

ORIGINAL ARTICLE

Scrofuloderma With Osteoarticular Tuberculosis in the Sanitary Area of Ferrol

B Monteagudo,^a JF García-Rodríguez,^b C de las Heras,^a J Labandeira,^c M Ginarte,^c C Durana,^d and JM Cacharrón^a

^aServicio de Dermatología and ^bUnidad de Enfermedades Infecciosas, Servicio de Medicina Interna, Complejo Hospitalario Arquitecto Marcide-Novoa Santos, Ferrol, La Coruña, Spain

^cServicio de Dermatología, Complejo Hospitalario Universitario, Facultad de Medicina, Santiago de Compostela, La Coruña, Spain

^dServicio de Anatomía Patológica, Complejo Hospitalario Arquitecto Marcide-Novoa Santos, Ferrol, La Coruña, Spain

Abstract. *Introduction.* Scrofuloderma results from direct extension of an underlying tuberculous focus such as bone, joint or even the epididymus to the overlying skin, but is more frequent over a lymph node, mainly in the cervical region.

Methods. We analysed all cases of scrofuloderma with a bone or joint focus evaluated in the sanitary area of Ferrol, with a current population of 220,000, during a 15-year period. We describe the clinical, histopathological, and microbiological data of patients.

Results. We found 6 cases of scrofuloderma with osteoarticular tuberculosis. This series includes five men and one woman, aged 37 to 80. Visceral involvement was found in 3 patients (50%).

Conclusion. Osteoarticular tuberculosis comprises 10% of all extrapulmonary tuberculous infections. There is a high probability of visceral involvement in patients with scrofuloderma. Underlying bone involvement should be ruled out in all patients with scrofuloderma, especially in those with incomplete response to medical treatment.

Key words: scrofuloderma, cutaneous tuberculosis, osteoarticular tuberculosis.

ESCROFULODERMIA CON TUBERCULOSIS OSTEOARTICULAR EN EL ÁREA SANITARIA DE FERROL

Resumen. *Introducción.* La escrofulodermia se produce por la extensión directa a la piel de un foco tuberculoso subyacente a nivel óseo, articular o incluso del epidídimo, pero sucede con mayor frecuencia sobre un ganglio linfático, sobre todo los cervicales.

Métodos. Analizamos todos los casos de escrofulodermia de origen óseo o articular vistos en el área sanitaria de Ferrol, población actual de 220.000 habitantes, en un periodo de 15 años. Describimos los datos clínicos, histopatológicos y microbiológicos de los pacientes.

Resultados. Encontramos 6 casos de escrofulodermia con tuberculosis osteoarticular. Esta serie incluye 5 varones y una mujer, de entre 37 y 80 años de edad. Se encontró afectación de órganos internos en tres pacientes (50%).

Conclusión. La tuberculosis osteoarticular constituye el 10% de todas las infecciones tuberculosas extrapulmonares. Hay una alta probabilidad de afectación interna en pacientes con escrofulodermia. Se debe descartar afectación ósea subyacente en todos los pacientes con escrofulodermia, sobre todo en los que muestran una respuesta incompleta al tratamiento médico.

Palabras clave: escrofulodermia, tuberculosis cutánea, tuberculosis osteoarticular.

Introduction

Tuberculosis continues to be a serious health problem in Spain. Approximately 35 new cases per 100 000 population are identified each year, although this rate can exceed 70 per 100 000 in areas such as Galicia.¹ The high incidence of tuberculosis in Galicia has been associated

Correspondence:
Benigno Monteagudo-Sánchez.
Rosalía de Castro, 38, 3^ºB.
15706 Santiago de Compostela. Spain
E-mail: benims@hotmail.com

Manuscript accepted for publication March 12, 2007

with high unemployment levels and the lack of an effective prevention and control program.² Cutaneous tuberculosis accounts for just 0.015 % of all diagnoses made in hospital outpatient dermatology units, and just under 1.5 % of all extrapulmonary forms of tuberculosis.³ The emergence of resistant strains combined with the presence of patients with AIDS, increased use of immunosuppressive drugs, and immigration from countries with a high tuberculosis burden could all lead to a rise in the incidence of tuberculosis in Spain.⁴

Extrapulmonary forms of tuberculosis account for 10 % of all cases, and 1 in 10 patients with extrapulmonary infection have bone tuberculosis. The most common bone infection site is the spine (40 %–60 % of all cases), followed by the metaphyses of long bones. The disease course is indolent and diagnosis is generally delayed due to a lack of specific signs and symptoms.^{5,6}

The aim of this prospective study was to evaluate data on scrofuloderma with underlying osteoarticular involvement, with particular emphasis on clinical, radiological, and microbiological findings.

