Letters to the Editor

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Style versus substance in artistic depiction: reply

In his article ‘Style versus substance in artistic depiction’, Bruce Rothschild reopens the issue regarding the interpretation of hands and fingers that give the impression of being deformed by a number of artists, Rubens in particular. He asks whether this was a stylistic effect desired by the artist or whether a joint swelling was actually being depicted.

Since time immemorial, afflictions have been described (for example, leprosy and the plague in the Bible) or depicted (for example, foot paralysis and temporal arteritis on Egyptian bas-reliefs, goitre, ascites, paralyses of the lower limbs, and whether a joint swelling was actually being depicted. In paintings by a number of artists, Rubens in particular. He asks whether this was a stylistic effect desired by the artist or whether a joint swelling was actually being depicted.

In early societies, portrayals of diseases and illnesses enabled the transference of the disorder to the object, recalled the punishment to anyone who violated the social order and maintained the faith. They were honoured or worn as prophylactic amulets.

At the individual level, depending on whether one was an artist, like Rubens, who was affected by rheumatism (labelled ‘chronic gout’), the depiction of an affliction that might be one’s own was a way of expressing it to present and future generations, even a way of exercising it.

If, like Leonardo da Vinci, the artist was also an anatomist, he took advantage of his observations and his knowledge in order to refine his portrayals. The interpretation of Leonard de Vinci’s drawings is particularly interesting as it can be analysed afterwards by both historians and physicians. Bruce Rothschild was surprised to discover on one of Leonardo’s drawings of a fetus, probably dating from the period 1510–1512, a swollen, deformed finger, probably dating from the period 1510–1512, a swollen, deformed finger, even though arthritis had never been observed in utero. He drew the conclusion that, in most cases, the portrayal of a rheumatic finger or hand was only for stylistic effect.

Between 1478 and 1518, Leonardo da Vinci was present at and carried out 30 or so dissections at the Santa Maria Nova Hospital in Florence and the Santo Spiritu hospital in Rome, and it was only after he had made his numerous drawings, including drawings of fetuses, that he additionally acquired a reputation as an anatomist.

Nevertheless, he took liberties with realism in drawings of fetuses. For example, the diameter of the head is often too small; the hands rest on the knees instead of being crossed on the chest or alongside the body; the arms are proportionately too long; the feet are stretched out in front while the knees are bent; and the fingers and toes are spread, a position that only occurs when the fetus is moving.

Consequently, one may wonder whether Leonardo did a number of his drawings not on the spot but from memory or from notes jotted down quickly during dissections (one should remember that, at that time, the Church was not really in favour of dissections, especially those of stillborn babies).

In these conditions, the rheumatoid arthritis of the finger spotted by Bruce Rothschild on the drawing of the fetus could be an error in the portrayal; if not, why could not Leonardo da Vinci have had memories from an encounter with a young child who suffered from juvenile polyarthritides?

Amongst the illustrious Florentine patrons of the arts from the Medici family, Julien, Duke of Nemours (1479–1516) was prone to fevers and pains in the joints from the age of 9 onwards; Recent X-rays of his exhumed adult skeleton revealed deformations with ankylosis of the metacarpophalangeal joints of the left hand and signs of periostitis. The Medicis were afflicted with gout, but in those days all types of rheumatism were called gout, and most of the members of the Medici family had gout. In addition, a recent X-ray examination of their skeletons leaned more towards the diagnosis of spondyloarthritis.

Leonardo da Vinci met Julien, Duke of Nemours, who was afflicted from a very young age with juvenile (?) polyarthritis (oligoarticular type). Was he his model?

Spondyloarthropathies have a long history; the diagnosis of ankylosing spondylitis was made after analysis of the skeleton of Ramses II, and those of other pharaohs or even that of Moses of the Bible. The same diagnosis was suspected in Erasmus of Rottember, a contemporary of da Vinci. Garrod described juvenile rheumatism in a 3-year-old child in his treatise ‘Gout and rheumatic gout’ dating back to 1876.

Surprisingly, in the biography of Leonardo da Vinci it is stated that towards the end of his life in 1517, while he was organizing festivities in Amboise (France), he purportedly suffered partial paralysis of the left hand. But his fetus drawings are from an earlier period.

Is the rheumatic finger the new enigma in the da Vinci Code?

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Mixed connective tissue disease: should the diagnosis be more restrictive? Comment on the article by Bodolay et al.

Sir, We read with great interest the original contribution of Bodolay et al. [1], and we would like to comment on some issues in regard to this study. Mixed connective tissue disease (MCTD) was originally described by Sharp et al. [2] in 1972 in patients with a combination of features found in different connective tissue diseases and a characteristic serological marker, the presence of antibodies against U1 small nuclear ribonucleoprotein (RNP) autoantigen. The existence of MCTD as a distinct disease entity has been a matter of controversy among rheumatologists since it was first described. Specific diagnostic criteria allow us to classify and to separate MCTD from other autoimmune systemic diseases.

