The Stories I want to tell you… my adolescents.

G. Calcagno

I want to tell you about…

- Lorena
- Angela and Melania
- Carlo and Andrea
- Adolescents and young adults suffering from rheumatic diseases, living a complex TRANSITION towards Adult rheumatology departments.

THE SOCIETY FOR ADOLESCENT MEDICINE®
...a Multidisciplinary Organization of Health Professionals

JOURNAL OF ADOLESCENT HEALTH

Transition from child-centered to adult health-care system for adolescents with chronic conditions. Position paper of the Society for Adolescent Medicine

Blum RW et al. 1993;14:570-6.

Transition is an active medical process

...the purposeful , planned movement of adolescents and young adults with chronic physical and medical conditions from a child-centered to an adult-oriented health care system.

Transition is a process……

- "A guided educational and therapeutic process rather than an administrative event"
- Transition to adult care should take place once the major developmental tasks of adolescence are complete(Viner. R)
- Is that really age 18 yrs?

TRANSFER

..is when a paediatrician hands a patient over to an "adult-oriented health system"

or

…when a Specialist meets the youth (now an adult patient) for the first time

When does the transition begin and end?

This is controversial !

TRANSFER

- **Transfer usually occurs during a very delicate phase in the adolescent's life**

- **Chronologic onset (age cut off) vs. social transitions (school completion)**

- **Elements of transition begin in the paediatric clinic (transition will take place over 2-5 yrs)**

TRANSITION

"… an active process involving adolescents' medical, psychological, social and educational needs, when moving from a paediatric-adolescent condition to that of an adult …"

TRANSITION

It involves each patient over 4 fundamental phases:

- **Consolidation of his/her sexual identity**
- **Forming social relationships out of the family**
- **Reaching his/her own independence**
- **Finding his/her own vocation**

Lorena, 13 years old

- Suffering from a fever, attributed to recidivous tonsillitis for 6 months
- Asthenia, weight loss
- High levels of acute phase reactant proteins

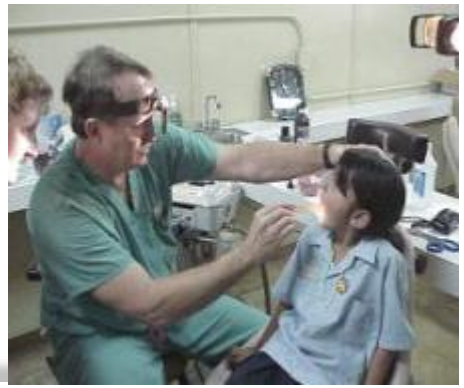
- ESR 96 mm/h, CRP 23.5 mg/dl
  RBCs 3860 x 109, WBCs 860 x 109
- Ferritin 110 ng/L
- Total proteins 9.1 g/L, g-glob. 32%, IgG 2360 mg/dl
- ANA, anti-DNA, ENA, aCL absent
- Thyroid function test within normal range
- Blood culture test, virologic test, and Tine test - negative

REUMA

Admission into Hospital

- Looking painful, sad, irritable
- Pale complexion, severe asthenia, headache
- Head bent on right side
- Ache on right ear
- Heart, chest and abdomen normal on examination

REUMA



ENT examination, skull x-rays on paranasal sinuses and mastoid sinus: no alterations

Evaluation of B and T lymphocyte levels:

normal

Chest x-ray: negative

Full scan of abdomen: negative

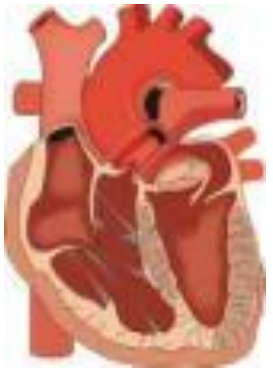
CT scan of abdomen: negative

REUMA

Heart examination:

ECG, echocardiography test: normal

pulse evaluation at radial artery - good



Neurological examination: normal

Ophtalmological examination: normal

REUMA

POSSIBLE DIAGNOSES

Infectious causes:

bacterial, viral, protozoarian and mycotic infections excluded

Cancer causes:

LDH, α-HDBH, uricaemia, VAM, peripheral blood: within range

Medullary and lymph node biopsy : within range

REUMA

- Lorena has constantly high temperature
- Eats very little and is losing weight
- More and more often she is tired, sad, depressed
- Cannot go to school
- Has no enthusiam, isolates herself from
-class-mates

What is the cause of this progressive deterioration?

REUMA

Lorena

- Keeps her head in an anthalgic position
- Has a Laterocervical mesoadenia

ECHO COLOUR DOPPLER NECK SCAN

- Volume of Laterocervical lymphnodes slightly increased
- Significant thickening of wall (4 mm) and
- Reduced lumen on both carotid arteries

REUMA

Lorena has:

- Bilateral carotid wall intima-media thickening
- Elevated phlogosis, hypergammaglobulinemia
- Anemia
- Syistemic Symptoms

Carotid intima-media thickening, likely inflammatory

CONCLUSIONS

Having considered:

- objective tests, age, sex
- outcomes of instrumental tests
- different pressure > 10 mmHg on arms

right arm 105/65 , left arm 85/40

TAKAYASU'S ARTERITIS

Classification criteria for Takayasu arteritis

- ❖ Angiographic abnormalities (conventional, CT, or MR) of the aorta orits main branches (mandatory criterium) plus at least one of the following four features:

- Decreased peripheral artery pulse(s) and/or claudication of extremities
- Bood pressure difference>10mmHg
- Bruits over aorta and/or its major branches
- Hypertension (related to chidhood normative data)

Ann Rheum Dis 2010 May 69 (5):798-806

THERAPY

- Prednisone 2 mg/Kg/day
-Anti-aggregation Aspirin therapy

- General condition visibly improved
- Better appetite and muscular strength
- Progressive stabilizing of acute phlogosis

