</td>
<td>Second costal cartilage peculiarly bulged forward; cartilage not altered; cartilage thickness increased; no evidence of malignancy or inflammation; occasional calcific deposits with splitting into fibers; Auffaserung</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brelauer-Chirurgische Gesellschaft</td>
<td>1</td>
<td>26, F</td>
<td>No data</td>
<td>No data</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hertling</td>
<td>1</td>
<td>24, M</td>
<td>No shadows indicating calcification of cartilage</td>
<td>Cartilage perhaps somewhat pale; calcareous deposits of various sizes; atrophic processes; degeneration of muscle; complete wasting; fibrillation (Auffaserung) of the ground substance as well as formation of fibrous tissue at site</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Himep</td>
<td>1</td>
<td>20, M</td>
<td>Affected cartilage widened; otherwise normal</td>
<td>No necrosis; no change in consistency or color of cartilage; slight thickening toward middle of cartilage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Satani and Fujii</td>
<td>1</td>
<td>26, F</td>
<td>No data</td>
<td>No granulation or pus; cartilage not distinctly altered</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gill, Jones, and Pollack</td>
<td>1</td>
<td>29, M</td>
<td>Soft tissue swelling; no bony abnormality</td>
<td>Spindle-shaped enlargement of cartilage; intercostal tissues edematous; cartilage appeared normal on cut section; opaque streaks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Geddes</td>
<td>1</td>
<td>27, M</td>
<td>No data</td>
<td>Cartilage and perichondrium swollen, no swelling of other contiguous structures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Legard and Monnercann</td>
<td>4</td>
<td></td>
<td>Increase in size and porosity of anterior extremity of ribs; mottled appearance and few scattered calcific deposits; soft tissue swelling; X-rays in 2 cases normal</td>
<td>In 3 cases adjacent rib showed a bluish de-vitalized (delayed) appearance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paterniti</td>
<td>1</td>
<td>32, F</td>
<td>Ribs normal</td>
<td>Cartilage swollen for 3 cm. near costo-chondral junction; perichondrium opaque and rather thickened; no gross changes of appearance or consistency of cartilage itself</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brune and Smoak</td>
<td>1</td>
<td>55, F</td>
<td>No data</td>
<td>No data</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laksell</td>
<td>1</td>
<td>22, F</td>
<td>No radiopaque areas in costal cartilages; skeletal survey normal</td>
<td>Perichondrium slightly thickened</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*American Journal of Medicine*
Spontaneous pain usually persists longer than tenderness. Although in some cases pain lasted only one week, it is usually described as lasting a few weeks to several months. Gradual subsidence over a period of weeks was the most frequent finding, with exacerbations not uncommon.

The palpable swellings seem to reach a maximum size, then either remain stationary or slowly regress. Exacerbations and remissions of the swellings have been claimed. Very few of these lesions have been observed to undergo complete regression. Some cases have been followed up in which the swelling was present sixteen to twenty-six months after onset.\(^{30,31,32}\) A few patients have given histories of such swellings being present for three to five years.\(^{6,8}\) A prolonged course is the rule.

In most cases no roentgenographic abnormalities are reported. (Table 1.) Lesions have occurred in cartilages which showed calcific deposits and in those which did not. Routine laboratory work, including complete blood count, urinalysis, sedimentation rate and serologic tests for syphilis, has been reported as normal in several cases. De Haas\(^{30}\) found the blood calcium, phosphorus and alkaline phosphatase levels to be normal in two patients. The total cholesterol and uric acid levels of these patients were "on the high side." Laake\(^{29}\) found normal urinary excretion of estrone and follicle-stimulating hormone in four young women with Tietze's syndrome.

**Diagnosis and Differential Diagnosis.** The rather characteristic clinical picture should suggest the diagnosis. Confirmation is largely a matter of exclusion. Involvement of the costal cartilage by systemic disease should be ruled out. Positive diagnosis is made when a biopsy specimen showing essentially normal costal cartilage is taken from a patient with the typical clinical findings. Needle biopsy of these lesions has proved unsuccessful. Surgical biopsy is necessary to rule out the many specific lesions which may cause swellings of or about the costal cartilages. A partial list of such lesions would include both benign and malignant neoplasms, e.g., chondroma, osteochondroma, multiple myeloma, osteogenic sarcoma, Ewing's tumor, Hodgkin's disease and

