Diagnostic difficulties in Hodgkin's disease

Fátima Pais*, Idália Esteves**, António Couceiro***, Raquel Pina****, José Ilídio****

Abstract

The authors present a case of Hodgkin's disease. The diagnosis was made when the disease had already two years of evolution. Some comments are made about the difficulty on the diagnosis of this disease.

Key words: Hodgkin's disease, lymph node tuberculosis.

Introduction

The histopathological diagnosis of Hodgkin's disease (HD) requires the presence of large cells characterized by one or more large vesicular nuclei with prominent nucleoli, inserted in an appropriate context.[1,2] The binucleated form is called Reed-Sternberg (R-S), although it had already been described by Tuckwell and others thirty years before Sternberg (1898) and Reed (1902). The mononuclear variant is called lacunar cell, or simply Hodgkin cell.[1]

The histological diagnosis of HD is not always easy, and often requires multiple ganglionary biopsies until a characteristic focal area is identified, within a condition that may be reactive ganglionary hyperplasia. The clinical case presented here highlights this diagnostic difficulty.

Case report

Female aged 32 years, married, an office worker, born and living in Porto. In August 1992 she developed erythema of the neck and left anterior side of the chest, associated with intense itching, and a painful cervical adenopathy on the left side of the base of the neck, of around 3 cm in diameter. Aspiration cytopuncture, followed by incisional biopsy of the adenopathy, not performed at our hospital, revealed a non-specific inflammatory lesion. The bacteriological exams and BK tests in direct and culture exams were negative.

One week after the biopsy, an exteriorized fistula formed at the incision site on the skin, which gradually increased in size. In December 1992, due to a Mantoux (IU) test higher than 40 mm, the patient was sent to the STDR (Tuberculosis and Respiratory Disease Service) of Gaia with suspected ganglionary tuberculosis. She began anti-bacillary treatment with Isoniazid, Pyrazinamide, Rifampicin and Ethambutol, which was maintained for two months, followed by therapy with the first three drugs only. In January 1993, due to the appearance of new cervical adenopathies on the left and right sides, exeresis of the right cervical ganglion was performed, the histological exam of which again revealed "reactive ganglion with non-specific characteristics and without signs of malignancy". In February 1993 she developed a nodular erythema on the legs anterior part, which was medicated with corticoids for two months, concomitantly with the anti-bacillary therapy, which led to regression of the erythema. In March 1993, a new exteriorized fistulous course appeared, this time on the right, which healed after local treatment. Again, the bacteriological exams, and BK and fungi tests were negative. Actinomycosis and cat scratch disease were ruled out. In July 1993 the therapeutic regimen was reduced to two drugs (Rifampicin and Isoniazid) and aspiration biopsy of the left cervical ganglion was performed, which was inconclusive. In view of the progressive increase and suppuration of the left cervical fistulous course, despite the anti-bacillary and antibiotic treatment, neck drainage surgery was performed; the histological exam of the skin sample revealed a "necrotising inflammatory process, probably of infectious cause".

*Resident to the Supplementary Internal Medicine Internship

**Pneumology Hospital Assistant

***Pathological Anatomy Hospital Assistant

****Director of the Pneumology Service

Pneumology Service of Vila Nova de Gaia Hospital Centre

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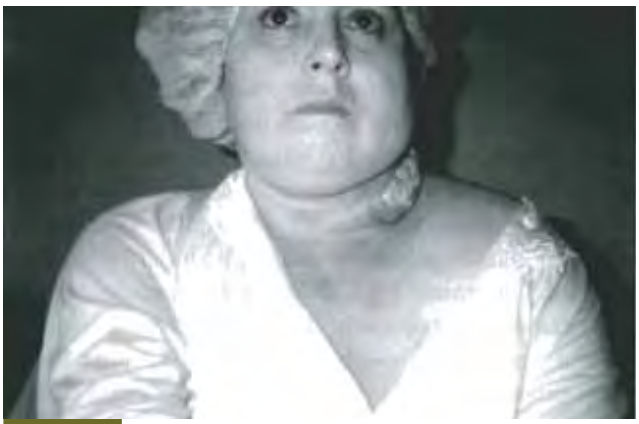