May 2003

To decrease steroid doses: MTX 20 mg/sqm

LORENA

Was well until January 2004

Phlogosis indices almost normal, γ-globulines normal

She attends school, with very good results

She's happy, she goes to a dance school

She has her first period

Prednisone is gradually reduced to 5 mg/day
MTX and aspirin: unchanged

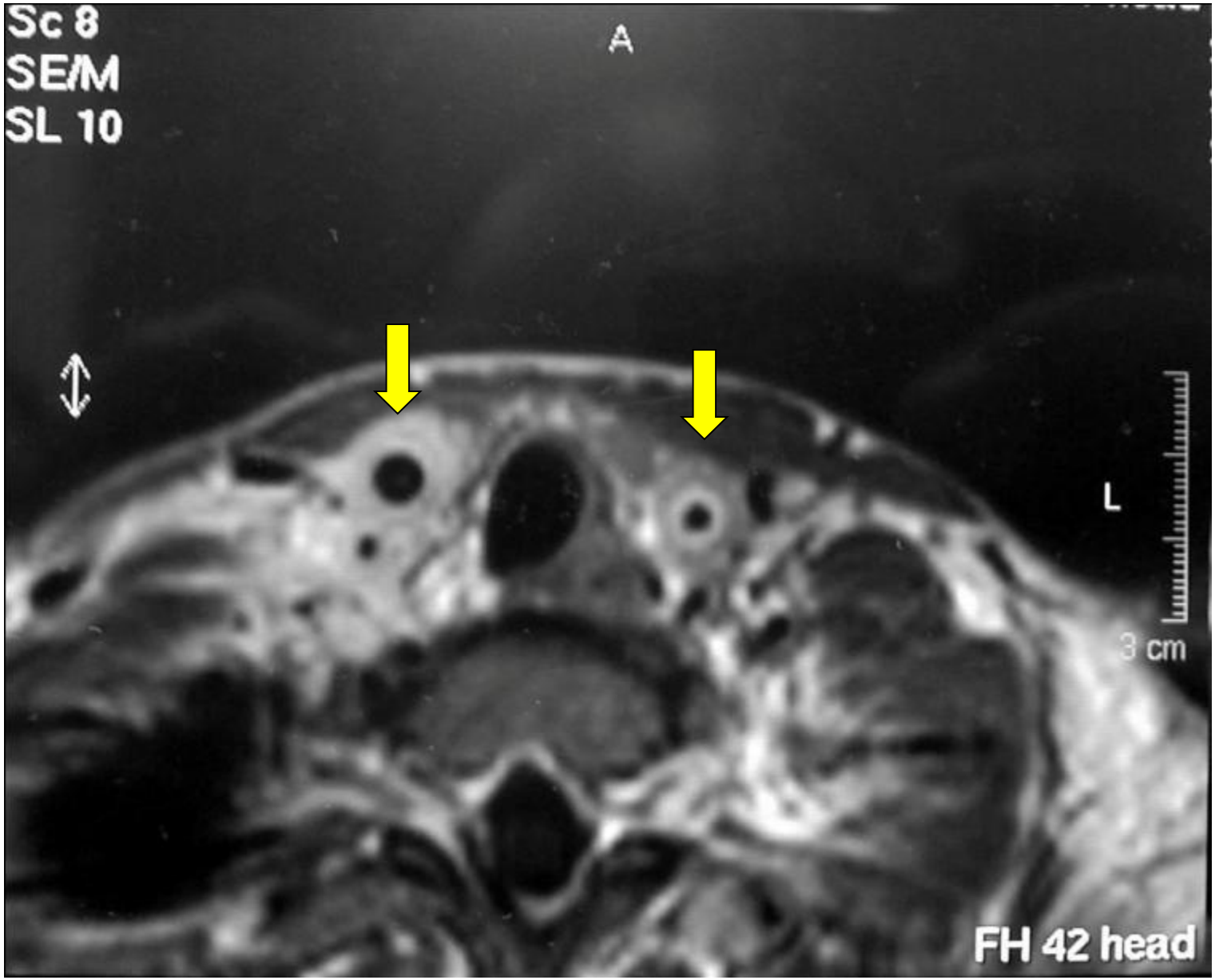
February 2004

Coinciding with the occurrence of a fever with flu-like symptoms

Two syncopes in the space of a few days

We were aware that this could mean a progression of the disease, despite negative phlogosis indices and clinical symptoms

