LANGERHANS CELL HISTIOCYTOSIS-20 YEARS OF SURGICAL FOLLOW-UP HIGHLIGHTS THE DEVASTATING LONG-TERM SEQUELAE

Allison Murdoch[1], Lakshmi Sundararajan[2], Dermot Murphy[3], Robert Carachi[1], Jairam Sastry[3], Milind Ronghe[3], Roderick Duncan[4], Allan Howatson[5,] Robert Carachi[1]

[1]Department of Paediatric Surgery, Royal Hospital for Sick Children (RHSC), Glasgow. [2]Department of Paediatric Surgery, University Hospital of Wales, Cardiff. [3]Department of Paediatric Oncology, RHSC, Glasgow. [4]Department of Paediatric Orthopaedic Surgery, RHSC, Glasgow. [5]Department of Pathology, RHSC

NHS Greater Glasgow and Clyde

BACKGROUND

Langerhans Cell Histiocytosis (LCH) is a rare, non-malignant disease that manifests in diverse ways. It is the result of an abnormal proliferation of pathologic Langerhans cells, accompanied by other inflammatory cells.

The diagnosis of LCH is usually made following a biopsy. The gold standard of diagnosis of LCH is the identification Langerhans cells *(Figure 1)* or ultrastructural Birkbeck granules *(Figure 2)*

- No other tissue or cell markers is unique to LCH

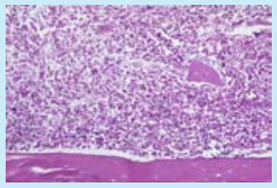


Figure 1: Langerhans Cell

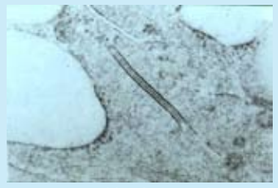


Figure 2: Birkbeck Granule

PURPOSE

Review of presentation and outcome of patients with Langerhans Cell Histiocytosis (LCH) attending The Royal Hospital for Sick Children, Glasgow between January 1990 and December 2009.

RESULTS

Population

- There were 30 children-16 boys & 14 girls

Age at Diagnosis

There were 16 boys & 14 girls.

Ages range 5 months to 15 years at diagnosis

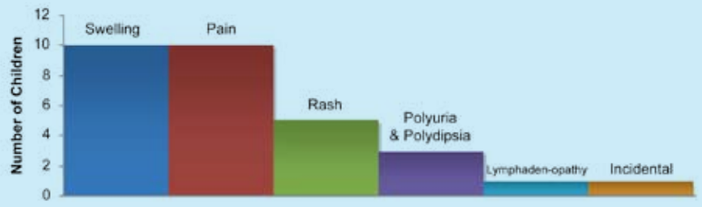
Median age 2 ½ years (IQR 1.5 yrs to 4.2 yrs)

11 children were < 2 years of age; 2 of whom were < 6 months.

Presenting Symptoms

LCH can present with symptoms in different systems of the body, with varying extent of involvement and severity.

Figure 3: Primary Presenting Sympto



Bony lesions presenting with pain or swelling are the common

If a skin lesion is the only manifestation, further investigations reveal the true extent of the disease.

- 4 (13%) of our children presented primarily with skin involvement, yet 3 of them were subsequently diagnosed with **Multisystem Disease involving bone, skin, lungs, liver, ears, hypothalamus**

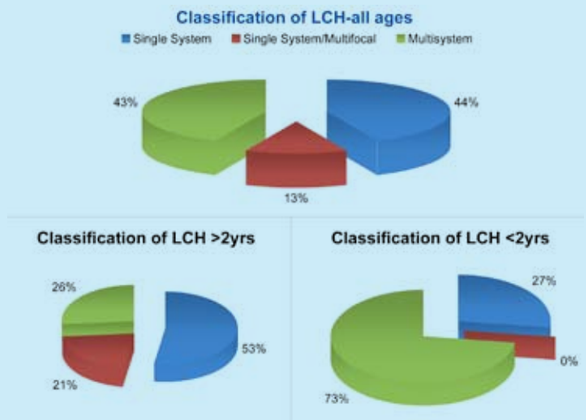
CNS Involvement (in the form of Diabetes Insipidus) presented in 3 (10%) of the cases