FIG. 1

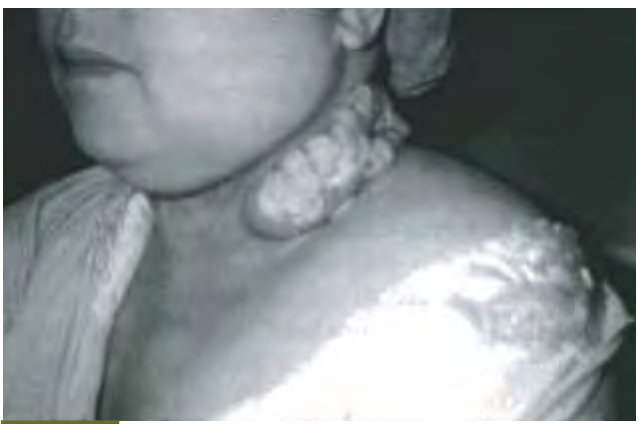


FIG. 2

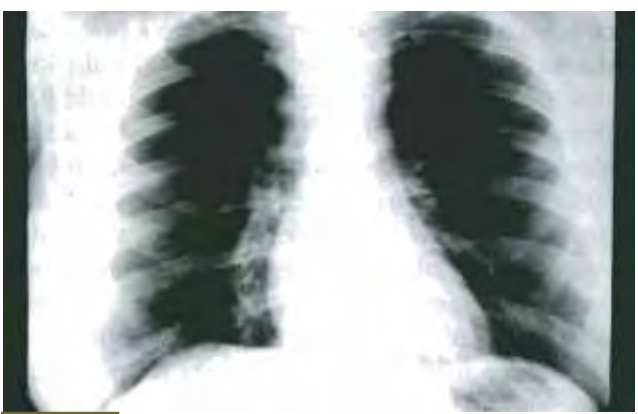


FIG. 3

Two weeks after surgery, the fistula reopened and the nodular erythema appeared for the second time; the anti-bacillary drug regimen was therefore altered to Rifampicin, Isoniazid and Streptomycin daily, and the erythema disappeared. The clinical situation remained the same until March 1994, when CAT scan of the neck, chest and abdomen was performed, with the following findings: "Multiple left cervical adenopathies with thickened, irregular central and peripheral ring necrosis. Left mediastinal and axillary adenopathies. Small nodular lesion in the right suprarenal region. A hypothesis of tuberculous adenitis is considered". In April 1994, the patient was referred to the hospital CHVN-Gaia for admission, with a hypothesis of ganglionary tuberculosis. There were no constitutional symptoms.

The patient's personal history included extraction of a benign node in the left breast at the age of 19. Smoker of 20 cigarettes/day for 17 years. The family history contained nothing of relevance.

On objective examination, she was conscious and collaborative, with good general condition. Pulse = 80 beats per minute, rhythmic, ample and regular; BP=120/60 mm Hg; Respiratory rate = 16 cycles per minute. Pale and hydrated mucosa. Edema and erythema on the left side of the face, mainly around the jaw (*Fig. 1*). Normal oral cavity and oropharynx. Objective examination of the neck was made difficult by the existence of edema due to skin infiltration. A purulent wound of around 15 cm in length and 4 cm in depth, horizontal, on the left side of the base of the neck. The edges of the wound were very thickened, pulled back, and with clear signs of inflammation (*Fig. 2*). Clusters of cervical, supraclavicular and axillary adenopathies. The remainder of the objective examination was normal.

The patient had hemoglobin 8.6 g/dL ; mean corpuscular volume 75.8m^3; mean corpuscular hemoglobin concentration 29.5; white blood cells 18300x10(9) (neutrophils 77%; lymphocytes 14%; monocytes 7%); ESR 111 mm 1st hour; normal values for glycaemia, renal and hepatic function and ionogram; iron 13mg/dL; iron binding capacity 186 mg/dL; lactic dehydrogenase 560U/L; normal proteinogram; B and C viral hepatitis markers, human immunodeficiency virus antibodies and syphilis serum negative; antigen 60 IgG=1406; bacteriological exams of the pus, BK test, mycobacteria atypical and anaerobic mycobacteria, all negative; negative hemocultures. Chest X-ray showed bilateral widening of the mediastinum (*Fig. 3*). CAT scan of the neck, chest and abdomen (April 1994) showed: voluminous adenopathies in various compartments of the neck, particularly on the left; bilateral axillary adenopathies; mediastinal adenopathies in all the compartments, and in the