- Vascular scan
-MRA (magnetic resonance angiography)
- PET
- Scintigraphy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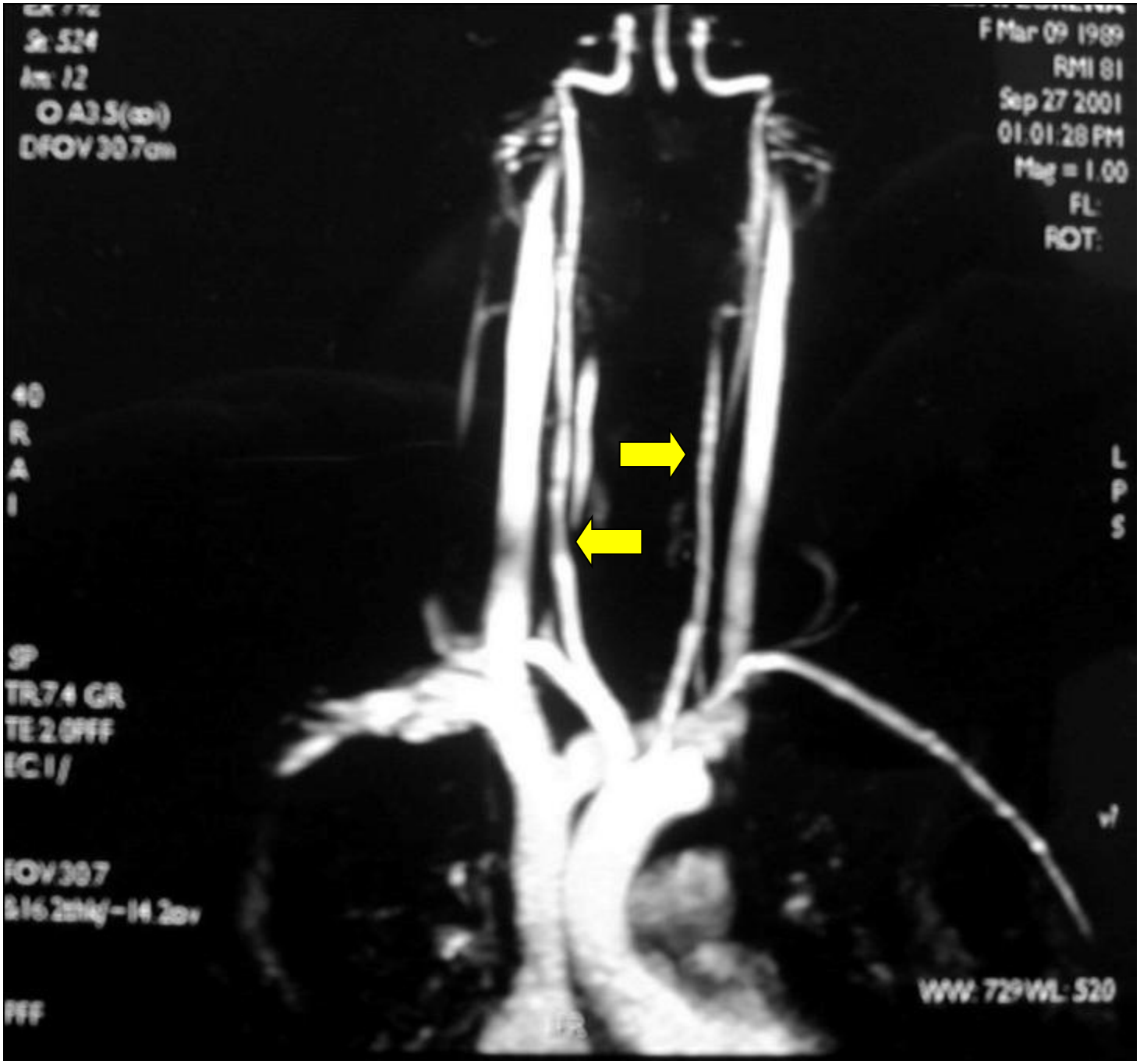
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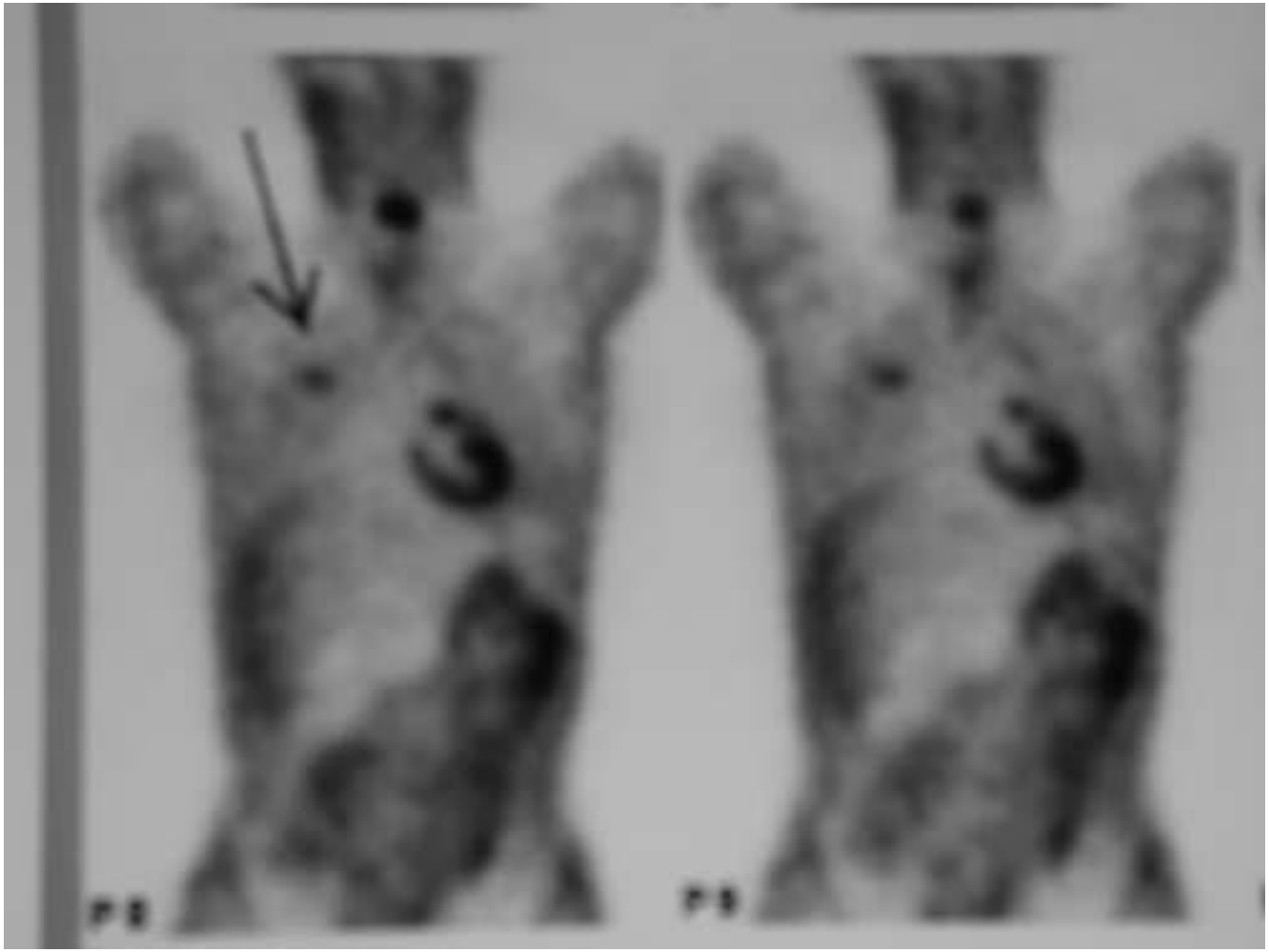
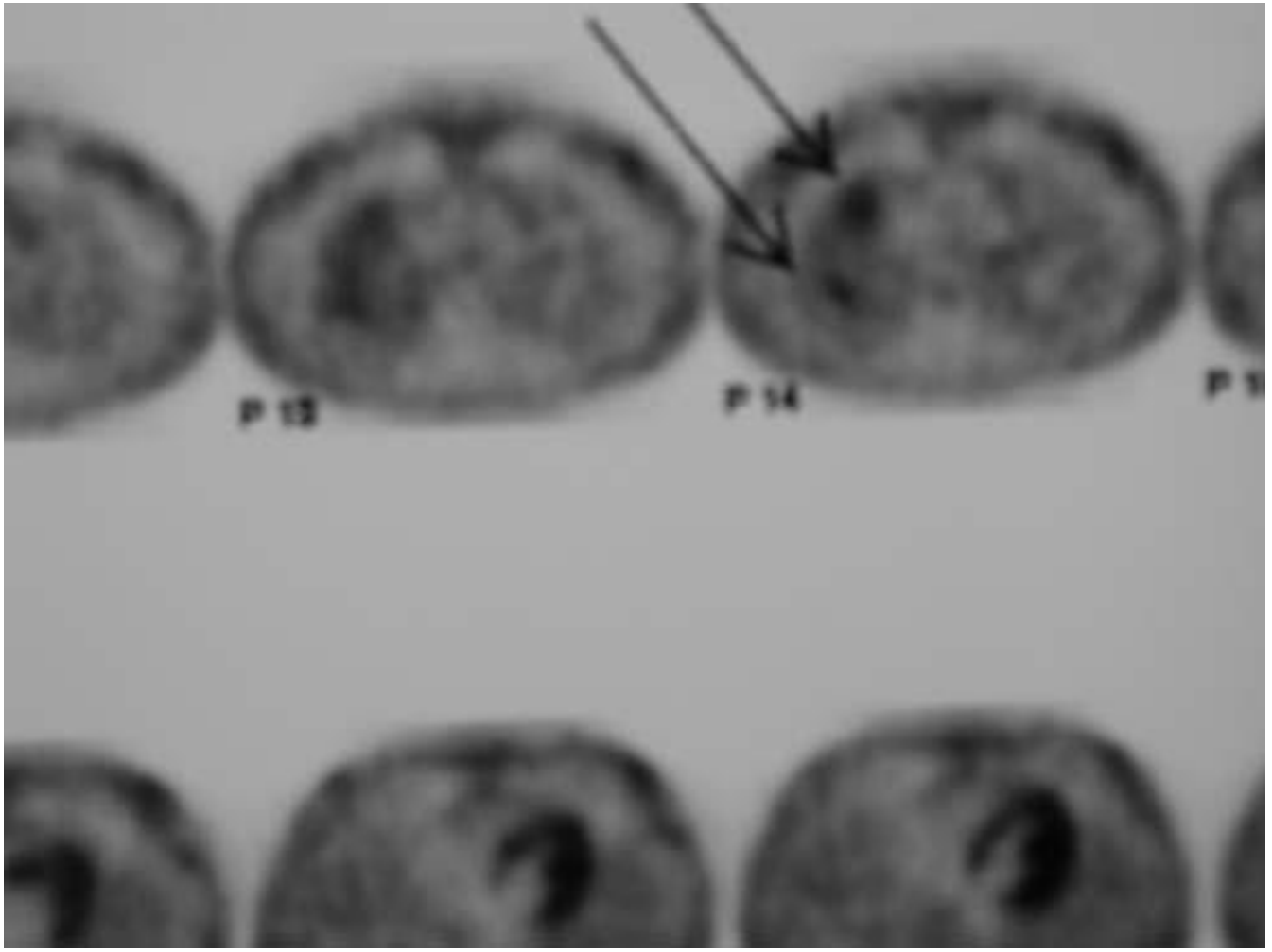
THERAPY