Materials and Methods

We prospectively studied 1139 consecutive cases of tuberculosis seen at a specialist tuberculosis unit between January 1991 and December 2005. The unit, which belongs to the infectious diseases unit of Complejo Hospitalario Arquitecto Marcide-Novoa Santos, Ferrol, Spain, receives the majority of referrals of patients over 12 years old who are diagnosed with tuberculosis at a

hospital or primary health care center in the health care area of Ferrol, which currently serves a population of 220 000. Of the 1782 patients diagnosed with tuberculosis during the study period, 1139 were referred to the unit. We recorded the following data: date of diagnosis, patient age and sex, medical history, organ involvement, prior general symptoms, skin signs and symptoms, time since onset of skin lesion, Mantoux test results, radiological findings (radiograph of the chest or other areas), results of laboratory workup, microbiological analysis, and histopathology, treatment prescribed, and therapeutic response. For patients who had undergone a skin biopsy, half of the specimen was used for histopathology (hematoxylin-eosin staining and Ziehl–Neelsen staining to detect acid-fast bacilli), and the other half was used for culture on Löwenstein–Jensen medium.

Results

A total of 1139 new cases of tuberculosis were seen in the specialist tuberculosis unit during the study period of 15 years. Of those, 33 (2.89 %) had osteoarticular tuberculosis. Only 6 patients had scrofuloderma with underlying osteoarticular tuberculosis. This corresponds to 0.52 % of the entire study group and 18.1 % of the patients with osteoarticular tuberculosis.

Table 1 shows the clinical characteristics—age, sex, date of diagnosis, medical history, prior general symptoms, location of skin lesion, and time since onset—of the 6 patients with scrofuloderma and underlying bone or joint disease. More men than women were affected (5 [83.3 %]

Table 1. Clinical Characteristics of Patients

| Patient | Sex/Age, y | Date | Medical History | Prior Symptoms | Site of Skin Lesion | Time Since Onset |
|---------|------------|------|--|---|--------------------------|----------------------------|
| 1 | M/48 | 1992 | Alcoholism, ITP, and stroke | Cough, expectoration, asthenia, anorexia, and weight loss for the past 4 months | Right lower jaw area | 1 month |
| 2 | M/37 | 1992 | None | None | Front left side of chest | 6 months |
| 3 | F/80 | 1995 | None | None | Left scapula | 8 months |
| 4 | M/70 | 1997 | Hypertension and anxiety–depression syndrome | Scrofuloderma on neck for the past 6 years | Presternal region | 3 years (presteral lesion) |
| 5 | M/57 | 1999 | Gastritis and pneumonia 5 years earlier | None | Left buttock | 1 year |
| 6 | M/59 | 2000 | Type 2 diabetes mellitus and hypertension | Weight loss and pain in right iliac fossa for the past 4 months | Front left side of chest | 2 weeks |

Abbreviations: F, female; ITP, idiopathic thrombocytopenic purpura; M, male.



Figure 1. Patient 4. Transverse hypertrophic scars on the neck as a result of tuberculous lymphadenitis. Ulcerated lesions seeping purulent exudate, located in the upper presternal and left parasternal regions.

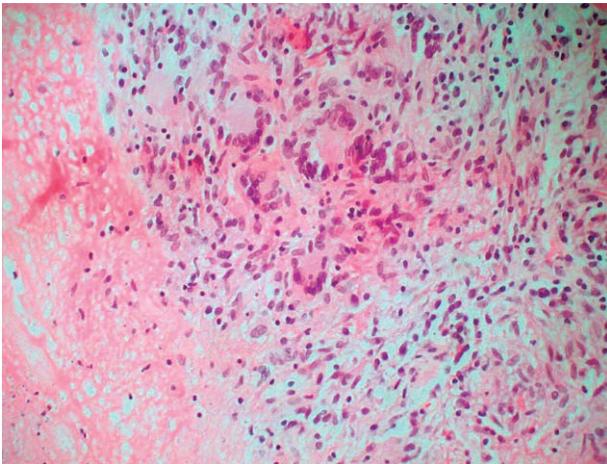


Figure 2. Patient 5. Epithelioid granulomas with necrotic centers (hematoxylin–eosin, $\times 150$).

and 1 [16.7%], respectively), and the patients' ages ranged from 37 to 80 years. No new cases were identified in the last 5 years of the study. The patients' medical histories were highly varied. Three of the patients reported general signs and symptoms prior to the diagnosis of tuberculosis: 2 had experienced considerable weight loss and 1 had had scrofuloderma lesions on the neck secondary to tuberculous lymphadenitis in the preceding 6 years. Time since onset of the skin lesions secondary to the bone involvement ranged from 2 weeks to 3 years, and the lesion sites were highly varied: front left side of the chest



Figure 3. Patient 5. Hip radiograph: bone-destructive and sclerotic areas in the left ischiopubic ramus and small areas of calcification in the soft tissues.