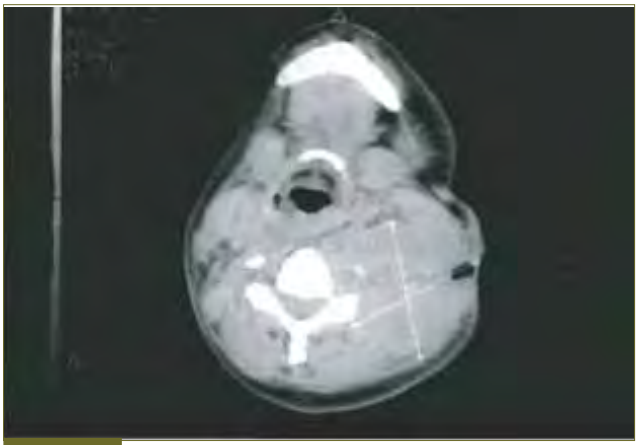


FIG. 4

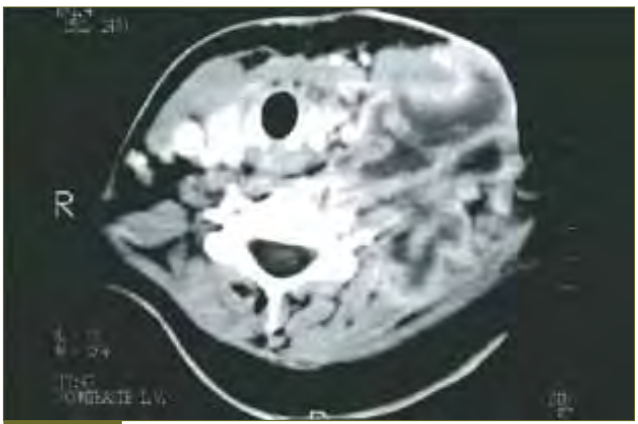
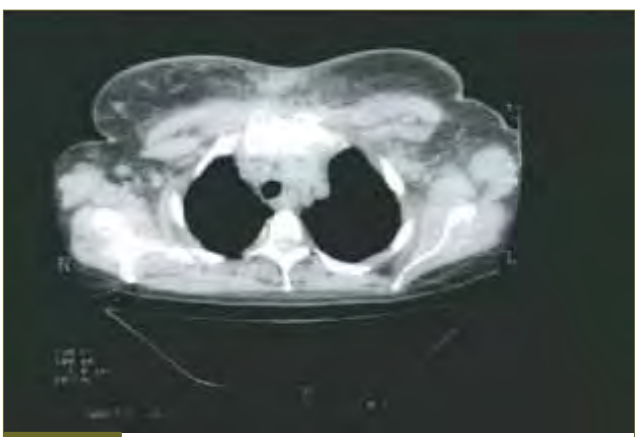


FIG. 5



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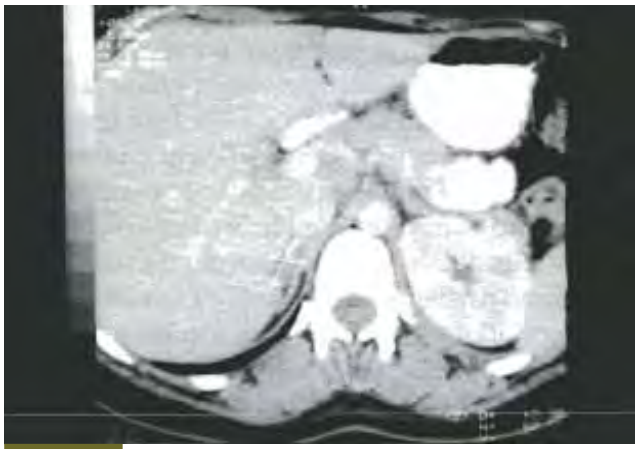

FIG. 7

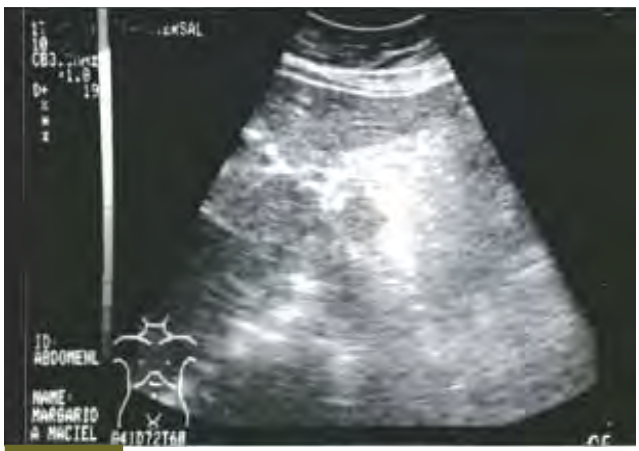

FIG. 8

retrocrural space of the lower mediastinum; no images of adenopathies below the diaphragm (*Fig. 4, 5, 6 and 7*). Myelogram showed "normal cellularity all the lines clearly represented, without alterations in maturation or excessive blasts; normal percentage values, except for the eosinophils, which were 7%; no foreign bodies in the bone marrow". Biopsy of the right axillary ganglion showed the existence of mixed cellularity Hodgkin's disease.