3 injections of Metilprednisolone1 gr/day,
followed by 1.5 mg/Kg of Deltacortene
and by Cyclophosphamide 2 mg/Kg orally, for 3 months
Administration of MTX interrupted

PET



PET



TAKAYASU'S ARTERITIS

Women whose wrist pulses are absent

Rare obliterative vasculitis in the larger blood vessels, affecting young women in particular (F:M=2.5:1)

SYMPTOMS:

Early phase **(before loss of pulse in the wrists) → systemic symptoms fever, malaise, nocturnal perspiration, anorexia, arthralgia/arthritis, mialgia, weight loss**

Later phase **→ inflammation, stenosis of the artery lumen, or aneurysms of the aorta and its branches, ischemia affecting limbs or organs**

SIGNS AND SYMPTOMS OF ORGANS INVOLVED

SKIN: malar rash , erythema nodosum

EYES: uveitis

HEART: dilatative cardiomyopathy , myocarditis, pericarditis

LUNGS: interstitial pneumopathy

KIDNEYS: mesangio-proliferative, membrano-proliferative, semilunar glomerulonephritis

GASTROINTESTINAL APPARATUS : ulcerous colitis

MUSCLE-SKELETON APPARATUS: arthritis, polymyositis

REUMA

THERAPY

-Steroids orally, 2 mg/Kg/day -

- until the disease is under control

- MTX subcutaneous, 20-25 mg/sqm/week

- Cyclophosphamide 2-3 mg/Kg first orally, then injected

- Mycophenolate 1.200 mg/sqm/day

- Vascular surgery (intraluminal stents, vascular grafts)

- Anti-TNF (Infliximab, Rituximab)

PROGNOSIS

- Correlated with an early diagnosis, a prompt medical and surgical treatment, so avoiding complications (aneurysms, arterial hypertension)
- Highly variable clinical course
- Survival at 5 years (83% of adults treated)

Feed Me
Fund Me
Leave me Alone

- **Compliance to drug treatment was difficult in the early years of the disease. The patient is now assuming Mycophenolate with adequate enough compliance**

- **TODAY Lorena is 22 years old, no longer studies, occasionally works as a shop assistant, goes from one adult rheumatology centre to another, does not want to be independent, she gets her mother to speak for her, she does not want to part from her paediatric rheumatologists**

The onset of adolescence is well known, but it is often difficult to say when it ends

– – – – – – – – – – – – –

Nowadays, due to their studies or to economic reasons, the number of youths who still live at home and depend on their parents is higher and higher, so delaying adulthood.

This phenomenon involves more frequently adolescents with a chronic disease, whose psycho-physical evolution and self-perception are abruptly altered by awareness of the disease

With more effective therapies available…

…many children with chronic, life-threatening diseases, such as cystic fibrosis, diabetes, Metabolic diseases and so on, may reach adult age in satisfactory conditions, but they still need constant assistance from the health care system

... in the last few years we have been witnessing a steady increase in the number of children with chronic rheumatic diseases

... and an increase in the number of rheumatic children who reach adolescence and adulthood with an active disease, leading to a condition of psycho-physical invalidity.