- Subsequently, **11 (36%) of children developed Diabetes Insipidus**

Classification of Disease

- Children under 2 years of age suffer more severe disease

Figure 4: Classification of Disease



- **73% of children aged under 2 years have Multisystem Disease**

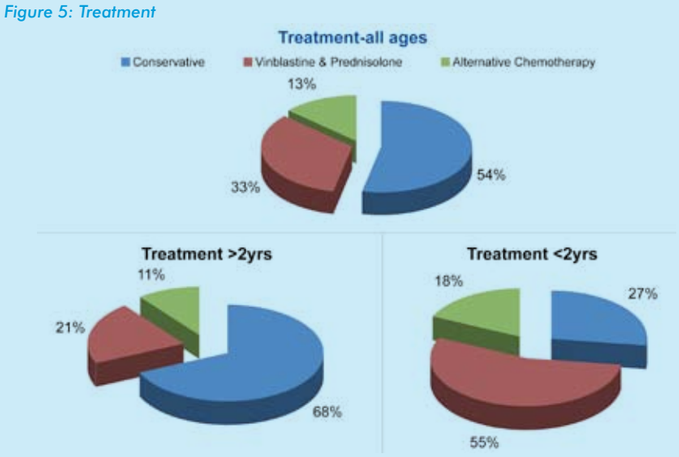
Table 1: Clinical Presentation by Age

No.		Age at Diagnosis (yrs, mths)	Primary Symptom	Classification	"Risk" "Special Site"	Treatment	Additional Therapy	Duration of follow-up (yrs, mths)
1	F	1/12	Skin lesion	**SS**		Conservative		4 9/12
2	M	5/12	Skin rash	**SS**		Conservative		11 6/12
3	M	8/12	Head lump	**MS**		Vinblastine & Prednisolone	DDVAP, GH, Thyroxine	11 3/12
4	F	9/12	Temporal swelling	**MS**		Vinblastine & Prednisolone		9 5/12
5	F	11/12	Skin rash	**MS**		Vinblastine & Prednisolone	DDVAP	12 5/12
6	M	1 1/12	Lymphaden-opathy	**MS**		Vinblastine & Prednisolone		6 2/12
7	M	1 3/12	Head lump	**SS**	CNS	Conservative		2 4/12
8	F	1 6/12	Ear polyps	**MS**		Vinblastine & Prednisolone	DDVAP	8 7/12
9	F	1 6/12	Head lump	**MS**		Vinblastine & Prednisolone		4 5/12
10	M	1 6/12	Mandibular swelling	**MS**	CNS	Vinblastine & Prednisolone; 2-CDA	DDVAP, GH, Thyroxine	11 7/12
11	F	1 10/12	Skin rash	**MS**		Vinblastine & Prednisolone; rpt & 6MP	DDVAP, GH	14 8/12
12	M	2 3/12	Polyuria & polydipsia	**MS**		Vinblastine & Prednisolone	DDVAP, GH	10 5/12
13	F	2 4/12	Scalp eczema	**MS-died aged 4 4/12**	Liver	Vinblastine & Prednisolone, 6MP then Cladribine	DDVAP	2 1/12
14	M	2 5/12	Incidental finding of head lump	**SS**		Conservative		7 1/12
15	F	2 6/12	Arm pain	**MS**		Vinblastine & Prednisolone		9
16	M	2 9/12	Groin pain	**SS Multifocal**		Conservative		9 4/12
17	M	2 10/12	Painful mic-turation	**SS**		Conservative inc circumcision		9 2/12
18	F	2 10/12	Facial swelling	**SS**		Conservative		1
19	M	2 10/12	Facial swelling	**SS**	CNS	Conservative		3
20	M	3 1/12	Polyuria & polydipsia	**MS**		Vinblastine & Prednisolone	DDVAP, GH, Zoladex	18 2/12
21	F	3 5/12	Polyuria & polydipsia	**SS**	CNS	Vinblastine & Prednisolone	DDVAP	2
22	F	3 7/12	Thigh pain	**SS**		Conservative		12 7/12
23	F	4 2/12	Thigh pain	**SS**		Conservative		4 9/12
24	M	4 4/12	Torticollis	**SS Multifocal**		Conservative		6
25	F	4 9/12	Back pain	**SS Multifocal**		Conservative		2 7/12
26	M	5 7/12	Pelvic pain	**SS**		Conservative		10 7/12
27	M	7	Facial lump	**SS**		Conservative		9 2/12
28	M	10 9/12	Shoulder pain	**SS Multifocal**		Conservative		5 11/12
29	M	12 8/12	Hip pain	**MS**		Indomethacin; Prednisolone; Vinblastine & Prednisolone	DDVAP, GH	7 6/12
30	F	15 2/12	Rib pain	**SS**		Conservative	DDVAP, GH	1 2/12

Treatment

- 16 children improved with expectant treatment (including biopsy)
- 10 (33%) of the children received Vinblastine & Prednisolone
- 4 (13%) required second line chemotherapy, including Mercaptopurine/6-MP, Cladribine/2CDA or Etoposide/VP-16