(2 patients), lower right jaw, left scapula, presternal region (Figure 1), and left buttock. We also identified 12 cases of scrofuloderma with underlying lymphadenitis during the study period. The majority of lesions were located in the lateral cervical region.

Table 2 shows the results of the diagnostic tests (histopathology and microbiology studies, laboratory workup, Mantoux test, and radiological tests), the treatment prescribed, and the therapeutic response. Purulent exudate was taken from all 6 patients for microbiological analysis, and a histopathologic study was performed in 3 patients. Colonies of *Mycobacterium tuberculosis* were found in Löwenstein–Jensen medium for all the samples (purulent exudate from 6 patients and biopsy specimens from 3 patients). Acid-fast bacilli, however, were only found in 1 of the 6 purulent exudates (auramine staining) and in 1 of the 3 biopsy specimens (Ziehl–Neelsen staining). The histopathologic study, performed in 3 patients, revealed granulomas composed of epithelioid cells and Langhans giant cells surrounded by lymphocytes; the granulomas were caseating in 2 of the patients (Figure 2) and noncaseating in the third. The results of the laboratory tests (blood count, biochemical workup, and urine test) were unremarkable except for findings that corresponded to previous diseases or substance abuse. The erythrocyte sedimentation rate was high in 2 patients.

Table 2. Diagnostic Tests and Treatment

| Patient | Histopathology and/or Microbiology Study | Laboratory Workup | Mantoux Test | Bone Involvement | Other Type of Involvement | Treatment and Response |
|---------|--|--|-------------------------------------|---|--|---|
| 1 | Exudate: Auramine– LJ+ (<i>Mycobacterium tuberculosis</i>) | Hemoglobin: 9.7 g/dL Platelets: 15 000/ μ L Albumin: 1.9 g/dL GGT: 93 U/L | + (12 mm) | X-ray: osteomyelitis in lower right jaw | Extensive pulmonary involvement: bronchogenic dissemination (on chest x-ray) | IRP (6-6-2 months). Treatment not completed, patient died after 2 months |
| 2 | Biopsy: Caseating granulomas ZN+ LJ+ (<i>M tuberculosis</i>) Exudate: Auramine– LJ+ (<i>M tuberculosis</i>) | Normal | + (35 mm) | X-ray: osteochondritis on left ninth rib (at chondrocostal junction) | Chest x-ray normal | IRP (6-6-2 months) and fistulectomy Complete response |
| 3 | Biopsy: Noncaseating granulomas ZN– LJ+ (<i>M tuberculosis</i>) Exudate: Auramine– LJ+ (<i>M tuberculosis</i>) | Normal | – | X-ray and chest CT: bone-destructive mass with poorly defined edges on left scapula Scintigraphy: uptake in left scapula | Chest x-ray normal | IRP (6-6-2 months), fistulectomy, and bone curettage Complete recovery |
| 4 | Exudate: Auramine– LJ+ (<i>M tuberculosis</i>) | ESR: 63 mm/h | Not done | Chest CT: bone-destructive mass in sternal manubrium and anterior intrathoracic and extrapleural collection (abscess) | Scrofuloderma of the neck secondary to tuberculous lymphadenitis LLL involvement (on chest x-ray) consistent with old tuberculosis | IRP (6-6-2 months). Supervised. Rejected surgery. Treatment unsuccessful. |
| 5 | Biopsy: Caseating granulomas ZN– LJ+ (<i>M tuberculosis</i>) Exudate: Auramine– LJ+ (<i>M tuberculosis</i>) | Normal | Not done (positive 5 years earlier) | X-ray and CT scan of pelvis: bone-destructive lesions in left ischiopubic ramus and calcification of soft tissues | Chest x-ray normal | IRP (6-6-2 months) and fistulectomy Complete response |
| 6 | Exudate: Auramine+ LJ+ (<i>M tuberculosis</i>) | ESR: 96 mm/h | + (15 mm) | X-ray: osteochondritis on left fifth rib (at chondrocostal junction) | Intestinal tuberculosis LRL and LLL involvement (on chest x-ray) consistent with old tuberculosis | IRP (6-6-2 months). Complete recovery |

Abbreviations: CT, computed tomography; ESR, erythrocyte sedimentation rate; GGT, gamma-glutamyltransferase; IRP, isoniazid, rifampicin, and pyrazinamide; LJ, Löwenstein–Jensen staining; LLL, lower left lobe; LRL, lower right lobe.