- Who should look after them?
- How should assistance be organized?
- How should a structure be created for the transition into centres for adults?
- Who should give financial support?

YARD (Young Adult Rheumatic Disease) Staff

- Pediatric rheumatologists
- Adult rheumatologists
- Clinical specialist nurses
- Social workers
- Secretarial support
- Access to physio- and occupational therapies
- Access to vocational counsellors

(Lori Tucker, Vancouver, Canada – 18th PReS Congress, Bruges, 2011)

Goals of the pediatric rheumatology Transition Program

- Education related to health issues
- Assist separation and independence issues
- Encourage adherence
- Assist with education, vocation, finance, relationship issues
- Implement final transfer to adult health care providers (rheumatologist and others)

(Lori Tucker, Vancouver, Canada – 18th PReS Congress, Bruges, 2011)

Barriers to transition

- Inadequate resources-time, funding, services
- Limited physician and health care provider Knowledge
- -Across primary and specialty areas
- -Across disciplines
- Poor inter/intra agency coordination
- Financial
- Anxiety-Youth "I dont't want to leave the Children's Hospital, it feels like a home to me…"
- Parents
- Pediatric health care providers "No one can take care of these patients as well as we can…"

- *(Lori Tucker, Vancouver, Canada – 18th PReS Congress, Bruges, 2011)*

Does the transition in paediatric reumatology take place for everybody?

Success… or Failure

- Many Kids are failing transition
- Study of 100 youths with JAI followed by a Canadian paediatric rheumatology program.
- Youths were transitioned to adult rheumatology providers aged 18yrs.
- 52 patients had an unsuccessful transfer
- 17 did not contact the adult rheumatologist for an appointment
- 35 went to an initial appointment but were lost to follow-up at 2 yrs after transfer

- *Hazel et al, Paediatric Rheumatology 2010*

Social context and transdisciplinary considerations are important

- Social (country, health system) and cultural context is important
- Healthcare providers across many disciplines **should be coordinated**: rheumatologists, family doctors, allied health personnel, social workers, vocational counsellors

I want to tell you about Carlo and Andrea…….

- **2 siblings (12 and 11years old) of Egyptian father and Italian mother, living in the north of Italy, with a medical history of recurrent fever attacks which started at the age of 14 and 6 months, respectively.**
- **Fever was accompanied by cervical adenopathy, severe exudative pharyngitis, oral aphtosis, abdominal pain and diarrhoea, sometimes with bloody stools.**
- **At the age of 10 and 9 years, screening for autoinflammatory disorders was performed revealing a single mutated FMF gene (E148Q). Since they fulfilled Tel Hashomer criteria, colchicine was started.**

While on holiday, they are urgently admitted into our department…

- **Despite colchicine, both still presented shorter fever attacks, recurrent abdominal pain with diarrhoea, oral and genital aphtosis, mialgia and asthenia. Blood tests and abdominal ultrasound were normal.**
- **An ophthalmic evaluation showed panuveitis in both.**
- **Recurrence of oral and genital ulcers, abdominal pain and uveitis strongly suggested the diagnosis of Behcet's Disease, even though HLA B51 was not detected**

The two siblings affected by Behcet's Disease (BD) had also a single mutated FMF gene

FMF is a genetic auto-inflammatory disease, characterized by attacks of fever and painful serositis.

Behcet's disease (BD) is an inflammatory disorder associated with vasculitis. Clinical manifestations of both diseases can mimic each other, and the coexistence of both diseases has been reported in some patients.

- Thalidomide (at an initial dose of 1mg/kg daily) was started along with colchicine.
- A positive clinical response was obtained in both patiens within a few months
- The patients went back to their hometown

A year later…

- The teenagers (especially the elder) refused to go to school (muscular and articular pain, which limited deambulation)
- Another year later, the elder brother is on a wheelchair, and is obese, despite frequent attacks of diarrhoea - referred by him – which involved admission into various hospitals in the country, two colonoscopies and blood tests which proved always negative for a re-activation of the disease
- After another year, their paediatric neuro-psychiatrist concludes that it is an amplification pain syndrome combined with a significant state of depression, starting a pharmacological and psychological therapy

- How could have depression – perhaps more serious than the disease itself – occurred after the final diagnosis, been avoided?

Child  Adolescent  Young adult

The transition from chilhood to adolescence for a subject with a chronic rheumatic disease since his/her early childhood is very complex, and differs from one country to another, depending on the different cultures and health care systems.

Issues which complicate transition

- Patients seeing multiple medical services, not coordinated with one another
- Patients with disease activation around the time of transfer
- Psychological aspects in patients affected by these diseases are underestimated

I want to tell you about…

- Angela and Melania
- Two sisters (27 and 9 years old) with PAN refractory to different drugs who had a persistent improvement over 5 years of thalidomide
- Angela had been diagnosed and treated for JIA since she was 5 years of age.
- **Melania's first clinical features occurred at three years of age. She had an acute stroke. Following hypertension, renal disease and neuropathy, PAN was diagnosed. Steroids, azathioprine and cyclophosphamide were given, with scarce benefit. After another ischemic cerebrovascular event, thalidomide was effective in controlling the disease activity. No side effects have been observed.**
- **After Melania's diagnosis, her mother brought Angela, the elder sister, to our attention.**

At 13 years

- Occurrence of:
- Neurological symptoms (**facial paraesthesia** and **left ptosis, reversible within a short period**) with a negative CAT

- Gastroenterological symptoms (**massive haemorrhage** followed by **right hemicholectomy** or: "**chronic granulomatous enteritis**")