Three different sets of criteria have been proposed by Sharp, Alarcon-Segovia and Kasukawa, but correlation among them is
not optimal. Bodolay et al. [1] in their study utilized the Alarcon-Segovia criteria which do not take into account the positivity to Sm antigen as an exclusion criterion. It is known that both the U1-RNP and Sm antigens are components of the spliceosome complex, whose function is to assist in splicing pre-messenger RNA to mature RNA, and that systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) also express autoantibodies to several protein components of spliceosome [3]. So it is probable that with more restrictive criteria, specifically taking into account the Sm antigen, some of the patients categorized in their study as MCTD will not be so classified. Smolen and Steiner [4] have shown in a cross-sectional study that 92% of patients who satisfied the Alarcon-Segovia criteria could also be classified as having MCTD according to the Kasuwaka criteria, but only 70% according to the Sharp criteria. We recently carried out a similar study in Barcelona; from a large series of patients with autoimmune systemic diseases treated at our out-patient clinic, we initially selected patients with positivity to anti-RNP antibodies by enzyme-linked immunosorbent assay (Inno-Lia ANA UpDate kit; Innogenetics, Ghent, Belgium). Fifty-one patients were identified with positivity to anti-RNP antibodies, and 21 of these were rejected because of the presence of Sm antibodies which are considered to be specific to SLE. Ribonucleic acid immunoprecipitation from HeLa S3 cell extracts was performed in the 30 remaining patients to confirm the presence of anti-U1-RNP antibodies, and only 22 patients out of 30 (75%) were positive. In order to study the presence of anti-RNP by enzyme-linked immunosorbent assay and RNA immunoprecipitation, serum samples were obtained at the same time to avoid the effect of epitope contraction that has been described in patients with MCTD [5]. Among patients who satisfied the Alarcon-Segovia criteria, a specific positive and negative accord with the Kasuwaka criteria was obtained in 79 and 40%, respectively, and in 75 and 50% with the Sharp criteria. When different sets of diagnostic criteria were applied, a tetrachoric correlation was statistically significant only between the Sharp and the Kasuwaka criteria (P = 0.044; r = 0.426), so the agreement among the different sets of criteria is only partial. Taking all these data together, it is our opinion that in order to better study and improve our knowledge of MCTD, the most restrictive criteria—clinical and immunological—should be used. The Sharp criteria which specifically exclude patients with anti-Sm antibodies and confirmation of anti-U1-RNP by RNA immunoprecipitation are recommended where possible.

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Mixed connective tissue disease: should the diagnosis be more restrictive?: reply

Sir, Thank you for the comment on our article [1]. The coexistence of several sets of classification criteria for mixed connective tissue disease (MCTD) indicates how difficult it is to give a precise definition of the disease. Recently four sets of criteria have been published, and these are generally used in international publications: the Sharp criteria, the Alarcon-Segovia criteria, the Kasukawa criteria and the Kahn criteria. The basis of these sets of criteria is the presence of anti-U1-ribonucleoprotein (RNP) autoantibodies. In fact only the Sharp criteria consider the excluding diagnosis of MCTD in the presence of anti-Sm [2-4]. In 1996 Amiques et al. compared the four sets of criteria to define MCTD. Their results indicated that the classification criteria with the best performance are those proposed by Alarcon-Segovia, with 62.5% sensitivity and 86.2% specificity.

The Alarcon-Segovia criteria are widely used because they contain five clinical symptoms (swollen hands, synovitis, biologically or histologically proven myositis, Raynaud’s phenomenon, acrosclerosis with or without proximal systemic sclerosis) and anti-RNP positivity. The presence of the anti-RNP antibody and at least three out of five clinical symptoms are necessary for diagnosis of MCTD. Use of this set of criteria is easy and fast; and for this reason we and some others use this classification. However, MCTD has never been diagnosed if a patient’s serum contains anti-Sm antibodies.

We have followed-up all our patients with MCTD since 1979. A total of 225 patients have fulfilled the diagnostic criteria for MCTD. All patients’ sera contained anti-U1RNP (70 kDa, A and C peptides) antibodies using the U1-RNP-specific antigen enzyme-linked immunosorbent assay test. Over these three decades we have gained more and more knowledge about the pathomechanism and the clinical aspects of MCTD.

Recently it has been discovered that the specific components of the spliceosome complex recognized by MCTD human sera include U1 RNA and the U1-specific polypeptides 70 kDa, A, and C, Hoffman [5] reported that U1 70 kDa reactive T cells have a typical T-helper phenotype and produce cytokines important in B-cell differentiation. They investigated the structure of T-cell receptors on human T-cell clones specific for the U1 70 kDa polypeptide, which were derived from MCTD patients. They found that tested human T-cell clones generated against U1 70 kDa were specific for epitopes within the RNA-binding domain of the protein. Their data suggest that U1-RNP, or a modified form of U1-RNP, may be important in immune targeting and may provoke the autoimmune response.

Long-term studies have shown that more organ damage may develop in MCTD than was first thought in 1972. Oesophageal hypomotility, heart involvement and pulmonary damage, such as interstitial lung disease and pulmonary hypertension, may develop in MCTD. In 1979 an early article on MCTD began ‘MCTD has overlapping clinical features of SLE, SSc, polymyositis and rheumatoid arthritis’. Our opinion is that the clinical manifestations of MCTD mean a symptom complex characteristic of MCTD and these are not overlapping features. Furthermore similar