The ENT exam was normal. Abdominal ultrasound (May 1994) showed signs of two adenopathies in the upper retroperitoneum, with maximum dimension of 2.6 cm (*Fig. 8*). Bone marrow biopsy showed the three lines of myelopoiesis in balanced proportions, with no signs of being affected by the lymphoproliferative process diagnosed.

Diagnosis: Hodgkin's disease, mixed cellularity, in stage IIIA.

Comments

This presentation of the case was prompted by the long diagnostic delay (2 years) in a treatable, curable

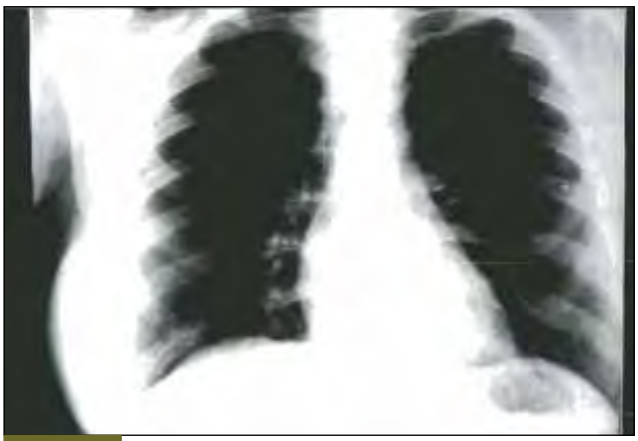

FIG. 9

patient,[2] probably justified by the fact that reactive ganglions had been biopsied, and the subsequent development of a wound that evolved with suppuration, constituting an additional difficulty to the diagnosis. In fact, although the R-S cell should be present for a diagnosis of HD,[1,2,3] it only becomes significant when it forms part of an appropriate context, as similar cells can appear in rare cases of carcinomas, melanoma, sarcomas, non-Hodgkin's lymphomas, and non-malignant diseases (thymoma, myositis, infectious mononucleosis, rubella) and any situation of lymphocyte depletion.[1,3] The R-S cell, thought to be the malignant cell of HD,[1,2,4,5,6] accounts for 1% to 2% of the cell population of the tumoral tissue.[1,7] Besides this sparseness, the R-S cells produce a series of cytokines that can induce an inflammatory response,[8] causing histological characteristics of HD to be similar to those of a chronic inflammatory/infectious process,[9] which is perfectly non-specific. The origin of the R-S cell is still uncertain, and subject to great controversy;[2] its scarcity in the tumoral tissue makes studies on this subject difficult.[1] There is strong evidence that it is derived from lymphoid B or T cells or histiocytes,[1,2,7,10,11,12] and it is likely that HD is a monoclonal neoplasia of the B cells, particularly in nodular form of lymphocytic predominance[1,12] or it may represent a final common route of various pathological processes induced by environmental, infectious or genetic factors.[2] These suggestions tie in well with the hypothesis of the etiological role of the Epstein-Barr virus in HD, which preferably affects the B lymphocytes, given that these are carriers of the C3d surface receptor to which the virions bind before entering the cell.[10] According to this hypothesis, HD is the result of the malignant transformation of the B lymphocyte, followed by an exuberant response of the host, which produces a heterogeneous population typical of polyclonal inflammatory cells surrounding the malignant R-S1 cell.

In the case presented, the fact that a ganglion was biopsied far from the site where the inflammatory/infectious process was more evident may have enabled a diagnosis of HD. In the case presented here, the left side of the neck (site where the adenopathies were detected first) and the right axilla (site of the diagnostic biopsy) do not constitute a pair of nodal zones in which involvement occurs directly by adjacency;[8] it is practically certain to be this type of involvement that occurs in the histological subtype in question.[8]

Since the start of the hospitalization, due to the intense suppuration of the neck wound, targeted antibiotic therapy was initiated for Gram+, Gram- and anaerobes, since the exams to look for an infectious agent gave no clarification. This therapy also led to the disappearance of the suppuration, with partial and extremely irregular healing of the wound. Given that we cannot safely rule out concomitance of a bacillary process, because the simultaneous nature of the two entities is described,[4] the specific therapy with Rifater and Streptomycin was maintained. The patient began chemotherapy cycles with MOPP / ABV hybrid scheme, which was well tolerated. This choice was based on the good results obtained with this therapy, which are extensively described in the literature.[1,2,5,13] At the end of the first cycle, the regression of the inflammatory process of the wound was evident, and it healed during the 2nd cycle.

A rapid decrease in the mediastinal adenopathies was also observed (*Fig 9*). The patient currently has criteria of complete remission. ■

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