- And:
- Occurrence of a **motor-sensitive deficit** on right arm and left leg

- **She assumed high doses of cortisone**

- **She started therapy with immuno-suppressing agents**

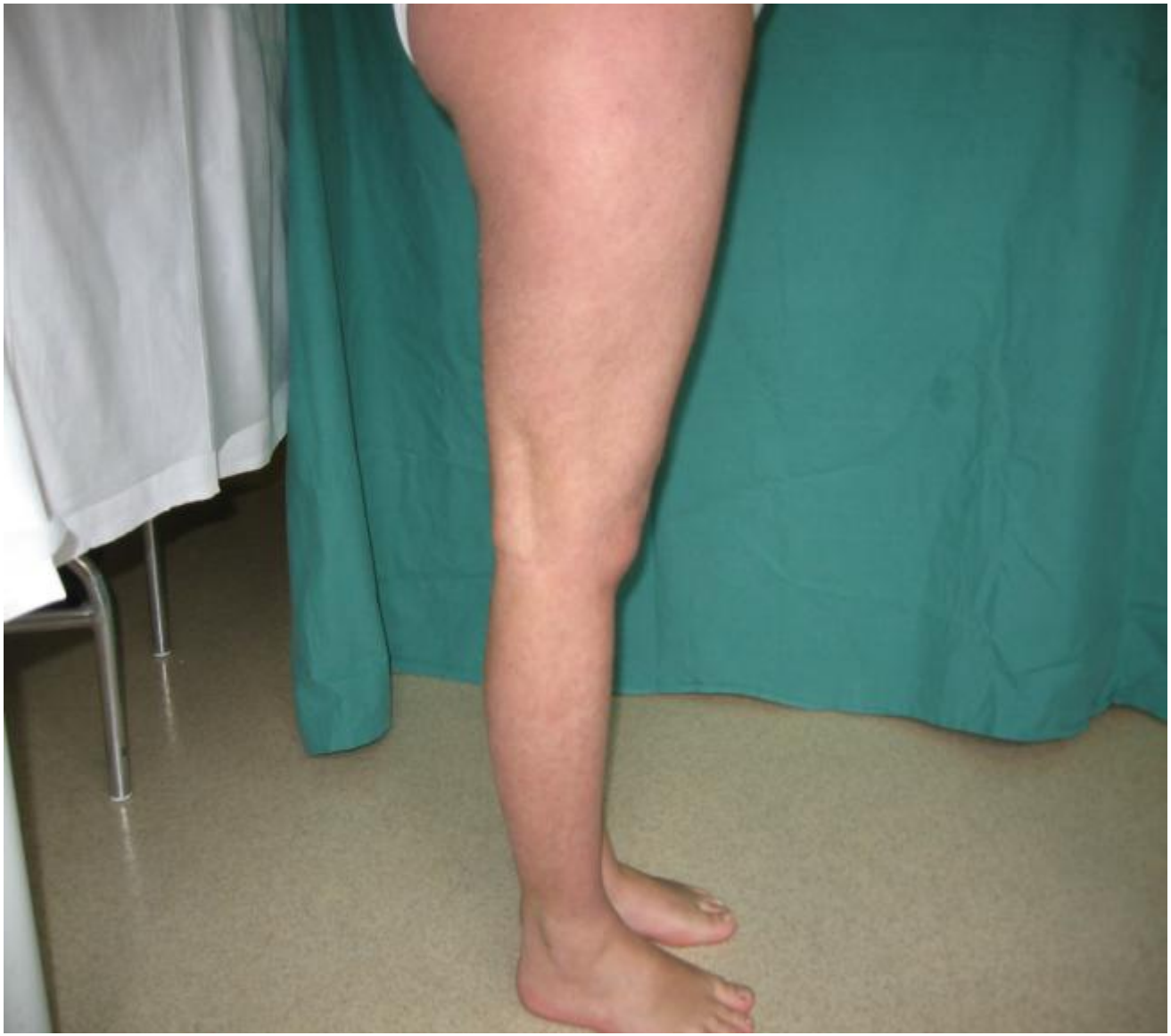
- **Methotrexate**
- **Cyclosporine**
- **Ciclophosphamide**

Low compliance, low symptomatological benefits

Worsening of her general conditions at 16 years of age – she is admitted into hospital

- Occurrence of
- Nephrovascular Hypertension (renal echo-doppler: increased resistance)
- Initial left ventricular dilation
- Osteoporosis
- Reduced pulse rate on right leg
- Paraesthesia (EMG: pathology of peripheral nerve sensitive fibres)
- Nodous polyarteritis is easily diagnosed, same as her sister