Bone involvement was detected by radiography, computed tomography, and scintigraphy. Affected bones included the ribs (in 2 patients) the lower right jaw, the left scapula, the sternum, and the left ischiopubic ramus (Figure 3). Chest radiography revealed pulmonary tuberculosis in 3 patients (50%). One of those patients had radiological signs of bronchogenic dissemination and 2 had signs that were consistent with old tuberculosis. The disease was associated with tuberculous lymphadenitis of the neck in 1 patient (patient 4) and intestinal tuberculosis in another (patient 6).

All the patients received specific tuberculostatic treatment with isoniazid, rifampicin, and pyrazinamide for 2 months, followed by isoniazid and rifampicin for a further 4 months. Three patients underwent surgery. The tuberculosis resolved in 4 of the patients following treatment, with residual scarring remaining. Patient 1 died due to respiratory failure before treatment was complete. Patient 4 rejected surgery and was prescribed supervised medical treatment in view of his psychiatric condition. The outcome, however, was not successful. He was finally prescribed an identical treatment regimen for a further 9 months, and the tuberculosis resolved.

Discussion

Scrofuloderma, also known as tuberculosis colliquativa cutis or scrofula, used to be the most common form of cutaneous tuberculosis in Europe. With some exceptions,^{7,8} lupus vulgaris⁴ is now found to be the most common form of the disease due to improved hygiene conditions and vaccination programs.⁹

Scrofuloderma occurs following the reactivation of *M tuberculosis* in previously infected or sensitized patients. It used to be more common in children, but it is now mostly observed in adult and elderly patients.³ It occurs when the tuberculosis extends directly to the skin from an underlying focus. Foci include bone and joint structures, the epididymis, the pleura (pleural empyema), and cervical lymph nodes in particular. Axillary, paratracheal, epitrochlear, and inguinal lymph nodes can also be a source of extension.⁹⁻¹² On rare occasions scrofuloderma can occur following bacillus Calmette–Guerin vaccination.¹³

Osteoarticular tuberculosis is often the result of a hematogenous or lymphatic spread of *M tuberculosis*. Although the lung is usually the primary source of infection, infected lymph nodes may also be involved. Cutaneous fistulas represent a rare form of disease onset. As we saw in our series, skin lesions occur on the limbs or trunk when there is phalangeal, joint, sternal, or rib involvement. Although rib lesions are only found in 1% to 3% of patients with osteoarticular tuberculosis,^{5,6} they occurred in 2 of our patients.

The initial lesion is a movable, solid, erythematous nodule that adheres to the skin. Once the nodule erodes, it perforates the skin, forming ulcers and fistulas that seep caseous or purulent exudate. The ulcers generally have blue borders with undermined edges and friable granulation tissue at the base. The course of the disease is chronic and spontaneous regression can occur after several years, leaving keloids and hypertrophic scars, which allow for retrospective diagnosis.^{3,4,10} Thirty percent of patients develop lupus vulgaris in or around this area.¹⁴

Between 1.7% and 38.2% of patients with cutaneous tuberculosis have internal organ involvement.¹⁴⁻¹⁶ In our series, the figure was 50%. This is similar to data from other series that have indicated that internal involvement, and pulmonary involvement in particular, is more common in patients with scrofuloderma.^{7,14}

Remarkable blood test results in patients with advanced disease include normocytic normochromic anemia, an increased erythrocyte sedimentation rate, elevated globulin levels, and hypoalbuminemia.⁴ In Galicia, 8% of patients with tuberculosis are also infected with the human immunodeficiency virus,¹ although coinfection was not observed in any of our patients. There were no immigrants in our series.