Figure 5: Treatment



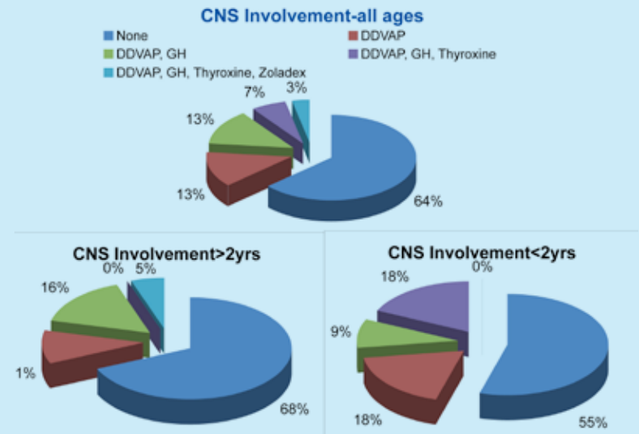
Children under 2 years of age need more intensive treatment

- **55% were treated with Vinblastine & Prednisolone**
- **A further 18% needed alternative chemotherapy**

Outcome & Long-Term Sequelae

- 1 patient died in spite of alternative chemotherapy
- Median follow up of 7.5 years (IQR 3.9 to 10.1 yrs)
- 11 (36%) children developed diabetes insipidus, of whom
  - » 7 were also deficient in Growth Hormone
  - » 2 were hypothyroid
  - » 1 child had panhypopituitarism requiring LHRH analogues

Figure 6: CNS Involvement



- More children under 2 years of age have CNS Involvement
- **45% suffer from Hypothalmic-Pituitary involvement**

CASE REPORT

A 2 ½ year old girl presented left forearm pain

- Clinically she had axillary & cervical lymphadenopathy
- X-ray & CT scans showed extensive destruction of left radius
- A biopsy confirmed the diagnosis of LCH
- She received a six month course of Vinblastine and prednisolone
- The left radius healed & the lymph nodes disappeared
- She has been well on follow-up for almost 9 years

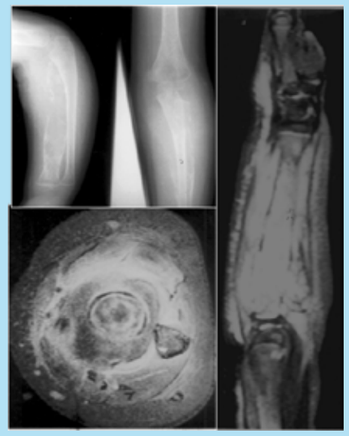


Image 1

CASE REPORT

A 2 ½ year old girl died in spite of all available treatment

- She presented with severe persistent scalp eczema, chronic ear discharge, polyuria & polydipsia, & poor weight gain
- She was dehydrated, anaemic, had a skin rash & palpable liver
- Skeletal survey showed multiple osteolytic lesions in the skull, clavicle, proximal humerus and pubic bones
- CT scans showed extensive destruction of mastoid, petrous, occipital & left zygomatic bones, the left middle ear & part of inner ear
- She was diagnosed of Multisystem LCH involving skin, bone, pituitary & middle ear was reached
- She commenced DDAVP &was treated with Chemotherapy
- She died 2 years after diagnosis with liver failure, cardiomyopathy, neutropenia & adenoviral enteritis

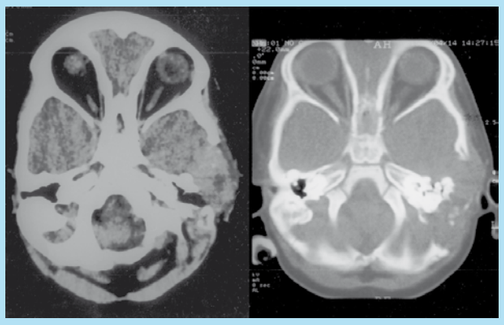


Image 2

CONCLUSION

1. Bony lesions were the commonest presentation-66% of children complained of pain or swelling, generally in the skull.
2. 75% of children presenting primarily with skin lesions were subsequently diagnosed with Multisystem Disease.
3. Localised disease may be treated conservatively with local therapy including a diagnostic biopsy.
4. In children under 2 years of age. 73% had Multisystem Disease. 55% were treated with Vinblastine & Prednisolone and a further 18% needed second line chemotherapy. 45% suffered from Diabetes Incipidus, of whom 9% were also deficient in Growth Hormone & 18% suffered from Hypothyroidism

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