Livedo reticularis agli arti inferiori



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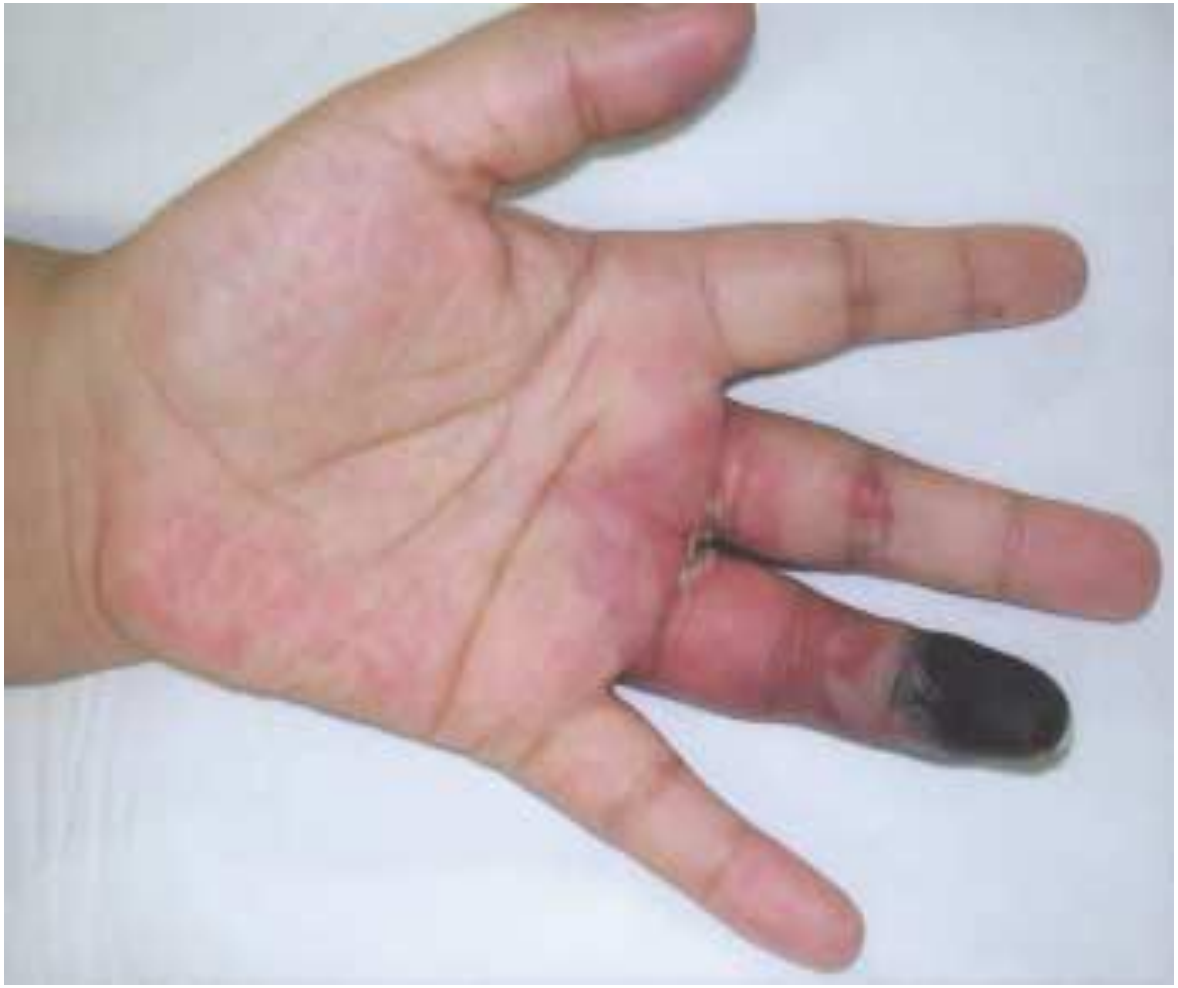
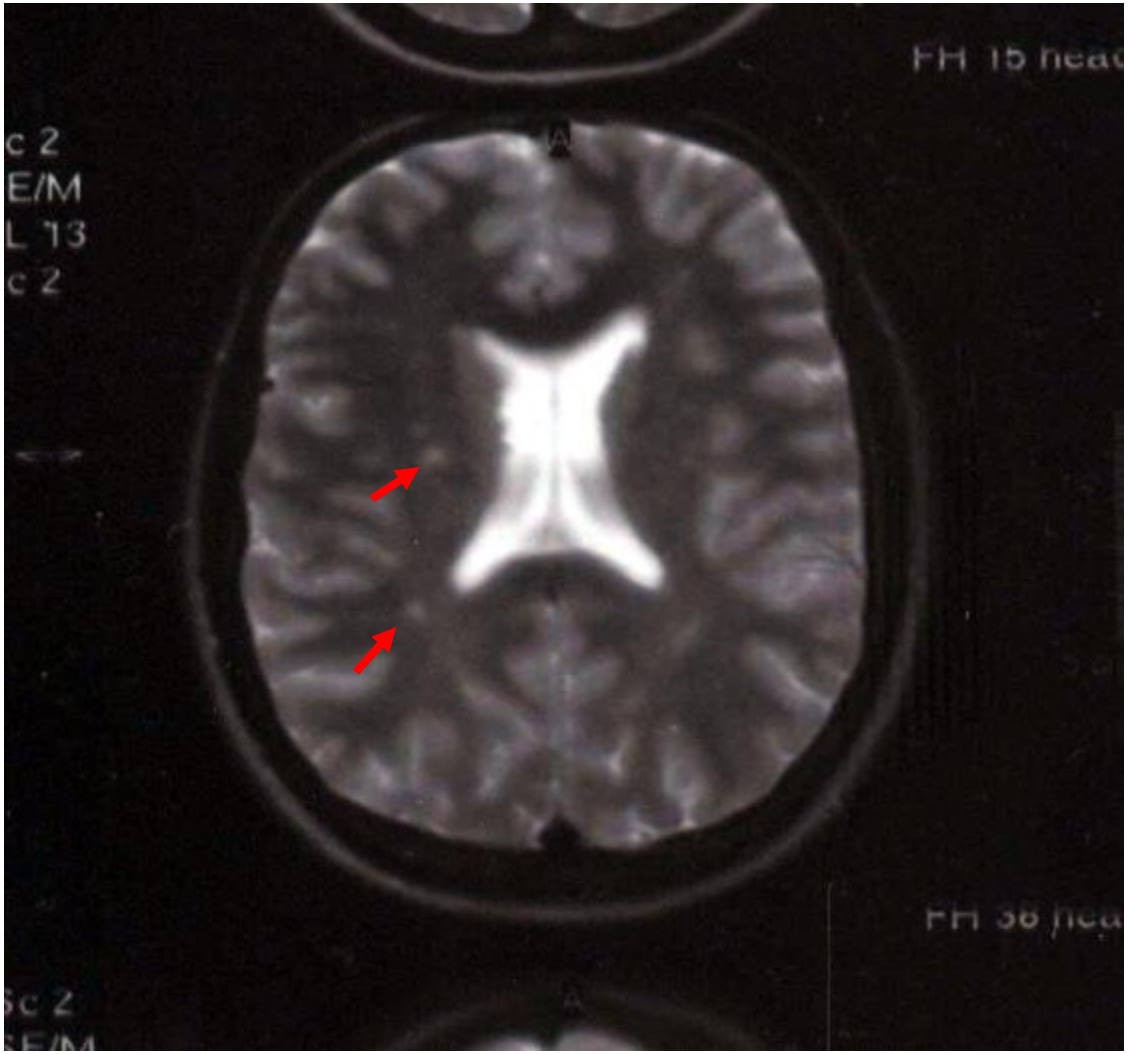
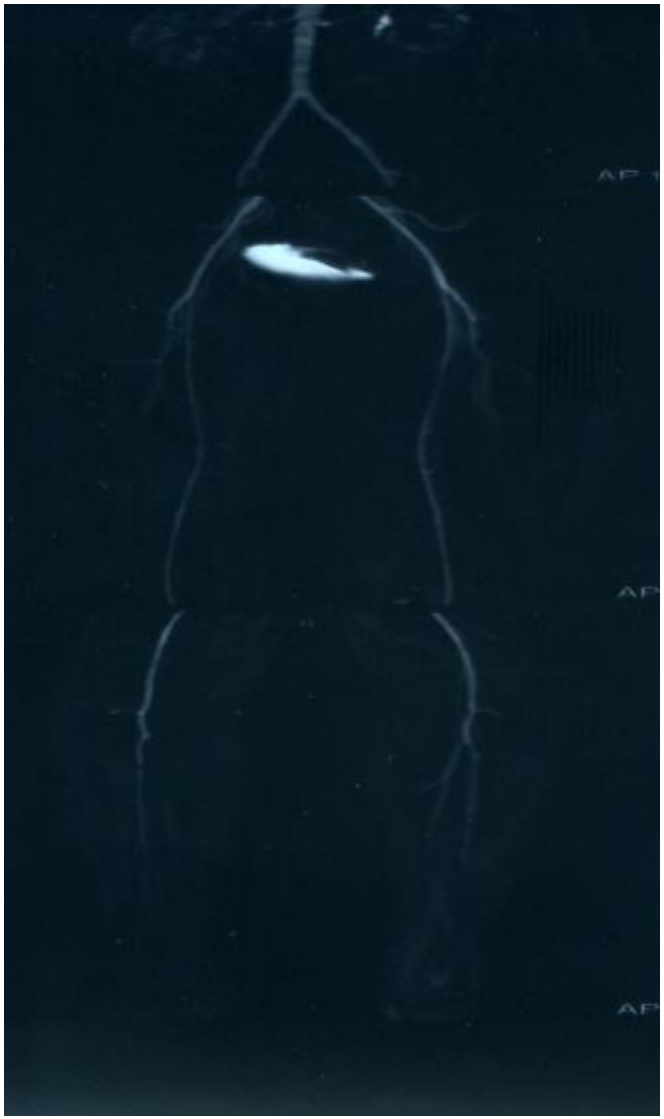
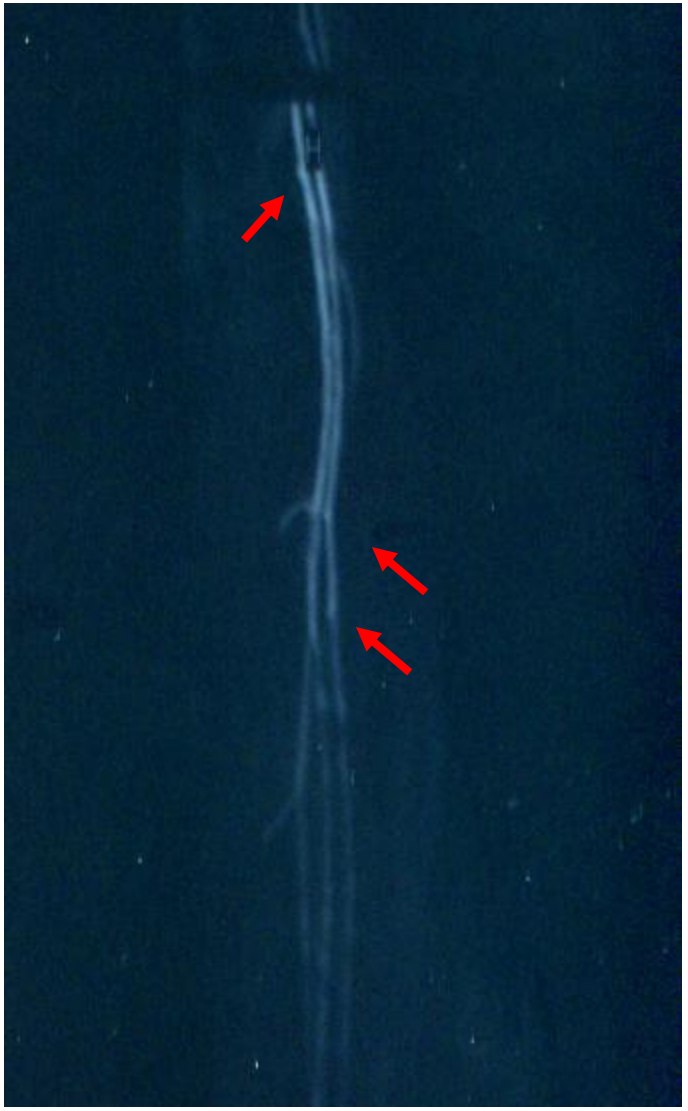