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</tr>
</thead>
<tbody>
<tr>
<td>De Haas(^{30})</td>
<td>1</td>
<td>57, F</td>
<td>Fairly marked calcification of costal cartilages</td>
<td>Gross: No data; Microscopic: No real abnormality</td>
</tr>
<tr>
<td>Chantraine(^3)</td>
<td>1</td>
<td>37, F</td>
<td>Negative</td>
<td>Gross: No data; Microscopic: Typical cartilaginous tissue with orderly cell arrangement; some center of calcification, nothing abnormal at the costochondral junction</td>
</tr>
<tr>
<td>Díbere(^1)</td>
<td>3</td>
<td>? , F</td>
<td>Normal bony anatomy without destruction or periosteal reaction; except for the almost absent physiologic calcification of first costal cartilage after age 30, no calcific deposits seen</td>
<td>Gross: No gross changes of bone, periosteum, cartilage or perichondrium; rib synchondrosis showed forward angulation to a greater than normal degree; the rib itself was somewhat bent in the same direction; Microscopic: Normal conditions throughout, both in bony and cartilaginous parts of ribs; inflammation and neoplasm could be ruled out with reasonable certainty</td>
</tr>
<tr>
<td>Beck and Bertheiner(^1)</td>
<td>4</td>
<td>22, F; 34, F; 11, M</td>
<td>Entirely negative in all patients</td>
<td>Gross: Cartilage approximately normal in size and thickness; it was buckled forward in an acute angle; immediately subjacent to the cartilage heavy ligamentous fibrous tissue bands visible; bifid rib in 1 case Microscopic: Removed cartilages entirely normal</td>
</tr>
<tr>
<td>Kayser</td>
<td>1</td>
<td>16, F</td>
<td>Nothing abnormal in thoracic wall costal cartilage normally calcified and showed no calcification</td>
<td>Gross: No evidence of adhesions or inflammation in overlying tissues; moderate degree of anterior angulation of second right costal cartilage at costochondral junction; periosteum smooth, not grossly thickened; cartilage appeared normal on section Microscopic: Normal cartilage and bone; no evidence of tumor or inflammation; adjacent bone showed numerous cement lines, suggesting waves of bone formation</td>
</tr>
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</table>

DECEMBER, 1956
Tietze's Syndrome—Kayser

metastatic tumors, especially carcinoma of the breast and lung. Many specific infections of costal cartilage have been described. Pyogenic organisms may give rise to chronic osteomyelitis of the nearby rib or to metastatic bacterial osteochondritis from a focus of infection elsewhere in the body. Lesions of costal cartilage have been described in tuberculosis, syphilis, typhoid and paratyphoid infections, and brucellosis.

Rheumatoid arthritis of the second to fifth chondroternal joints, costochondral separation, posttraumatic callus formation and other rarer entities have been mentioned as possibilities in the differential diagnosis.

Treatment. There is no specific treatment. Symptomatic measures which have been recommended include reassurance and analgesics, rest and local heat, short wave therapy, and local counterirritants. Roentgen radiation was used by Laake without convincing effect, and Chantraine found a local dose of 1,400 r to be ineffective in one case.

Partial or complete resection of the involved cartilage has been performed in refractory cases. Beck and Berkeheiser excised the involved cartilages in four patients, leaving behind a cuff of perichondrium to insure healing. They reported no recurrences following operation.

DISCUSSION

The etiology and pathogenesis of Tietze's syndrome remain unknown. The syndrome even defies positive inclusion in one of the known categories of disease: infectious, neoplastic, metabolic, degenerative, traumatic, etc. Indeed, it may be a disease, not of cartilage at all but of the surrounding ligaments.

The question may arise as to whether these lesions are not simply painful chondromas, since histologic distinction between chondroma and normal cartilage is sometimes difficult. Several differences are apparent: The typical chondroma is lobulated, whereas no lobulations have been reported in Tietze's syndrome; in the majority of chondromas of the chest wall, pain is a late symptom, if it appears at all; chondromas of the chest wall have no preference for upper or lower ribs; whereas Tietze's lesions show a predilection for the upper ribs, especially the second. The chondroma grows steadily and may reach enormous proportions, whereas the lesion of Tietze's syndrome appears to limit itself to slight or moderate swelling which is capable of spontaneous regression.

Tietze's syndrome is of clinical interest primarily because of its significance in the differential diagnosis of chest pain. The pain of Tietze's syndrome may mimic that of pleurisy, angina pectoris, intercostal neuritis and other more common syndromes.

A British physician in India candidly reported that a patient with pain in the chest first noticed the "lump" on his chest while the doctor was examining his back. It follows that a history of pain in the chest should lead to inspection and palpation of the thoracic wall, as well as auscultation of the heart and lungs.

SUMMARY

Tietze's syndrome consists of an initially painful, usually tender prominence of one or more of the upper costal cartilages for which no specific etiology can be found. Biopsy usually shows normal cartilage. The clinical course is benign but may be prolonged.

A case of this syndrome is presented and the findings in 159 cases from the literature are analyzed, with emphasis on the biopsied cases.

Acknowledgments: The author is deeply grateful to Arthur M. Rogers, M.D., formerly Associate Professor of Clinical Medicine, The University of Pennsylvania School of Medicine. His clinical skill was responsible for making the diagnosis in the case reported here. Doctors René Lefevre, Masashiro Sakai and Carlos Robles generously did many of the necessary translations.

ADDENDUM

The writer inadvertently omitted from this study a careful pathologic description of a resected specimen of the second left costal cartilage from a twenty-three year old man. The painful swelling in this case was due to a persistent fracture of the adjacent rib with subsequent callus production and the formation of pseudarthrosis. (Wepler, W. Ueber die sog. Tietzscbe Krankheit. Deutsche med. Wochenschr., 79: 137-139, 1954.)

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Tietze’s Syndrome—Kayser


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