The histopathologic study typically reveals caseating tuberculous granulomas in the deep and peripheral areas around the abscesses, whereas the findings are nonspecific in the abscesses and necrotic areas at the center of the lesion. Pus or tissue generally produce *M tuberculosis* colonies (as we saw in our patients) and can be used to rule out diseases caused by nontuberculous mycobacteria. Acid-fast bacilli are found using specific staining methods in approximately 50% of patients, and the tuberculin skin test result is generally strongly positive.^{7,8} Polymerase chain reaction is becoming increasingly popular as a means of detecting *M tuberculosis* DNA, although a negative result is not sufficient to rule out the disease.^{3,10}

Cutaneous tuberculosis is treated in the same way as tuberculosis, although surgery is sometimes necessary in patients with scrofuloderma and bone involvement.⁵

Differential diagnosis includes deep mycotic infections (sporotrichosis), actinomycosis, gummatous syphilis, chronic bacterial osteomyelitis, amebiasis, acne conglobata, and hidradenitis suppurativa.

Because early diagnosis and treatment are essential in tuberculosis control programs, it is important to be able to distinguish between different clinical forms of the disease. We have described 6 cases of scrofuloderma, a rare disease in Spain, in order to aid diagnosis. We stress the high likelihood of associated internal organ involvement and the importance of ruling out underlying bone involvement in these patients.

Conflicts of Interest

The authors declare no conflicts of interest.

References

1. Moreno S, Cobo J. Las múltiples caras del control de la tuberculosis. *Enferm Infecc Microbiol Clin*. 2003;21:279-80.
2. García Rodríguez JF, Vázquez Castro J, De Juan Prego J, Rodríguez Mayo M, Sesma Sánchez P, González Moraleja J. Epidemiología de la tuberculosis en El Ferrol. *Med Clin (Barc)*. 1995;104:365-8.
3. Ferrándiz C, Ribera M. Tuberculosis cutánea. In: Drobnic L, Giménez Camarasa JM, editors. *Infecciones en Dermatología*. Badalona: Baetulo Arts Gràfiques; 2002. p. 313-26.
4. Roche E, García Melgares ML, Vilata JJ, Fortea JM. Escrofuloderma de larga evolución. *Actas Dermosifiliogr*. 2005;96: 522-4.
5. Kaur S, Thami GP, Gupta PN, Kanwar AJ. Recalcitrant scrofuloderma due to rib tuberculosis. *Pediatr Dermatol*. 2003;20:309-12.
6. Kaur S, Thami GP, Kanwar AJ, Mohan H. Scrofuloderma with multiple organ involvement in a 5-year-old child. *Pediatr Dermatol*. 2001;18:328-31.
7. Farina MC, Gegundez MI, Pique E, Esteban J, Martin L, Requena L, et al. Cutaneous tuberculosis: a clinical, histopathologic and bacteriologic study. *J Am Acad Dermatol*. 1995;33:433-40.
8. Yates VM, Ormerod LP. Cutaneous tuberculosis in Blackburn district (U.K.): a 15-year prospective series, 1981-95. *Br J Dermatol*. 1997;136:483-9.
9. Mlika RB, Tounsi J, Fenniche S, Hajlaoui K, Marrak H, Mokhtar I. Childhood cutaneous tuberculosis: a 20-year retrospective study in Tunis. *Dermatol Online J*. 2006;12:11.
10. González López MA, Vázquez López F, Gómez Díez S, Pérez Oliva N. Lesión cutánea ulcerada y supurativa de evolución tórpida en el cuello de una mujer de 83 años. *Enferm Infecc Microbiol Clin*. 2005;23:177-8.
11. Ramesh V, Misra RS, Beena KR, Mukherjee A. A study of cutaneous tuberculosis in children. *Pediatr Dermatol*. 1999; 16:264-9.
12. Barbagallo J, Tager P, Ingleton R, Hirsch RJ, Weinberg JM. Cutaneous tuberculosis. Diagnosis and treatment. *Am J Clin Dermatol*. 2002;3:319-28.
13. Tan H, Karakuzu A, Arik A. Scrofuloderma after BCG vaccination. *Pediatr Dermatol*. 2002;19:323-5.
14. Motta A, Feliciani C, Toto P, De Benedetto A, Morelli F, Tulli A. Lupus vulgaris developing at the site of misdiagnosed scrofuloderma. *J Eur Acad Dermatol Venereol*. 2003;17: 313-5.
15. Pandhi D, Reddy BSN, Chowdhary S, Khurana N. Cutaneous tuberculosis in Indian children: the importance of screening for involvement of internal organs. *J Eur Acad Dermatol Venereol*. 2004;18:546-51.
16. Singal A, Pandhi D, Agrawal SK. Multifocal scrofuloderma with disseminated tuberculosis in a severely malnourished child. *Pediatr Dermatol*. 2005;22:440-3.