Encephalic Angio-NMR



Angio RMN- Total Body





Criteria for childhood polyarteritis nodosa

- Skin involvement (livedo reticularis, tender subcutaneous nodules, other vasculitic lesions)
- Myalgia or muscle tenderness
- Systemic hypertension
- Mono-neuropathy or poly-neuropathy
- Abnormal urine analysis and/or impaired renal function
- Testicular pain or tenderness
- Signs or symptoms suggesting vasculitis of any other major organ system (gastrointestinal, cardiac, pulmonary or central nervous system)
- *Should include conventional angiography if magnetic resonance angiography is negative*

❖The treatment with Thalidomide (50 mg/day)

- Has allowed to:
- gradually stop administering immuno-suppressive agents
- Avoid high doses of cortisone

Therapy

- **Thalidomide 50 mg/day**

- Anti-hypertensive therapy (Ace-inhibitors)
- Peripheral vasodilators (Nicardal)
- Prednisone
- Alendronate
- Calcium and Vitamin D

Outcomes

- Both sisters treated with Thalidomide went into remission.
- The use of Immuno-suppressors, Thalidomide in particular, compels us to inform the patients about risks involved, especially in the case of an unexpected pregnancy

SESSUALITY AND CONTRACEPTION

Sexuality, contraception and pregnancies are subjects that must be dealt with, both within the family, and in health care structures (with the help of various specialists – gynaecologists, adolescentologists, endocrinologists, psycologists, and so on).

When she's 22 years old

- Angela tells us she wants to get married, weel aware of the risks of having children, with the therapy she's following



TRANSITION

- Chronological age
- Maturity
- State of the disease
- Family
- Patient's compliance
- Independence

TRANSITION

Choosing the right time to move a youth to a department for young adults is the key to a successful transfer.

TRANSITION

Transferring patients based only on anagraphic age may lead to mistakes, either because the youth is not ready yet,
or it is too late, when he or she is no longer at ease in an environment where he still feels treated like a child.

What's the state of things here?

- Paediatric rheumatic centres are few, and in some parts of the south of Italy there are none
- A transition centre is inexistent, here in the south of Italy
- However, to start solving a problem it is fundamental to IDENTIFY the problem itself.